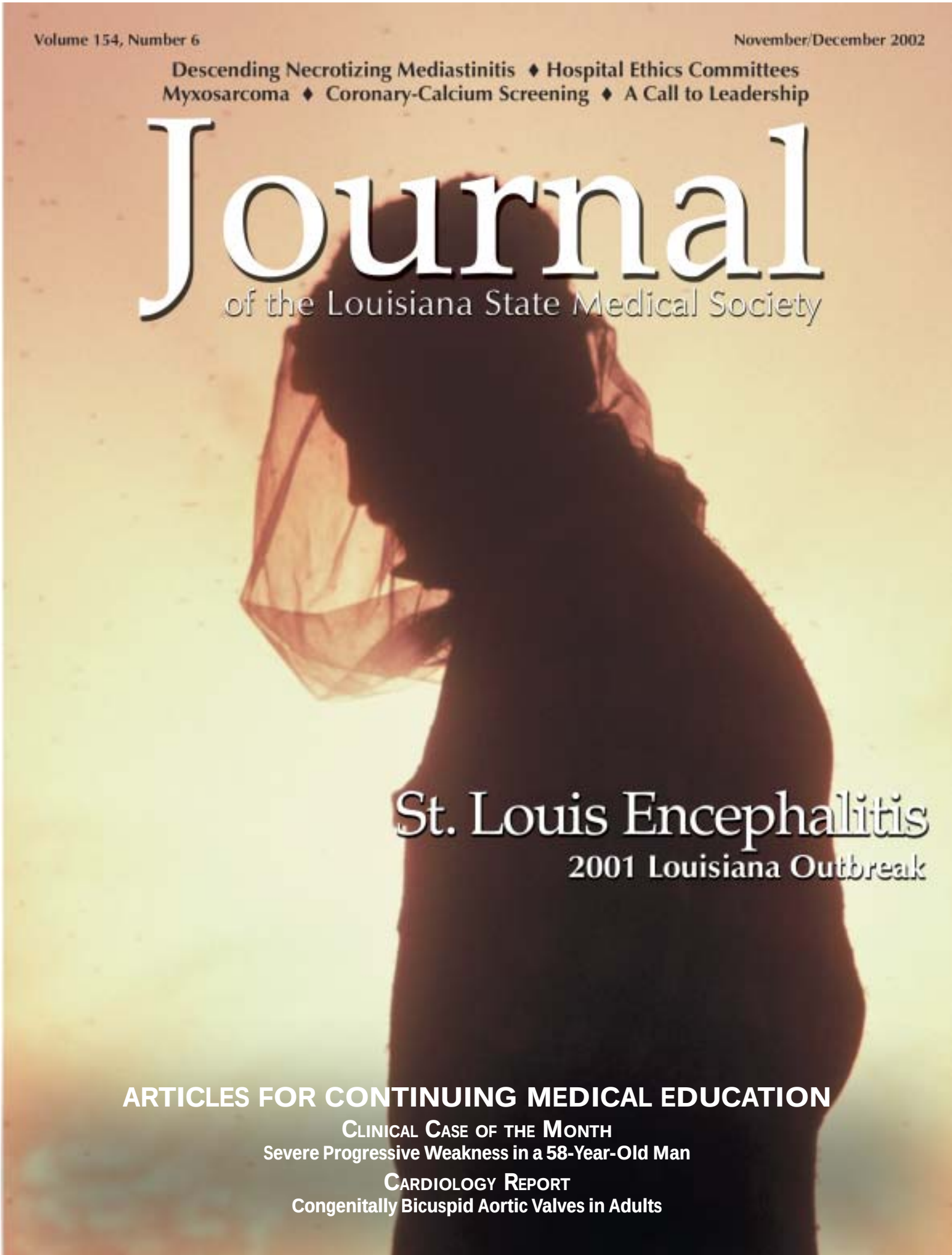
Volume 154, Number 6 November/December 2002

Descending Necrotizing Mediastinitis ♦ Hospital Ethics Committees
Myxosarcoma ♦ Coronary-Calcium Screening ♦ A Call to Leadership

Journal
of the Louisiana State Medical Society



St. Louis Encephalitis
2001 Louisiana Outbreak

ARTICLES FOR CONTINUING MEDICAL EDUCATION

Clinical Case of the Month
Severe Progressive Weakness in a 58-Year-Old Man

Cardiology Report
Congenitally Bicuspid Aortic Valves in Adults

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JOURNAL

ARTICLES

DEPARTMENTS

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The *Journal* is published for the benefit of the members of the Louisiana State Medical Society. Manuscripts should be of interest to a broad spectrum of physicians and designed to provide practical information on the current status, progress, and changes in the field of clinical medicine. The articles published are primarily original scientific studies but may include societal, socioeconomic, or medicolegal topics.

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Each submission is reviewed by the editor and is subject to peer review by one or more of the editorial consultants. Manuscripts are also subject to editorial revision and to such modification as to bring them into conformity with *Journal* style. The final decision to accept or revise falls to the editor. Criteria for acceptance include perceived interest to *Journal* readers, soundness of scientific observations and conclusions, timeliness, originality, presence of a substantial take-home message, and quality of writing.

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38°C 3.3 mg/dL 100 mL/hr

Drug names should be entered in the generic form. If the proprietary name is especially relevant to the study, it may be added in parentheses immediately following the first mention of the generic name. A generic name is lowercased; a proprietary name is capitalized.

Laboratory procedures which are unusual should show normal values in parentheses immediately following the reported value.

Names of organisms should include full genus and species at first mention; the genus name may be abbreviated at later mention of the same organism; capitalize genus, lowercase species; set entire name italic.

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Smith[1] Brown et al[2] Several authors[3,4,7-9]

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On the lower part of the same page, list three to five key words or short phrases that will assist indexers. When possible, use terms from *Medical Subject Headings* as used in *Index Medicus*.

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Location data for a journal article: Give abbreviated name of journal, year of publication, volume number, first and last page. Abbreviate name of journal in accordance with style used in *List of Journals Indexed* in *Index Medicus* (visit http://www.nlm.nih.gov/tsd/serials/lji.html); italicize name of journal to indicate that the name of the journal is to be printed italic; do not omit digits from first or last page numbers.

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Information for Authors (Expanded)

an article in a newspaper, (8) a reference to a book which has been accepted for publication but has not yet been published and (9) a reference to a website.

1. Brush JE Jr, Cannon RO III, Schenke WH, et al. Angina due to coronary microvascular disease in hypertensive patients without left ventricular hypertrophy. *N Engl J Med* 1988;319:1302-1307.
2. Hajdu SI. *Pathology of Soft Tissue Tumors*. Philadelphia, Pa: Lea & Febiger;1979:60-83.
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9. American Board of Internal Medicine. Diplomates certified as of 01/22/01. <http://www.abim.org.info/states.htm> (accessed 20 February, 2001).

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Type each table on a separate page; number tables in the order first cited; provide a title; avoid vertical rules; consult recent issues of the *Journal* for examples of tables.

Limit tables to one table (or one figure) per 1000 words of text.

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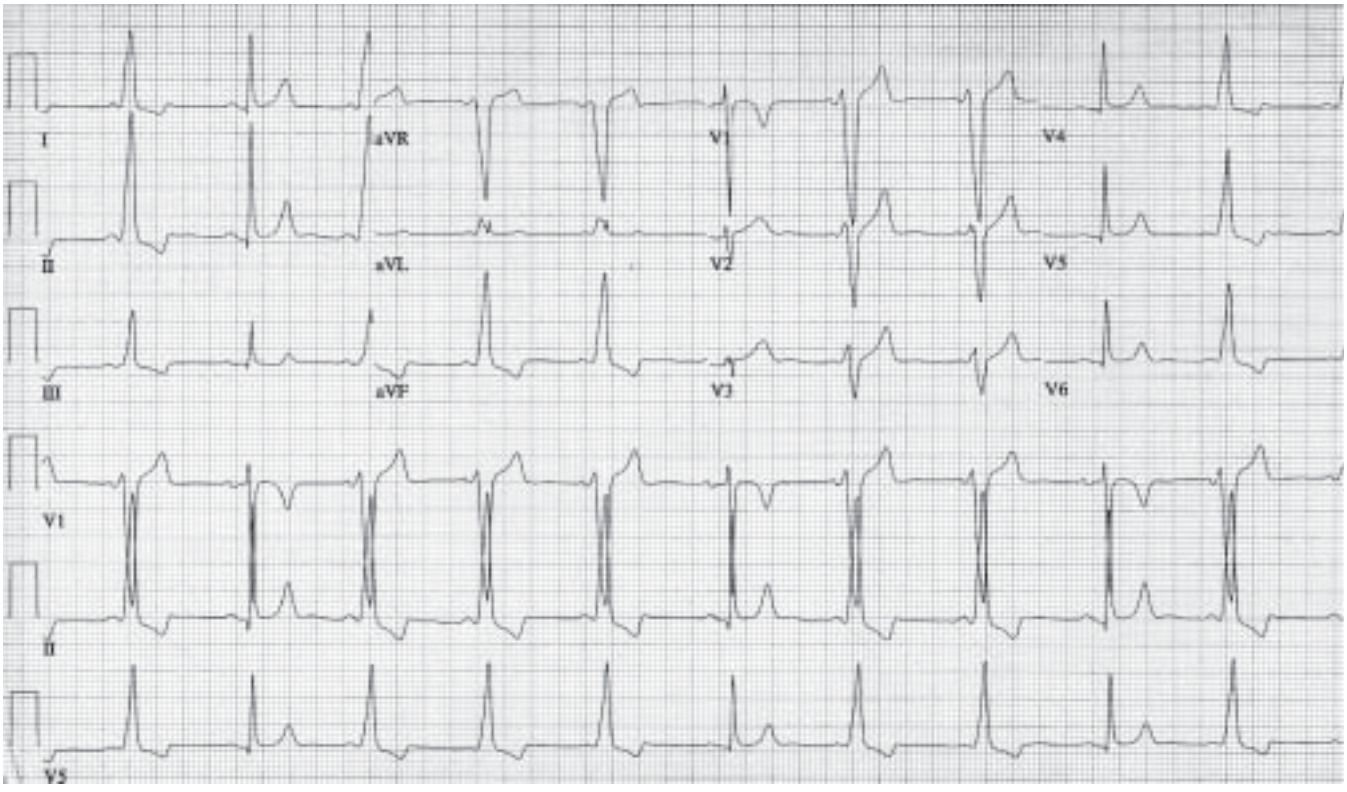
Intermittently Wide QRS Complexes

Viviana C. Falco, MD; Darrin M. Breaux, MD; and D. Luke Glancy, MD

A 31-year-old woman came to the hospital complaining of palpitations and chest pain. Her electrocardiogram is shown below.



What is your diagnosis?
Elucidation on page 286.

ECG of the Month
Presentation is on page 285.

DIAGNOSIS – *Sinus rhythm with Wolff-Parkinson-White type pre-excitation and spontaneous intermittent block in the accessory pathway.*

There is minimal sinus arrhythmia, and a sinus P wave precedes each QRS. Most complexes have the typical features of Wolff-Parkinson-White type pre-excitation: a short P-R interval, a wide QRS complex, and, in many leads, a characteristic slur of the initial part of the QRS called a delta wave. These findings indicate that atrioventricular conduction has occurred predominantly by way of the accessory pathway and, to a lesser extent, through the atrioventricular node and His bundle. Beats 2, 6, and 9, however, have normal P-R intervals and QRS complexes indicating normal atrioventricular conduction, the result of spontaneous, intermittent block in the accessory pathway.

The Wolff-Parkinson-White pattern of ventricular pre-excitation occurs in the electrocardiograms of approximately 0.3% of the population.[1,2] Although one Japanese study reported an equal prevalence in boys and girls,[3] most studies have found a male:female ratio of approximately 2:1.[4,5] Episodes of tachycardia occur in 25% to 50% of those with the pre-excitation pattern on the electrocardiogram.[2,4,5]

Because the accessory pathway provides a second connection between atria and ventricles, it also provides the substrate for atrioventricular reciprocating tachycardia, which nearly 90% of the time is orthodromic, ie, atrioventricular conduction via the normal pathway and ventriculoatrial conduction by way of the accessory pathway, in most instances producing a narrow-QRS tachycardia. In the minority of instances the reciprocating tachycardia is antidromic, ie atrioventricular conduction via the accessory pathway and ventriculoatrial conduction by way of the normal pathway, thus producing a wide-QRS tachycardia.

While paroxysmal atrioventricular reciprocating tachycardias constitute some 75% of the tachyarrhythmias in patients with Wolff-Parkinson-White type pre-excitation, atrial fibrillation makes up the majority of the remaining 25%.[4] Again, atrioventricular conduction is usually by way of the normal pathway, but occasionally is by way of the accessory pathway. When the accessory pathway can conduct very rapidly, there is a small, but definite, risk of atrial fibrillation inducing ventricular fibrillation. Intermittent, spontaneous block in the accessory pathway, as seen in this patient, indicates a long refractory period and makes rapid atrioventricular conduction unlikely.[6]

Intermittent pre-excitation has been reported to occur in 7% to 90% of patients with pre-excitation of the Wolff-Parkinson-White type.[2,6] This wide range in prevalences is due to the ways in which intermittence was documented – one electrocardiogram, multiple electrocardiograms, electrocardiograms plus Holter monitoring, etc. Some studies have found that the phenomenon was rate-related with the Wolff-Parkinson-White pattern of conduction disappearing at faster heart rates.[6,7] In our patient, however, no such pattern could be found in either her 10 electrocardiograms or the numerous electrocardiographic monitoring strips from the hospital. Some of these recordings did show all normal conduction, all Wolff-Parkinson-White type conduction, different QRS durations during Wolff-Parkinson-White conduction, and various patterns of intermittent conduction down the bypass tract, including bigeminy.

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This ECG of the Month is presented by the Section of Cardiology, Departments of Medicine, Louisiana State University Health Sciences Center and the Medical Center of Louisiana, New Orleans.

Sclerotic Bone Disease in an 8-Year-Old Dwarf

Priti B. Ram, MD; Sunil K. Ram, MD; and Harold Neitzschman, MD

An 8-year-old boy presented with growth failure, and the following radiographic images were obtained.

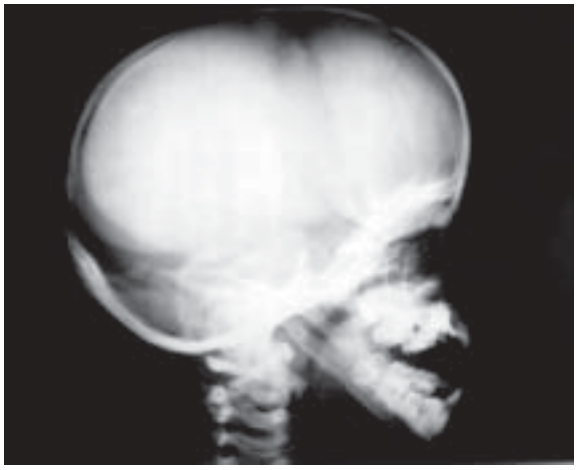

Figure 1. Lateral view of the skull.

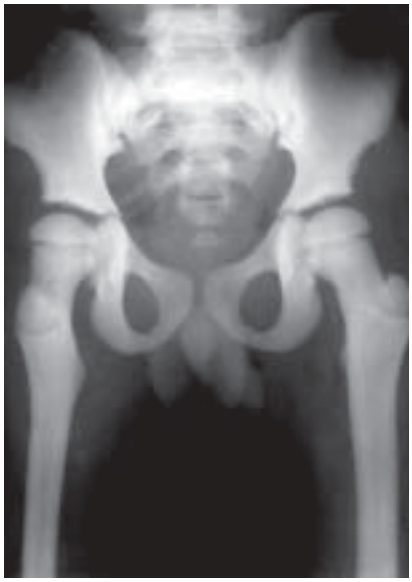

Figure 2. Anteroposterior view of the hip/pelvis.

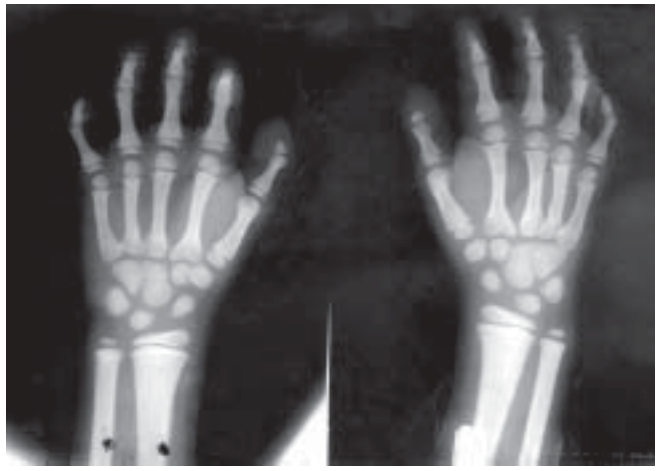

Figure 3. Anteroposterior view of the hands.

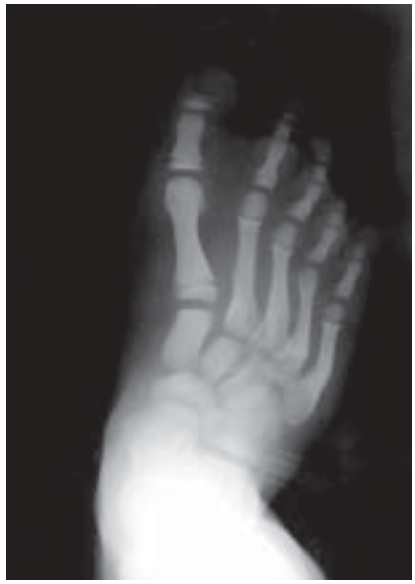

Figure 4. Anteroposterior view of the right foot.

What is your diagnosis?
Elucidation is on page 288

Radiology Case of the Month
Case presentation is on page 287.

RADIOLOGIC DIAGNOSIS – *Pycnodysostosis.*

INTERPRETATION OF IMAGES

Lateral view of the skull (Figure 1) demonstrates bony sclerosis, widening of the cranial sutures, and flattening of the mandibular angle.

Anteroposterior view of the pelvis (Figure 2) shows evidence of diffuse sclerotic disease and bilateral coxa valgus deformity. Anteroposterior views of the hand, wrist, and foot demonstrate hypoplasia of the distal phalanges (Figures 3 and 4). Bone age is appropriate for the chronological age.

DISCUSSION

Pycnodysostosis is an autosomal recessive skeletal dysplasia. It is characterized by short stature, osteosclerosis, bone fragility, clavicular dysplasia, acro-osteolysis of distal phalanges, loss of mandibular angle, and skull deformities with delayed suture closure.[1,2,3]

Pycnodysostosis is caused by a mutation in the gene encoding cathepsin K (CK), which is a lysosomal cysteine protease enzyme that degrades bone matrix proteins.[1,2] Patients are short-limbed dwarfs with large occipital prominences and parietal bossing. In addition, fractures are common in these patients. Patients have normal intelligence and normal sexual development.[3] French artist Henri de Toulouse-Loutrec is believed to have suffered from pycnodysostosis.[1]

Other forms of dwarfism and disorders of sclerosing bone disease should be included in the differential diagnosis of pycnodysostosis: Albers-Schonber disease (type II autosomal dominant osteopetrosis) caused by deficiency of carbonic anhydrase II, osteopathia striata (Voorhoeve disease), progressive diaphyseal dysplasia, hyperostosis corticalis generalisata (Van Buchem disease), and mixed sclerosing dysplasias (melorheostosis). Other causes of bone sclerosis should also be investigated including fluorosis, renal osteodystrophy, tuberous sclerosis, hypervitaminosis D, hypothyroidism, and phosphorus poisoning.[4]

Treatment of pycnodysostosis includes symptomatic management of fractures. The selective mutation of the CK gene, present only in osteoclasts, makes it a potential target for therapeutic intervention. Gene therapy, bone marrow transplantation of normal osteoclasts, and osteoclast-targeted enzyme replacement may have significant roles in the future treatment of these patients.

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The Radiology Case of the Month is a regular educational feature presented by the Departments of Radiology and Pediatrics at Tulane University Medical Center in New Orleans, Louisiana.

Abdominal Pain and Weight Loss in a Young Adult

Wei Sun, MD; Diana M.Veillon, MD; Mary L. Nordberg, PhD; Soheir Nawas, MD; and James D. Cotelingam, MD

A 34-year-old black man presented with a three-month history of abdominal pain, anorexia, and weight loss. Physical examination and radiologic studies revealed diffuse lymphadenopathy. Ascites and bilateral pleural effusions were also evident. The patient's condition deteriorated after admission, and he died prior to initiation of therapy. Histologic sections and special studies performed on a cervical lymph node biopsy performed shortly before the patient's death are shown in Figures 1-4. A bone marrow aspirate and biopsy were also performed and revealed no evidence of disease.

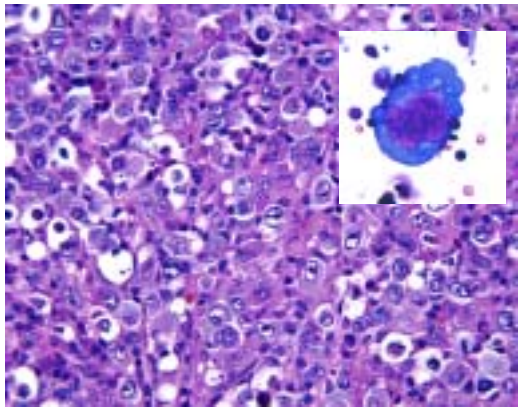

Figure 1. Lymph node biopsy (Hematoxlin and Eosin, original magnification X 400); Inset: Cytospin of lymph node suspension (Wright-Giemsa stain, original magnification X 400).

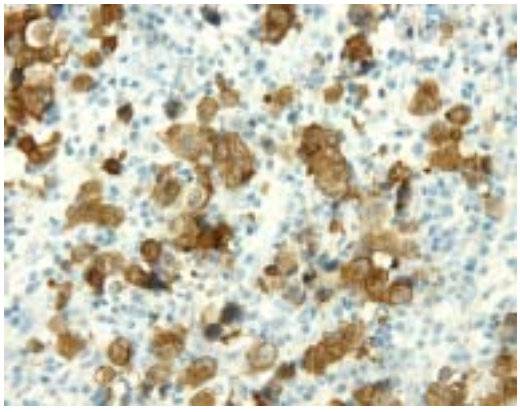

Figure 3. Immunohistochemical staining of the lymph node for anaplastic lymphoma kinase protein (ALK).

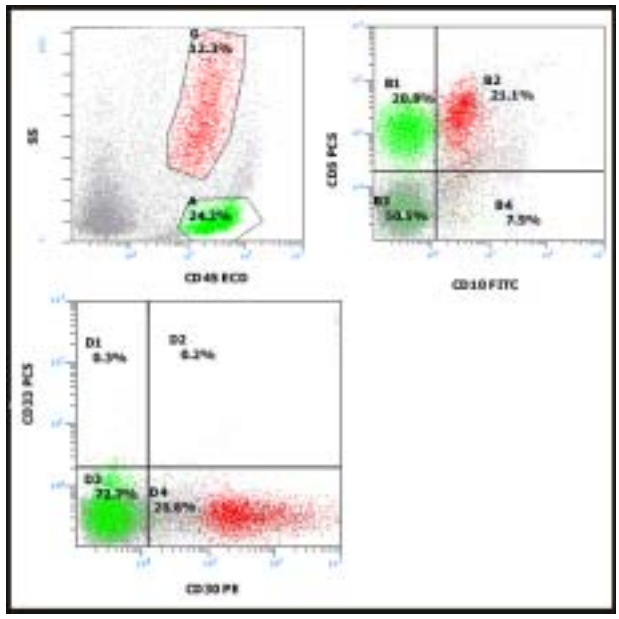

Figure 2. Flow cytometric studies performed on lymph node.

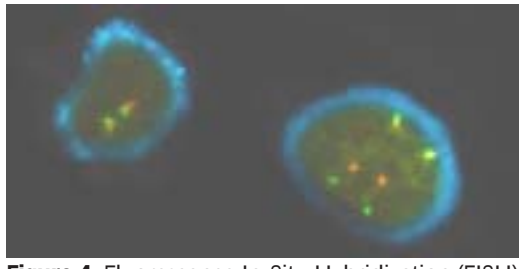

Figure 4. Fluorescence In-Situ Hybridization (FISH) for genetic rearrangement of the ALK gene: normal (upper left) and neoplastic (lower right).

What is your diagnosis?
Elucidation is on page 290.

Pathology Case of the Month
Case presentation is on page 289.

PATHOLOGIC DIAGNOSIS - *Anaplastic large cell lymphoma (ALCL).*

PATHOLOGIC INTERPRETATION

Hematoxylin and eosin stained sections of the lymph node reveal effacement of the architecture and a proliferation of large anaplastic cells with eccentric, horseshoe-shaped nuclei and prominent nucleoli. The atypical cells have abundant eosinophilic and often granular cytoplasm (Figure 1). Flow cytometric studies reveal a population of large atypical cells with expression of CD5, CD10, and CD30 (Figure 2). T-cell receptors (CD3, CD8, and TCR-heterodimers) also demonstrate abnormal expression patterns. By immunohistochemistry, the atypical cells are intensely positive for CD30, CD3, and anaplastic lymphoma kinase (ALK) (Figure 3). The cells lack B cell markers including CD20. Fluorescence In-Situ Hybridization (FISH) studies (Figure 4) are positive for disruption of the ALK locus, most likely the result of a translocation between chromosomes 2 and 5: t(2;5)(p23;q35). These results are consistent with a diagnosis of anaplastic large cell lymphoma.

DISCUSSION

Anaplastic large cell lymphoma (ALCL) is a T-cell lymphoma characterized by large pleomorphic cells with abundant cytoplasm and horseshoe-shaped nuclei. The cells are CD30 positive and frequently express epithelial membrane antigen (EMA) and cytotoxic associated proteins. Most tumors are positive for the ALK protein, but cases without ALK expression are also included in this group. Several morphologic variants have been described. These include a common variant (70%), a lymphohistiocytic variant (10%), and a small cell variant (5%-10%).[1] In a minority of cases more than one variant can be seen in an individual patient.[2] ALCL accounts for approximately 10%-30% of childhood lymphoma and 3% of adult non-Hodgkin's lymphoma.[3] ALK-positive ALCL most frequently presents in the first three decades of life and is observed predominantly in men (male: female ratio = 6.5:1). ALCL is associated with a high incidence of extranodal (61%) and cutaneous disease (25%).[4]

ALK-negative ALCL more frequently presents in older individuals and is slightly more common in women (male: female ratio = 0.9:1).[1] ALK-negative ALCL is less well-characterized, and it is controversial whether these tumors should be considered a variant of ALCL. Morphologically, ALK-negative ALCL is often composed of larger, more pleomorphic cells with more prominent nucleoli.[5]

The majority of ALCLs (50%) are of T cell origin, but 30% are of null cell phenotype. In the latter group, there is loss of several pan T-cell antigens, but evidence for a T-cell lineage at the genetic level can be identified.[6] The majority of ALCLs show clonal rearrangement of the T-cell receptor (TCR) genes, regardless of the immunophenotypic profile. For TCR gene rearrangement studies, polymerase chain reaction (PCR) technology is useful to independently target conserved regions within the variable and the joining regions that flank the complimentarity determining region 3 (CDR3) of the TCR gene. Clonality is easily discernible if the lesion is of T-cell lineage. Since no other distinctions can be found in cases with a T-cell versus a null-cell phenotype, T/null ALCL is considered a single entity.[2]

ALCL is associated with the t(2;5)(p23;q35) chromosomal translocation, resulting in fusion of the ALK gene with the nucleophosmin gene (NPM).[7] The resulting 80-kD fusion transcript, NPM/ALK or p80, is detected in 65% of cases of classic ALCL.[8] Dysfunctional regulation of the normal tyrosine kinase function of ALK is the mechanism by which the aberrant chimeric protein participates in lymphomagenesis. Variant translocations, other than the classic t(2;5) may also participate in ALK gene activation and the pathogenesis of ALCL.[9]

Both variant and classic types of ALK gene rearrangement can be detected by molecular cytogenetic methods including FISH. For ALK gene rearrangement, a two-color FISH approach was employed for analysis. A commercial DNA probe, designed for this translocation and its variants, was selected and prepared according to the manufacturer's protocol (LSI ALK Dual Color, Break Apart Rearrangement Probe (Vysis, Inc., Downers Grove, IL)). The DNA probe contains two differently labeled probes on opposite sides of the breakpoint of the ALK gene at 2p23. A 250 kilobase (kb) segment of the probe 3' to the t(2;5) ALK gene breakpoint region is labeled in an orange fluorochrome (SpectrumOrange) and the 300 kb segment 5' to the breakpoint region is labeled in a green fluorochrome (SpectrumGreen). In normal cells, hybridization of target DNA with the LSI ALK probe results in two immediately adjacent or fused orange/green (yellow) signals. Alternately, in tumor cells or cells where a t(2;5) or other chromosome rearrangement of the 2p23 ALK locus has occurred, one orange and one green signal will be seen. The remaining native ALK region (on the unaffected chromosome) will remain as the orange/green (yellow) fusion signal.

ALK protein expression can be detected by immunohistochemical staining with monoclonal or polyclonal

antibodies directed against the ALK protein. Monoclonal antibodies to the overexpressed ALCL tyrosine kinase receptor (ALK-1; ALKc) can be used diagnostically, and provide important clinical and prognostic information.[10,11]

ALCL is also characterized by the expression of CD30 (Ki-1), a cell surface cytokine receptor belonging to the tumor necrosis factor (TNF) receptor superfamily.[12] CD30 expression, however, is not specific for ALCL and can be seen in activated lymphoid cells, other non-Hodgkin's lymphomas, Hodgkin's disease, and even germ cell neoplasms. Therefore, the older term Ki-1 lymphoma is not favored.[13]

The differential diagnosis of ALCL may include metastatic carcinoma and Hodgkin's disease. Because of the prominent sinusoidal localization and frequent expression of EMA by the tumor cells, stains for cytokeratin rather than EMA should be used if the differential diagnosis includes metastatic carcinoma.[13] ALCL may also be extremely difficult to distinguish from some cases of Hodgkin's disease.[14] The lack of the t(2;5) chromosomal translocation and positive expression of CD15 suggest a diagnosis of Hodgkin's disease.[8]

ALCL is an aggressive disorder, but responds to combination chemotherapy. The prognosis of ALCL is comparable to that of other diffuse large cell lymphomas.[15] The most important prognostic indicator is ALK positivity, which has been associated with a favorable prognosis.[16] The overall 5-year survival rate in ALK-positive ALCL is close to 80%, in contrast to a 40% 5-year survival in ALK-negative cases. Relapses occur in approximately 30% of cases, but often remain sensitive to chemotherapy.[8]

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The Pathology Case of the Month is a regular educational feature presented by the Department of Pathology at Louisiana State University Health Sciences Center in Shreveport, Louisiana.

Severe Progressive Weakness in a 58-Year-Old Man

Scott Sondes, MD; John M. Kennedy, MD; Stephen Kishner, MD; Fred A. Lopez, MD; and Lowell Anthony, MD

Myasthenia gravis historically has been associated with significant morbidity and mortality rates, and most of those afflicted either died of the disease or became greatly disabled. However, modern understanding of the pathogenesis of this disorder has led to several effective treatments which have transformed the prognosis of this disease greatly.

A 58 year-old man presented to our facility complaining of a one-week history of increasing difficulty in "holding his head up." About eight months earlier, he had begun to experience generalized muscle weakness, which worsened in the evenings. This weakness progressed gradually until ambulation and activities of daily life became difficult. He could not even hold his head up without the use of a cervical collar (Figure 1). In addition, he complained of some difficulty with breathing and swallowing. He also reported a forty-pound weight loss over the preceding year. He denied fevers, chills, or malaise, and his symptoms were not associated with any pain, fatigue, sleepiness, cold intolerance, depression, orthopnea, or paroxysmal nocturnal dyspnea.

His past medical history was significant for hypothyroidism diagnosed one year earlier and congestive heart failure diagnosed 4 months earlier. His medications included lisinopril, furosemide, digoxin, spironolactone, levothyroxine, and aspirin. With the exception of the levothyroxine, the patient was taking these medications as prescribed. He was allergic to penicillin and sulfa-

CME INFORMATION

TARGET AUDIENCE

The November / December Clinical Case of the Month is intended for family physicians, general internists, general practitioners, emergency medicine physicians, pediatricians, radiologists, and neurologists.

EDUCATIONAL OBJECTIVES

The Clinical Case of the Month is a regular educational feature presented by the Louisiana State University Department of Medicine in New Orleans. Medical students, residents, postdoctoral fellows, and faculty collaborate in the preparation of these discussions. After reading this article, physicians should be able to better identify and understand the pathophysiology, clinical presentation, diagnosis, and treatment of myasthenia gravis.

CREDIT

The LSMS Educational and Research Foundation designates this educational activity for a maximum of one (1) hour of category 1 credit toward the AMA Physician's Recognition Award. Each physician should claim only those hours of credit that he / she actually spent in the educational activity.

DISCLOSURE

Dr. Sondes has nothing to disclose.
Dr. Kennedy has nothing to disclose.
Dr. Kishner has nothing to disclose.
Dr. Lopez discloses that he is a member of the LSMS *Journal* Board and the LSMS *Journal* Editorial Board.
Dr. Anthony has nothing to disclose.

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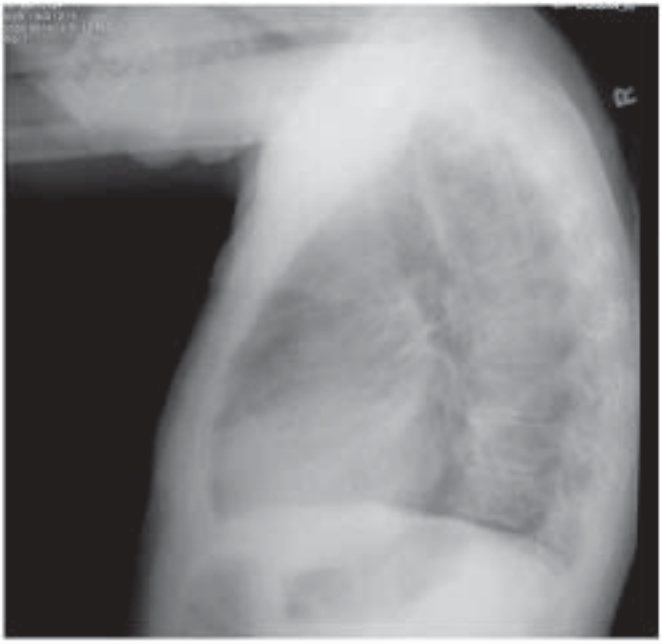

Figure 1. Lateral view of chest and neck demonstrating profound cervical weakness.

based medications. The patient's mother had a history of unspecified "thyroid problems". He denied any history of heavy alcohol use, illicit drug use, and had stopped smoking cigarettes ten years previously.

On physical exam, he was alert and oriented but in mild respiratory distress. His vital signs were: temperature 36.6° C, pulse 119 beats per minute, respirations of 28 per minute, blood pressure of 128/69, and an oxygen saturation of 97% in ambient air. Cardiovascular examination revealed mild tachycardia without gallop(s) or murmur. Lungs were clear to auscultation bilaterally. The neurological exam was notable for mild bilateral ptosis, and motor strength of 4/5 in the extremities, but only 2/5 with neck extension. Reflexes and cerebellar function were normal. The remainder of the physical exam was unremarkable.

Significant lab values included a hemoglobin of 10.4 g/dL (normal 14.0-18.0 g/dL) with a normal mean cell volume, thyroid stimulating hormone of 9.19 ug/dL (normal 0.5-5.0 ug/dL), and arterial blood gas pH of 7.43 (normal 7.35-7.45), pCO2 of 53 mmHg (normal 35-45), pO2 of 63 mmHg (normal >90), and bicarbonate of 30 mEq/L (normal 24-30).

After admission, an edrophonium test was performed in order to assess for myasthenia gravis. Ten milligrams of edrophonium were injected, and the patient reported a dramatic subjective improvement of his respiratory difficulty though minimal to no objective improvements in muscle strength elsewhere were appreciated.

On the fifth hospital day, the patient underwent nerve conduction studies (NCS) and electromyography (EMG) in order to better elucidate the cause of weakness. Pyridostigmine, which the patient had been taking for several days, was stopped 18 hours prior to NCS/EMG. During NCS/EMG, the patient was evaluated for polyneuropathy and polyradiculopathy. These tests were negative. Additional EMG testing also ruled out a myopathy as another possible cause of weakness, a concern because of the patient's history of hypothyroidism and elevated serum level of thyroid stimulating hormone. Lastly, repetitive stimulation at 3Hz was performed on the right abductor digiti minimi (ADM) and the left obicularis oculi (OBO). Testing showed an 11% decrement in the amplitude of the motor unit action potential (MUAP) after repetitive stimulation of the right ADM and a 33% decrement in the amplitude of the MUAP after stimulation of the OBO. Both of these findings were electrophysiologically consistent with myasthenia gravis. Pyridostigmine without steroids was continued, and the patient experienced marked improvement in the strength of all affected muscles in the following week. Antibodies to acetylcholine were not drawn due to the positive EMG/NCS findings and the improvement in symptoms after pyridostigmine was started. His other medications including levothyroxine were continued. At follow-up appointments 1 month and 3 months after discharge, the patient's symptoms of dysphagia and weakness had completely resolved.

DISCUSSION

Myasthenia gravis affects approximately 1 in 25,000 persons in the United States and may present at any age, although usually in women of child-bearing age and men greater than 60 years of age.[1] Patients characteristically develop rapid fatigability of the skeletal muscles, which improves with rest. Most patients experience weakness of extraocular and eyelid muscles early in the course of the illness and in approximately 15% of patients the weakness remains localized to these areas, resulting in ptosis and diplopia[2]. The bulbar muscles may also be affected, causing difficulty in swallowing and nasal speech. Approximately 85% of patients will develop more generalized muscle weakness. This weakness is usually most pronounced in the proximal muscles and neck extensors, as was the case in our patient. The muscles of respiration can also be severely affected, and the patient may require mechanical ventilation and monitoring in an ICU. Of note, the physical exam should demonstrate a complete lack of involvement of the sensory nerves; reflexes and proprioception should also be normal. In addition, the intensity of symptoms in this disease frequently fluctu-

ates creating an almost diurnal pattern.

Myasthenia gravis is an autoimmune disorder in which an autoantibody is directed against the nicotinic acetylcholine receptor. By a number of different mechanisms, these antibodies decrease the effective number of acetylcholine receptors, resulting in decreased numbers of contractions of individual muscle fibers.[3] Even though the pathogenesis of disease is relatively well-understood, little is known about what actually precipitates the cascade of immune-associated events. Recent research suggests a possible role of molecular mimicry in which exposure to microbial antigens induces the production of antibodies which cross-react with various epitopes located on the acetylcholine receptor.[4] Such research may lead to the development of molecularly-targeted therapies that block specific steps in the presentation of MHC class II molecules to T-cells that initiate immune responses.

The diagnosis of myasthenia gravis is primarily clinical and suggested by the history and physical examination findings. However, several tests can be helpful in diagnosing myasthenia gravis. The Tensilon test involves administering a short-acting, acetylcholinesterase inhibitor, edrophonium chloride. This leads to a transient, often dramatic, relief of symptoms in approximately 80% of patients with myasthenia gravis. However, false positives and false negatives have been known to occur, and in the presence of an equivocal test, additional evidence of disease is needed before potentially harmful therapies are initiated[5].

The ability to detect acetylcholine receptor antibodies has greatly assisted in the diagnosis of myasthenia gravis.Eighty percent to ninety percent of patients with myasthenia gravis will test positive by radioimmunoassay for the presence of acetylcholine receptor antibodies in the serum.[6] Of the approximately 15% of patients in which the antibody is not found, experiments have shown that when their immunoglobulin is transferred to mice, a similar neuromuscular defect occurs.[7] These patients have disease which is indistinguishable from that of antibody-positive myasthenia gravis. Recent discoveries have shown that the majority of these patients produce antibodies to a tyrosine kinase specific to muscle cells.[8] These antibodies are believed to interfere with a pathway crucial to normal function at the neuromuscular junction.

The diagnosis of neuromuscular transmission disturbances consistent with myasthenia gravis can also be made with the use of EMG / NCS. The neuromuscular junction in suspected myasthenia gravis is best studied by repetitive nerve stimulation. Under normal conditions, repetitive nerve stimulation will not produce a detectable abnormality. With myasthenia gravis, however, repetitive nerve stimulation can result in recordable neuromuscular transmission abnormalities. In myasthenia gravis there is a post-synaptic neuromuscular junction defect due to acetylcholine receptor antibodies. This leads to a reduction in the number of potential acetylcholine interactions thereby reducing the safety margin normally present in neuromuscular transmission. Once the nerve being tested is repetitively stimulated in a myasthenia gravis patient, a decrement in the amplitude of the compound motor action potential may be noted (typically >10% by the fourth action potential) due to the reduction of available acetylcholine receptors.

TREATMENT

Modern treatments of myasthenia gravis have transformed this previously grave disease into an illness that can usually be controlled and allow afflicted individuals to lead essentially normal lives. The mainstay of symptomatic therapy for mild-to-moderate disease is an acetylcholinesterase inhibitor like pyridostigmine. Side-effects of these medications include muscle fasciculations, abdominal cramping, diarrhea, and weakness. Immunosuppressive therapy with corticosteroids (ie, prednisone) is necessary in those more severely affected and those not optimally controlled with acetylcholinesterase blocking agents. Other immunosuppressive agents such as azathioprine and cyclosporine can be used as steroid-sparing agents. Severe or refractory cases may be treated with plasmapheresis or intravenous immune globulin.

Mention should also be made of surgical treatment of myasthenia gravis with thymectomy. Regardless of whether or not the patient has a co-existent thymoma, removal of the thymus gland is often associated with improvement of symptoms. Nearly all patients with generalized myasthenia gravis who are between puberty and approximately 60 years of age should be considered for thymectomy. A retrospective Mayo Clinic study comparing groups of patients with or without thymectomy showed that 85% of patients who underwent thymectomy experienced either a remission or at least improvement in symptoms.[9] This result was significantly better than in those individuals who did not undergo thymectomy.

SUMMARY

Myasthenia gravis is an autoimmune post-synaptic neuromuscular junction disorder that is usually identified clinically. Assistance with the diagnosis can be pursued with edrophonium chloride administration (ie, Tensilon test), electromyography with repetitive nerve stimulation, and serologic testing for acetylcholine receptor antibodies. Medical and surgical treatments can poten-

tially improve the symptoms and outcome of those affected by myasthenia gravis. When confronted with a patient with weakness made worse by fatigue, myasthenia gravis should always be included in the differential diagnosis.

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The Clinical Case of the Month is a regular educational feature presented by the Louisiana State University Department of Medicine in New Orleans. Medical students, residents, postdoctoral fellows, and faculty collaborate in the preparation of these discussions.

CME QUESTIONS

To earn CME credit, read the preceding CME article and complete the registration, evaluation, and answer form on page 335. Mail or fax the registration, evaluation, and answer form to the Educational and Research Foundation. Answers must be postmarked or faxed prior to December 31, 2003. Participants must attain a minimum score of 75% to receive credit.

For each question, choose the one answer that is most correct.

1. All of the following statements are true regarding myasthenia gravis except:
   a) Myasthenia gravis affects approximately 1 in 25,000 persons in the United States.
   b) Myasthenia gravis may present at any age, although usually in younger women and men greater than 60 years of age.
   c) Patients characteristically develop rapid fatigability of the skeletal muscles which improves with exercise.
   d) Most patients experience weakness of extraocular and eyelid muscles early in the course of the illness.

2. True or False. In myasthenia gravis, the physical exam typically reveals marked abnormalities in sensation, reflexes, and proprioception.

3. Myasthenia gravis is an autoimmune disorder in which an autoantibody is directed against the:
   a) Acetylcholine receptors
   b) White matter of the brain
   c) Facial nerve
   d) Benzodiazepine receptors

4. Treatment options for patients with myasthenia gravis include all of the following except:
   a) Steroids.
   b) Thymectomy.
   c) Imipenem.
   d) Acetylcholinesterase inhibitor.
   e) Plasmapheresis.

Congenitally Bicuspid Aortic Valves in Adults

D. Luke Glancy, MD

The congenitally bicuspid aortic valve occurs in more than 1% of the population. Although it may never cause difficulty and first be discovered at autopsy, more often it results in some hemodynamic abnormality. Its clinical manifestations are varied, and its early recognition is essential if we are to prevent the dreaded complication of infective endocarditis.

Because it usually causes no significant disturbance in infancy or childhood, the congenitally bicuspid aortic valve (CBAV) is not included in most statistical analyses of the incidence of congenital heart disease. If it were, the incidence of congenital heart disease would rise from approximately 0.7% of live births to approximately 2.0%. Thus, CBAV occurs nearly twice as frequently as the combined total of all of the cardiac malformations usually recognized as being congenital: ventricular septal defect, atrial septal defect, patent ductus arteriosus, tetralogy of Fallot, coarctation of the aorta, etc. Although CBAV may be an incidental autopsy finding (Figure 1), more often it presents clinically.[1] These presentations usually are in adult life, rather than in childhood, and form the basis of this report (Table).

ANATOMIC CONSIDERATIONS

Approximately one-half of CBAVs have right and left cusps with the corresponding coronary arteries arising above them.[1] The other one-half have anterior and posterior cusps, and then both coronary arteries arise above the anterior cusp. Most CBAVs have a raphe (false commissure), a thin ridge of tissue that usually is in the middle of the cusp and does not reach its free margin.[1] The raphe is in the anterior cusp when the cusps are anterior and posterior and in the right cusp when the cusps are right and left (Figure 1). In heavily calcified valves, the raphe often is obscured (Figure 2).

Most CBAVs examined at autopsy or after surgical excision are stenotic,[1] but an echocardiographic study has found that most valves are regurgitant.[2] This discrepancy may be due to exclusion from the echocardio-

CME INFORMATION

TARGET AUDIENCE

The November/December Cardiology Report is intended for family physicians, general internists, general practitioners, emergency room physicians, pathologists, cardiologists, cardiac surgeons, cardiovascular nurses, coronary care unit nurses, emergency room nurses, and surgical intensive care unit nurses.

EDUCATIONAL OBJECTIVES

After reading this article, the healthcare provider should 1) know the various manifestations of a congenitally bicuspid aortic valve (CBAV), 2) comprehend the diagnostic and therapeutic options for each of these manifestations, and 3) appreciate the importance of recognizing a CBAV while the patient is still well.

CREDIT

The LSMS Educational and Research Foundation designates this educational activity for a maximum of one (1) hour of category 1 credit toward the AMA Physician's Recognition Award. Each physician should claim only those hours of credit that he/she actually spent in the educational activity.

DISCLOSURE

Dr. Glancy discloses that he is Editor of this journal.

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Table. Presentations of Congenitally Bicuspid Aortic Valves in Adults.

- Aortic Stenosis
- Aortic Regurgitation
- Aortic Stenosis and Regurgitation
- Infective Endocarditis
- Coarctation of the Aorta
- Ejection Sound on Routine Exam
- Systolic Ejection Murmur on Routine Exam
- Dilated Ascending Aorta on Chest X-Ray
- On Echocardiogram
- Aortic Dissection
- Incidental Autopsy Finding

graphic study of valves so heavily calcified that their morphology is obscured; such valves would more likely be predominantly stenotic rather than predominantly regurgitant.[3] In addition by progressive, dystrophic calcification, some valves r,egurgitant early in life, may become primarily stenotic later. Finally, stenotic features of a valve are easier to recognize anatomically than are regurgitant ones. All studies of CBAVs have found normally functioning valves to be in the distinct minority.[1,2]

AORTIC STENOSIS

Aortic valves intrinsically stenotic at birth are usually unicommissural, unicuspid valves, and those presenting in persons over age 70 years are usually tricuspid valves that are stenotic not because of commissural fusion, but due to immobilization of the cusps by fibrous tissue and calcium deposits.[4-6] In adults less than 70 years old, stenotic aortic valves usually are bicuspid (Figure 2). Many of these valves have little or no commissural fusion, are not stenotic at birth, and become stenotic over many years because of fibrous thickening and subsequent dystrophic calcification. These degenerative changes, which in part are anatomic markers of turbulent blood flow, are likely to occur in middle age in patients with bicuspid valves, which are more likely to have abnormal patterns of blood flow across them, and in old age in those with tricuspid valves. In both instances, the degree of stenosis is related to the extent of the calcium deposits.[3] Evidence is accumulating that atherosclerotic plaques in the cusps themselves play a role in the genesis of aortic stenosis and that lowering atherosclerotic risk factors may slow the development and progression of aortic stenosis.[7] Rheumatic heart disease is becoming rare in the United States, and nowhere is it a significant cause of aortic stenosis without coexistent mitral valvular disease.[8]

The patient with aortic stenosis is more often a man than a woman and usually enjoys an asymptomatic period of many years. After angina pectoris, syncope, or frank congestive heart failure develop, however, the prognosis is ominous, and with rare exception mechanical intervention is indicated.[9] This usually consists of aortic valve replacement, although in some young adults with pliable valves, more commissional fusion, and less

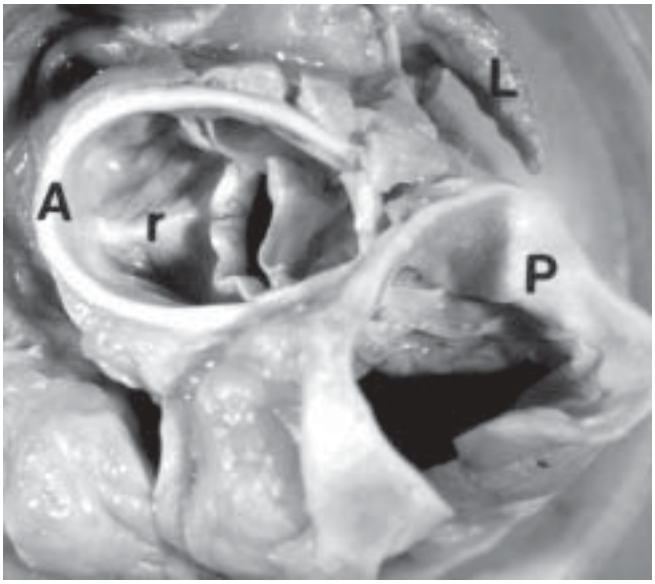

Figure 1. A congenitally bicuspid aortic valve first diagnosed at autopsy in a 49-year-old woman who died of carcinoma of the breast. The aorta (A) has been removed back to the level of the valve whose right cusp is larger than the left cusp and contains a median raphe (r). Both cusps are thin and delicate with only minimal fibrous thickening of the tips of the cusps centrally. There is no calcium deposition or commissural fusion, and the valve probably functioned normally during life. L = left atrial appendage; P = opened pulmonary trunk. (Courtesy of William C. Roberts, MD)

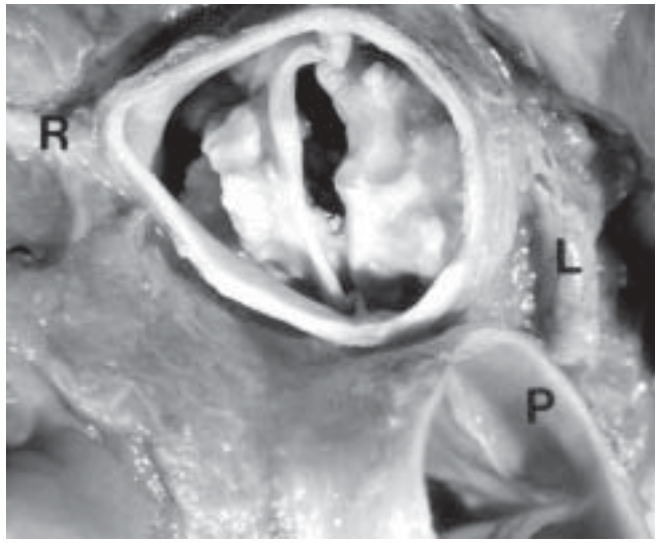

Figure 2. Looking down on a severely stenotic, congenitally bicuspid aortic valve and the proximal portions of the right (R) and left (L) coronary arteries. Both aortic valvular cusps are immobilized by heavy calcium deposits leaving only a slit-like orifice. The patient, a 58-year-old woman, died of cardiac failure. P = opened pulmonary trunk. (Courtesy of William C. Roberts, MD)

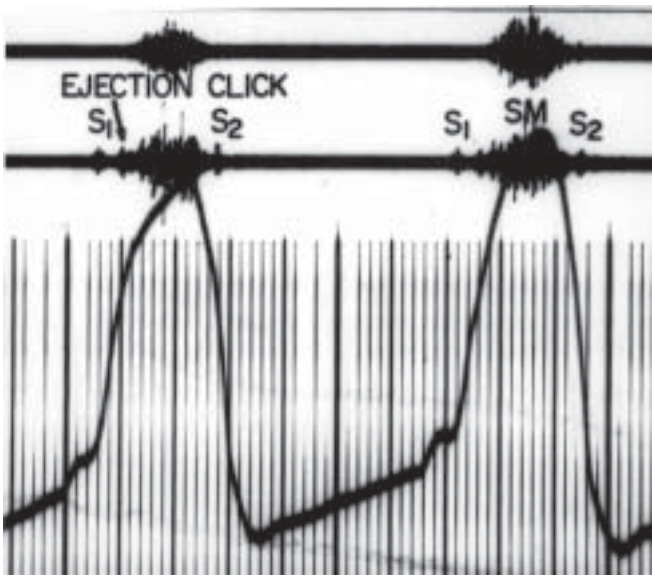

Figure 3. Phonocardiograms (above 2 tracings) and apexcardiogram (below) in a patient with a stenotic congenitally bicuspid aortic valve. The upper phonocardiogram, recorded at the high-frequency setting over the second left intercostal space, shows the characteristic diamond-shaped systolic ejection murmur (SM). The lower phonocardiogram, recorded at a medium-frequency setting over the fourth left intercostal space, also shows the first (S_1) and second (S_2) heart sounds and the ejection sound or click. The last suggests that the valve is still mobile. The apexcardiogram shows a large, sustained, left ventricular systolic pulsation preceded by the presystolic pulsation of left ventricular distention caused by atrial systole.

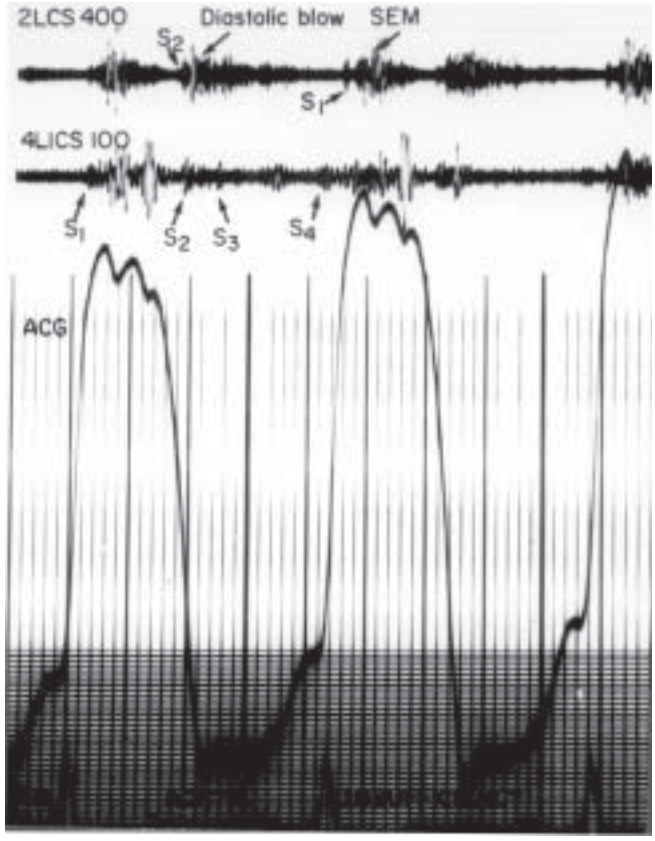

Figure 4. Phonocardiograms, recorded at the high-frequency setting over the second left intercostal space and the low-frequency setting over the fourth left intercostal space (LICS), and apexcardiogram (ACG) in a patient with severe aortic regurgitation. The top tracing shows the first heart sound (S_1), the systolic ejection murmur (SEM) due to the large stroke volume, and the long, decrescendo, blowing, aortic regurgitant murmur beginning with the second heart sound (S_2) and lasting throughout most of diastole. The middle tracing also shows intermittent third (S_3) and fourth (S_4) heart sounds. The apexcardiogram shows a large, hyperdynamic, left ventricular systolic impulse. (Courtesy of Kevin P. O'Brien, MD)

extensive calcium deposits, aortic valvuloplasty, either surgical or by balloon catheter, gives good, but rarely life-long, palliation.[10] Although angina may result from aortic stenosis alone, the symptom suggests coexistent coronary arterial disease.[9]

The salient diagnostic findings in aortic stenosis due to CBAV are a harsh, systolic ejection murmur, usually loudest in the 2nd right intercostal space; a systolic ejection sound if the valve has not been immobilized by calcium deposits (Figure 3); slowly rising and / or small carotid arterial pulses; evidence of left-ventricular enlargement by physical examination, electrocardiogram, chest x-ray, or echocardiogram; and a thickened, often immobile, aortic valve on echocardiogram.[5] Because many other conditions cause systolic ejection murmurs and because the intensity of the murmur is not a reliable guide to severity, the presence and severity of aortic stenosis often are misdiagnosed.

AORTIC REGURGITATION

Although trivial regurgitation, detected only by Doppler echocardiography, of each of the other three cardiac valves is so common that it is not necessarily considered abnormal, any amount of aortic regurgitation is abnormal. While the causes of pure aortic stenosis are few, CBAV is only one of many causes of pure aortic regurgitation and is strongly suggested by a systolic ejection sound.

The characteristic finding on physical examination in patients with aortic regurgitation is a descresendo, early diastolic murmur usually heard best along the left sternal border with the diaphragm of the stethescope while the patient is leaning forward holding his breath in full exhalation. Hemodynamically important aortic regurgitation causes a long, decrescendo, diastolic murmur; a systolic ejection murmur; full and brisk pulses; a wide systemic arterial pulse pressure; a low diastolic pressure; signs of left ventricular enlargement; and, in the most severe cases, a third heart sound and the diastolic,

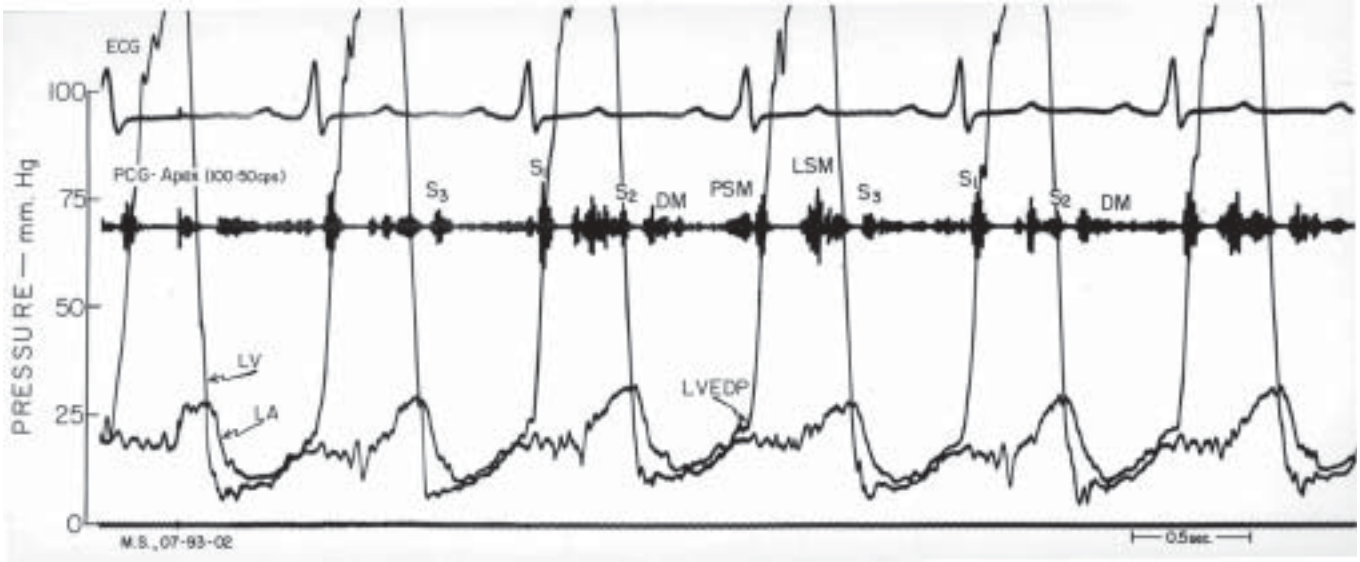

Figure 5. Simultaneous electrocardiogram (ECG), phonocardiogram (PCG) recorded at the low-frequency setting over the left ventricular apex, and directly recorded left atrial (LA) and left ventricular (LV) presssure tracings in a patient with severe aortic regurgitation and the Austin Flint murmur. The apical, low-pitched, diastolic murmur (DM) of Austin Flint begins with a third heart sound (S_3) and lasts throughout diastole, at times with presystolic accentuation (PSM). The late systolic murmur (LSM) of mitral regurgitation is the result of volume overload of the left ventricle. A small early diastolic pressure gradient between LA and LV and a reverse end-diastolic gradient with the left ventricular end-diastolic pressure (LVEDP) markedly elevated and higher than the A wave in LA are typical findings in patients with severe aortic regurgitation who have the Austin-Flint murmur.[11] S_1 = first heart sound; S_2 = second heart sound. (Courtesy of Kevin P. O'Brien, MD)

apical rumble of Austin Flint (Figures 4,5).[11] Although the prognosis with symptoms is not as bleak in patients with aortic regurgitation as in those with the same symptoms and aortic stenosis, angina, syncope, or dyspnea at a low level of exertion, occurring spontaneously or during exercise testing, in a patient with chronic, *severe*, aortic regurgitation is an indication for valvular replacement or repair.[9] A left-ventricular internal diameter of > 75 mm during diastole or > 55 mm during systole, progressive left ventricular dilatation, and a low ejection fraction, singly or in combination, also are indications for surgical intervention.[9] The surgeons have become increasingly adept at repairing regurgitant aortic valves, but many patients still require valve replacement.

AORTIC STENOSIS AND REGURGITATION

Because together they impose both volume and pressure loads on the left ventricle and thus cause inordinately high wall tension, the combination of severe regurgitation and severe stenosis, although uncommon, is especially poorly tolerated (Figure 6). Indications for operative intervention are symptoms and signs of left ventricular dysfunction or enlargement.

INFECTIVE ENDOCARDITIS

William Osler in 1886 was the first to note the unusual susceptibility of the CBAV to infective endocarditis.[12] To give patients prophylactic antibiotics during procedures, such as dental work, likely to cause transient bacteremia is perhaps the most compelling reason to recognize the CBAV while the person is well. Infective endocarditis on a CBAV often results in acute, severe, aortic regurgitation with catastrophic and potentially fatal results (Figures 7-9).

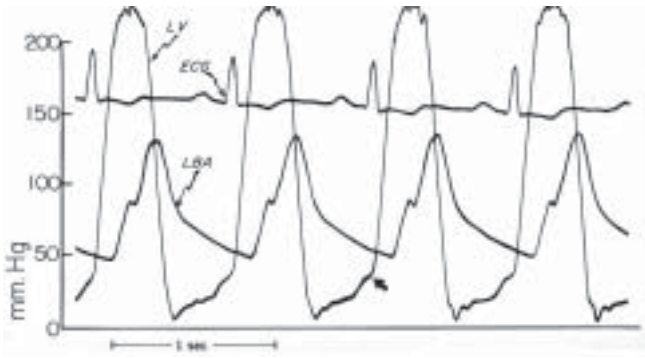

Figure 6. Simultaneously recorded electrocardiogram (ECG) and left ventricular (LV) and left brachial arterial (LBA) pressure tracings. The 100mmHg peak-to-peak systolic pressure gradient between LV and LBA and the slowly rising pressure and relatively low anacrotic notch on the LBA tracing indicate severe aortic stenosis. The wide pulse pressure (85mmHg) and low diastolic pressure (50mmHg) in the LBA indicate severe aortic regurgitation. The combined pressure and volume loads have raised left ventricular end-diastolic pressure (arrow) to 30mmHg (normal = 4 to 12).

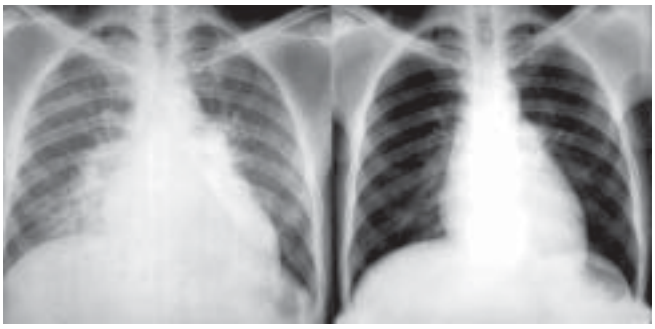

Figure 7. Posteroanterior chest x-rays in a 48-year-old man with acute, severe, aortic regurgitation due to infective endocarditis on a congenitally bicuspid aortic valve show generalized cardiomegaly and pulmonary edema before aortic valve replacement (left) and clearing of the edema and a slight reduction in heart size after operation (right).

WITH AORTIC COARCTATION[13]

CBAV may be an incidental finding in patients presenting with other forms of congenital heart disease, especially aortic coarctation, and a common scenario is for a patient to develop symptomatic aortic stenosis years to decades after repair of the coarctation. Thorough evaluation for CBAV by echocardiography at the time of presentation with aortic coarctation and, if the valve is bicuspid, institution of life-long follow-up and antibiotic prophylaxis for dental work, etc. are essential for preventing infective endocarditis and detecting subsequent aortic valvular dysfunction.

EJECTION SOUND OR SYSTOLIC EJECTION MURMUR ON ROUTINE EXAMINATION

Because the CBAV has only two commissures, it is tethered to the aorta differently from the normal valve, does not open fully, and often produces a clicking sound when it reaches its maximal excursion. This ejection sound or click occurs at the onset of the carotid arterial upstroke. It may be heard over the entire precardium and may be of maximal intensity in the second right intercostal space (the so-called aortic area), at the cardiac apex, or along the left sternal border (Figure 3). In contrast, pulmonic ejection sounds often are heard only in the second left intercostal space and may decrease or disappear with inspiration.[14] An ejection sound often is mistaken for an unusually loud and snappy first heart sound and must also be distinguished from the mid- and late-systolic clicks of mitral valvular prolapse. Because bicuspid valves do not open as completely as tricuspid aortic valves, ejected blood has less laminar flow and more turbulence. Consequently an ejection systolic murmur may be heard even in the absence of a measurable pressure gradient. The long-term study of Kitchiner et al suggests that although

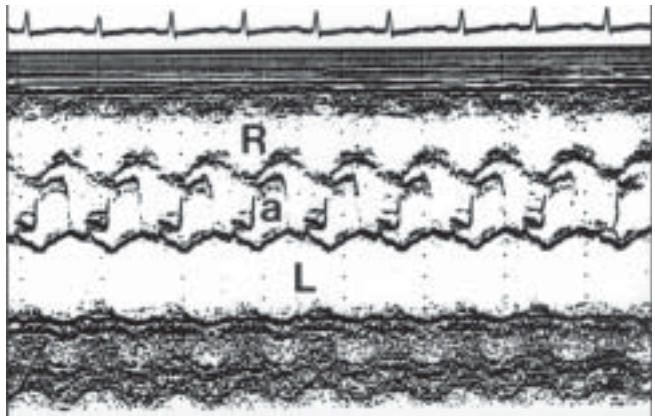

Figure 8. M-mode echocardiogram on a 32-year-old man with florid heart failure due to acute, severe, aortic regurgitation resulting from infective endocarditis on a congenitally bicuspid aortic valve with anterior and posterior cusps. The aortic valve (a) opens widely during systole, and the fuzzy-appearing material on its anterior cusp is a large vegetation. The line of closure of the cusps during diastole is close to the posterior aortic wall and far removed from the anterior wall, a finding suggesting that the valve is bicuspid. The vertical dots are 1 cm apart. The patient died of heart failure in the operating room after aortic valve replacement. L = left atrial cavity: R = right ventricular cavity.

infants and children with no hemodynamic abnormality or mild stenosis when their bicuspid aortic valve is discovered have a better prognosis than those with moderate or severe stenosis, after 30 years few will have normal valvular function or only mild stenosis.[15]

DISCOVERY BY ECHOCARDIOGRAPHY

On both the M-mode and the 2-dimensional echocardiogram, the CBAV has several distinguishing features that are rather reliably recognized by the observant echocardiographer (Figure 8). Consequently echocardiography is not only the means of verifying a CBAV that has been suspected clinically, but also allows for serendipitous discovery in a patient being studied for another abnormality, either congenital or acquired.

MISCELLANEOUS PRESENTATIONS

Because of both turbulent flow across the valve and what appears to be an inherent abnormality in the aortic wall, CBAV is associated with dilatation of the ascending aorta, and discovery of this aortic abnormality by chest roentgenogram or other imaging modality may lead to discovery of the valvular malformation.[2] Furthermore, through the same mechanisms CBAV is associated with aortic dissection and may first be detected during that catastrophic event.[16] Finally, the bicuspid aortic valve may be an incidental autopsy finding (Figure 1).

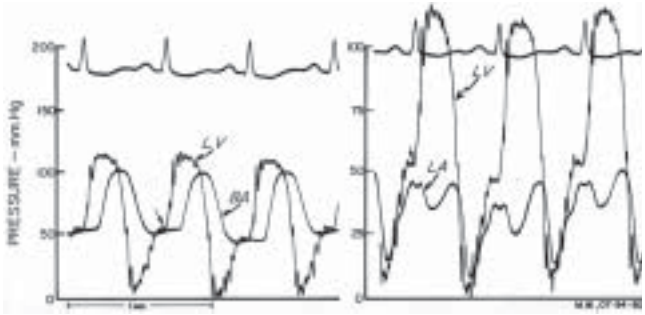

Figure 9. Simultaneous left ventricular (LV) and brachial arterial (BA) pressure tracings (left) and LV and left atrial (LA) tracings (right) in a 53-year-old man with infective endocarditis, an acutely and severely regurgitant, congenitally bicuspid, aortic valve, and a loud Austin-Flint murmur. LV and BA pressures equalize during diastole (straight arrow on left), the ultimate sign of severity in aortic regurgitation. The small LV-BA systolic pressure gradient indicates that the bicuspid valve is mildly stenotic. LA pressure is markedly elevated due to the markedly elevated LV end-diastolic pressure of 50mmHg (straight arrow on right). LA pressure exceeds that in LV by a small amount in early diastole. The pressures equalize in mid diastole due to the torrential aortic regurgitation, and the mitral valve closes prematurely. LV end-diastolic pressure exceeds left atrial pressure. This patient also died of cardiac failure early after aortic valve replacement.

CONCLUSION

The CBAV occurs in more than 1% of the population. Although it may never cause difficulty and first be discovered at autopsy, more often it results in some hemodynamic abnormality. Its clinical manifestations are varied, and its early recognition is essential if we are to prevent the dreaded complication of infective endocarditis.

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The Cardiology Report is a regular educational feature presented by the Section of Cardiology, Department of Medicine at the Louisiana State University Health Sciences Center Department of Medicine in New Orleans.

CME QUESTIONS

To earn CME credit, read the preceding CME article and complete the registration, evaluation, and answer form on page 335. Mail or fax the registration, evaluation, and answer form to the Educational and Research Foundation. Answers must be postmarked or faxed prior to December 31, 2003. Participants must attain a minimum score of 75% to receive credit.

For each question, choose the one answer that is most correct.

1. True or False. The incidence of congenitally bicuspid aortic valve (CBAV) is more than that of all forms of right ventricular outflow tract obstruction (pulmonic stenosis, tetralogy of Fallot, pulmonary arterial branch stenoses, etc.), but is less than the incidence of ventricular septal defect in all of its manifestations.

2. Which of the following is *not* true of an ejection sound or click due to a CBAV?
   a) May be best heard in the aortic area, along the left sternal border, or at the cardiac apex
   b) Is often mistaken for the first heart sound
   c) Occurs in mid systole
   d) Occurs when the valve reaches its fully opened position
   e) May be accompanied by a systolic ejection murmur

3. A person with a CBAV is more likely than a person with a tricuspid aortic valve to have or develop all but which of the following?
   a) Coronary artery disease
   b) Coarctation of the aorta
   c) Aortic dissection
   d) Aortic stenosis
   e) Aortic regurgitation
   f) Infective endocarditis

4. An asymptomatic 23-year-old man is found on a routine physical examination to have an ejection click, but no cardiac murmur, and transthoracic echocardiography confirms a bicuspid aortic valve. Current management should include:
   a) A transesophageal echocardiogram to get a better look at the valve.
   b) Antibiotic prophylaxis against infective endocarditis.
   c) Cardiac catheterization to rule out silent aortic stenosis.
   d) Cardiac surgical consultation.
      Fast CT to confirm that the valve is truly bicuspid.

St. Louis Encephalitis Outbreak in Louisiana in 2001

Shelley Coats Jones, MD; Jim Morris, BS; Greg Hill, RS; Myra Alderman, RN; and Raoult C. Ratard, MD

A description of the St. Louis encephalitis (SLE) outbreak in Northeast Louisiana is presented. In the fall of 2001 there were 63 cases of St. Louis encephalitis in Monroe and West Monroe and seven additional cases in the neighboring parishes of Richland, Morehouse and Franklin. All cases had a clinical presentation of encephalitis and were confirmed serologically. Clinically most cases presented with fever, meningitis syndrome with altered mental status. Tremors were common (56% of cases). There were three deaths. Age-group distribution showed a predominance among 45 and older. The epidemic curve based on diagnosis date showed an explosive outbreak starting August 8, 2001, reaching a peak by the second week, and progressively slowing down. The curve showed that by the time the first case was diagnosed, 60% or more of the cases were already infected. Most of the cases come from low socio-economic areas. Houses were often run down, many with screens in disrepair. Backyards were usually large, with heavy brush and many trees. There was an abundance of sources of mosquito larvae, particularly for Culex quinquefasciatus which is the main vector. Mosquito pools confirmed the presence of SLE virus. As soon as the first case was reported, a campaign of health education and increased mosquito adulticiding were implemented.

St. Louis Encephalitis (SLE), an infection due to an arbovirus, more specifically a flavivirus, is endemic in Louisiana and most of the USA. There are 20 to 50 cases reported per year in the USA with epidemics occurring at 10-20-year intervals. In the past 30 years, the major outbreaks occurred in 1975-76 (with nearly 3000 reported cases) and in 1990[1]. Factors contributing to the cyclic recrudescence of the virus are only partially understood[2]. Several species of mosquitoes are involved in the transmission, however in the southern United States Culex quinquefasciatus is by far the most prominent vector[3].

In Louisiana most cases are sporadic, but the state has experienced a few outbreaks. In the 1960s there were 27 sporadic cases, in the 1970s 20 sporadic cases. In the 1980s there was an outbreak of 12 cases in New Orleans in 1980, and seven sporadic cases. In the 1990s there were seven sporadic cases and two outbreaks, in 1994 in New Orleans (16 cases) and in 1998 in Jefferson Parish (14 cases). Five of the seven sporadic cases of the 1990s occurred in 1998, the year of the Jefferson outbreak. The largest outbreak of SLE occurred in Monroe and West Monroe in 2001. The last cases reported from Monroe had been from 1976.

POPULATION AND METHODS

A case definition was necessary to differentiate infection from disease and allow a consistent method to evaluate the progress of the outbreak.[4] Cases were defined using standard case definitions for public health surveillance.[5]

Spinal fluid and serum were tested. Using the date of onset as a guide serum were classified as acute (collected less than 8 days after onset) or convalescent (convalescent serum collected at least 15 days after onset). Serologic tests done included an immunofluorescence (IFA) from MRL Diagnostics ® performed by the Office of Public Health (OPH) laboratory, an enzyme immunoassay (EIA) from the CDC performed by the Office of Public Health and the CDC laboratory at Fort Collins, CO. Both methods were used to test for IgM and IgG antibodies. The plaque reduction neutralization tests were all performed at the CDC laboratory in Ft. Collins, CO.

Epidemic curves were used to monitor the progress of the outbreak. Three epidemic curves were constructed using the following dates: (1) date of blood collection, a surrogate for date of diagnosis, (2) date of onset from questioning the case or close family members. For those

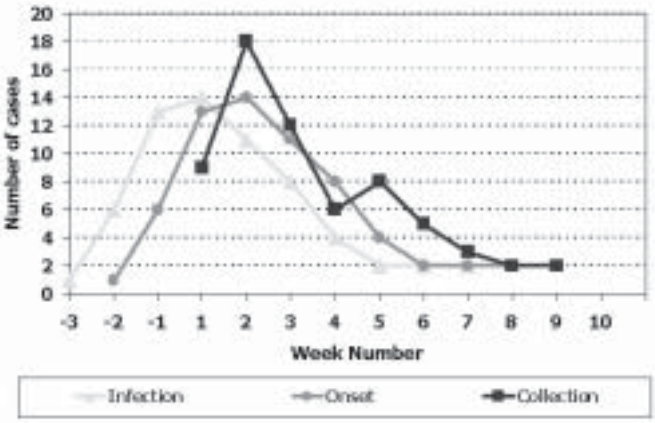

Figure 1. Epidemic curves according to date of blood collection, date of onset, and date of infection.

cases who could not remember date of onset or those with no family members able to answer questions regarding onset, the mean delay between onset and blood collection (4 days), and (3) date of infection, estimated from the date of onset minus 7 days (a short estimate of the incubation period). These epidemic curves are presented in Figure 1. Week 1 (August 6 to 12, 2001) is the week during which the first cases were diagnosed. Week -1 was the week before.

A simple questionnaire was obtained for all cases. It included demographic data, date of onset, summary clinical information, exposure, hospitalization dates, risk factor and environmental observations at the place of residence.

Culex quinquefasciatus densities were determined by using ovitraps.[6] The presence of SLE virus was tested by the CDC laboratory at Fort Collins, CO using a TaqMan reverse transcriptase-PCR assay. Bird serologies were tested using EIA techniques measuring IgG.

RESULTS AND COMMENTS

Cases

There were a total of 70 cases of St. Louis encephalitis: 34 were confirmed serologically by a positive IFA in the serum or CSF performed by the OPH laboratory and a positive EIA and a positive seroneutralization performed by the CDC laboratory at Fort Collins Co. The remaining 36 cases were confirmed by an IFA and EIA performed at the OPH laboratory.

Epidemic curves

The first case was diagnosed August 8, 2001. The epidemic curve showed a sharp increase from 9 cases the first week to 18 the second week. Then the number of cases gradually decreased over the following 9 weeks. The total number of cases in Monroe and West Monroe was 63.

In addition there were:

- three cases in Morehouse parish, north of Ouachita parish; two occurred in week 4 and one in week 7
- three cases in Richland parish, east of Ouachita parish; two occurred in week 6 and one in week 10
- one case in Franklin parish, south of Ouachita parish in week 9.

The epidemic curve based on week of infection showed that by week 1 when the first cases were reported, there were at least 34 cases already infected using a 7-day incubation period, or 45 cases using a 15-day incubation period. This means that by the time the first cases were reported, between 54% and 71% of the cases were already infected. It shows that by the time the outbreak is initially recognized, it is too late to prevent a large number of cases. Therefore a different strategy is necessary to get an early warning.

Age and Gender distribution

The age and gender distribution of cases is presented in Table 1 and Figure 2. Typically SLE cases occur predominantly among the elderly. In this outbreak the incidence of cases (new cases / 100,000 population) increased with age group up to a certain point, there was a decrease among those over 60.

Geographical distribution

The two major sites affected were the cities of Monroe and West Monroe with 34 and 29 cases respectively;

Table 1. Age and Gender Distribution of Cases in Ouachita Parish.

Age	M	F
0-14	1	0
15-29	3	3
30-44	9	11
45-60	9	14
60-99	7	6

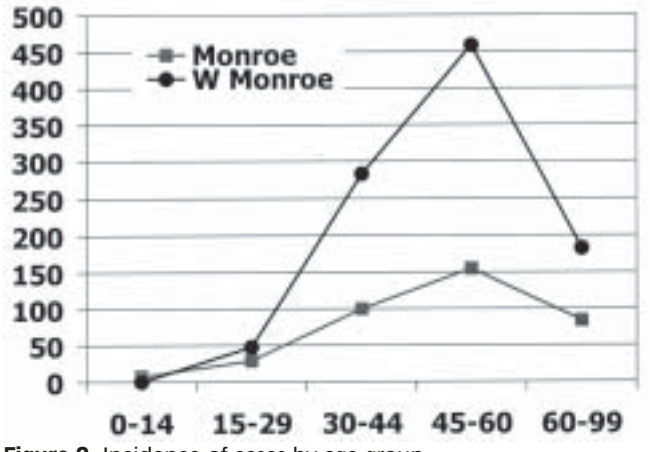

Figure 2. Incidence of cases by age group.

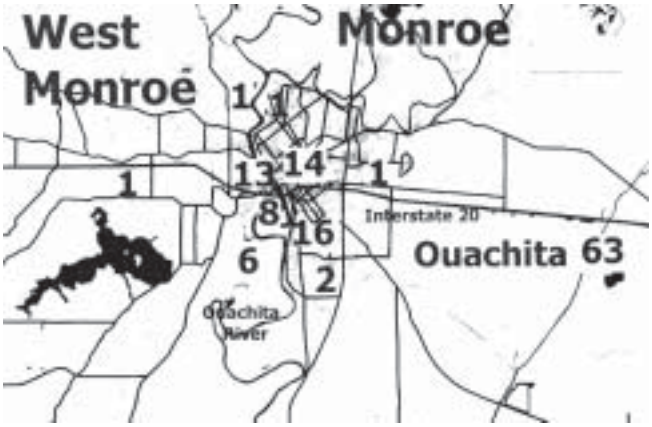

Figure 3. Monroe and West Monroe and Ouachita Parish, Louisiana.

thus, incidence rates were 64.0 and 178.2 / 100,000. Cases were concentrated in a relatively small area at the intersection of Ouachita river and Interstate 20 (Figure 3). The area that included 57 cases (13+14+16+8+6 on the map) covers approximately 6 miles from north to south and 3 miles from east to west. This is a low socio-economic area with large lots, numerous trees and heavy undergrowth, houses often run down, houses elevated off the ground on short brick pilings, window screens in disrepair, trash in the yards, and numerous ditches. Backyards were usually large, with heavy brush and many trees.

Clinical data

Initial signs and symptoms observed are described in Table 2. Fever, headaches, altered mental status (confusion, disorientation, or coma) tremors and muscle weakness were the most common signs and symptoms. All cases were hospitalized.

The observed symptoms match the expected picture of SLE which include fever, altered consciousness (slight disorientation, confusion, delirium, or somnolence) generalized motor weakness as the three predominant presenting features.[7]

Admitting diagnoses were varied and were probably influenced by timing. At the beginning of an outbreak, encephalitis is not suspected. As the outbreak progresses, the medical community becomes aware, and the admitting diagnosis rapidly shifts to encephalitis. Admitting diagnoses were fever, fever / nausea / vomiting, encephalitis, meningitis, and headaches. Among diagnoses was urinary tract infection in two cases. Upper respiratory tract infection, urinary tract infection, and gastro-intestinal illness are reported in the literature as common initial clinical presentations of arboviral encephalitis.

A large proportion of cases had some pre-existing conditions such as diabetes, chronic alcoholism, gastrointestinal, hematologic, renal, liver and other miscellaneous chronic conditions. Only one had reported an immunodeficiency. Overall 28 out of 44 (63%) patients for whom a previous history of disease was collected, had some chronic conditions.

Table 2. Initial Signs and Symptoms.

Initial Symptoms	Present	Absent	%
Fever	39	21	67.6
Headache	34	26	56.7
Tremor	31	29	51.7
Altered mental status including	28	32	46.6
Inlcuding			
Confusion	20	40	33.3
Disorientation	16	44	26.4
Coma	4	56	6.7
Muscle Weakness	25	35	41.8
Neck Stiffness	20	40	33.3
Light Sensitivity	18	42	30.0
Vomiting	16	44	26.7
Joint Pain	11	49	18.3
Rash	3	57	5.0

Three cases died: a 51-year-old man, a 78-year-old woman, and an 81-year-old woman. They all had other serious medical conditions (chronic renal failure, diabetes and coronary heart disease, and hypertension). The prevalence of complicating medical condition was 61% among the survivors and 100% among the deceased. This difference was not significant (p=0.55, Fisher's exact), which is not surprising given the very small sample size.

Entomologic data

In this area large number of Culex quinquefasciatus were present. Culex quinquefasciatus, also called the southern house mosquito, is the main vector of SLE encephalitis in the southern USA. Five weeks into the outbreaks, the prevalence of infection by SLE virus was at 3 to 5 / 1,000, a very high prevalence given that a prevalence of 1 / 1,000 is deemed sufficient to cause an outbreak.

Culex quinquefasciatus is an ubiquitous species particularly abundant in tropical and subtropical countries. Females lay a single raft of 140-340 eggs on heavily polluted, small water collections after each blood meal. Eggs hatch in 1-2 days. The larval and pupal stages lead to an adult 8-12 days after egg laying. Breeding places and biting activity are the most important determinants of the geographical distribution of the infection. Breeding places comprise all types of large man-made containers and collections of ground water, storm sewer catch basin, ground pools, ditches, run off from sewage plants, small artificial containers, cesspits, drains, septic tanks, unused wells, storm water canals. Culex quinquefasciatus can travel up to 3,600 feet / night. Its

life span is 2 weeks in nature. The biting activity involves feeding at night particularly on birds. Humans are not a usual target. Biting humans occurs toward the middle of the night. Since most of the population is indoors late at night, human biting occurs most often in areas with poor housing and ready access of mosquitos to humans sleeping indoors. Culex quinquefasciatus population density is evaluated by catching egg laying females in gravid traps. A gravid trap is a small (gallon size) open container filled with heavily polluted water. On top of the container rests a tube connected to a mosquito net cage. The tube contains a fan that "sucks up" the females as they approach to lay eggs and directs them to the cage.

In the target area, large numbers of Culex quinquefasciatus were found ranging from 0 to 500 mosquitoes / night / gravid trap. More details on the entomologic aspects of this outbreak will be presented in another article in preparation.

Housing inspections were carried out for 43 patients: 48% had central air conditioning, 32% had window units, and 20% had no air conditioning all. Fifteen percent admitted to having their windows open. Fifty eight percent had window screens with holes. For 58% of the patients there was at least one obvious path for mosquitoes to enter the house: windows left open, no screens on open windows, screens with holes.

Only one of the patients queried used mosquito repellent (1 / 44=2%).

Bird data

Miscellaneous types of birds were involved in the outbreak. Rates of infection, as demonstrated by the presence of antibodies, showed a wide range according to species: 48% in sparrows, 24% in chickens, 63% in pigeons (rock doves), 100% in turkeys.

Sentinel chickens are used as an early warning system. Chickens placed in cages are bled regularly (every week or every other week). Serologic tests performed on these chickens would show conversions in case of encephalitis viral activity in the area. In Monroe in 2001 there was no early warning from the chicken sentinel flocks. The main reason is that the chickens were not located in the high risk area. In the high risk, areas prevalence rates of infection among sparrows were around 50%, but the chickens were placed in a low risk area where the prevalence of infection among sparrows was only 5%.

CONCLUSIONS

In the past 40 years there had been relatively few cases of SLE and few outbreaks which led to some complacency. This major outbreak was a wake-up call for public health (including mosquito-control programs). It is very obvious that when the first human cases are reported, it is already very late and a large proportion of the cases are already infected–hence the crucial importance of an effective early warning system. An effective early warning system must be based on a good understanding of the local epidemiologic and entomologic situation. The location of the sentinel chickens must be carefully selected in an area of high transmission potential.

Nineteen parishes, covering 60% of the Louisiana population have a significant, local, mosquito-control program. Extension of mosquito control activities to an additional 10 parishes deemed at high risk would provide coverage for 75% of the population. Two of these parishes have already started the process of planning / implementing a new mosquito control program.

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Myxosarcoma: A Rare Primary Cardiac Tumor

Aditya K. Samal, MD; Hector O. Ventura, MD; Adam Berman, MD; Chika Okereke, MD; Yvonne E. Gilliland, MD; and Gladden W. Willis, MD

We describe the case of a patient with myxosarcoma of the left ventricle, a very rare type of primary cardiac sarcoma, who presented with features of acute pericarditis and discuss the management of this condition.

Primary cardiac tumors are rare, with autopsy series reporting an incidence of 0.0017% - 0.28%.[1-3] Most cardiac tumors are benign, the most common being atrial myxoma. After myxoma, sarcomas are the second most common primary cardiac tumors.[3] However, they are quite rare, with one series reporting them as representing 4% of all cardiac tumors in children and 18% in adults.[4] Despite the best treatment available, survival usually ranges from 6 months to 2 years.[3-5] We describe an unusual case in a young woman with a rare form of cardiac sarcoma, myxosarcoma of the left ventricle, which grew rapidly and resulted in the patient's death less than 3 months after the onset of symptoms.

A 31-year-old caucasian, mother of three, who was 28 weeks pregnant, presented to the emergency department after 1 day of sharp, pleuritic chest pain, not associated with fever, cough, or shortness of breath. There was no history of recent travel or any significant medical history. At the time of initial presentation, she was tachycardic and afebrile, with stable blood pressure and normal O_2 saturation. Physical examination revealed no abnormalities except the presence of tachycardia and a pericardial rub. Electrocardiogram showed sinus tachycardia and low voltage (Figure 1a); chest x-ray (Figure 2a) and cardiac enzymes were normal. The patient was admitted to the hospital with the diagnosis of acute pericarditis and was started on indomethacin therapy. Echocardiography confirmed the presence of a small-to-moderate-sized pericardial effusion (Figure 3a); other parameters were normal. The patient's symptoms resolved, and she was discharged home on indomethacin.

After completing a 10-day course of indomethacin, the patient returned to the emergency department with complaints of recurrent chest pain. The patient was restarted on indomethacin and was referred to the cardiology clinic. At the time of follow-up, she was stable, and a repeat echocardiography revealed a small pericardial effusion. The patient was started on prednisone for failed indomethacin treatment. On follow-up, the prednisone dose was titrated down; however, because of recurrent pain, the patient was started on a daily does of 10 mg of prednisone to continue until her delivery.

The patient was admitted to the hospital for induction of labor at 38 weeks of pregnancy. A cardiology consult was requested for pre-operative clearance because of the history of pericarditis. At that time, the patient was mildly short of breath and continued to be tachycardic. Her blood pressure was normal. Cardiac examination was normal except for tachycardia and elevated jugular venous pressure. The electrocardiogram did not differ significantly from that performed previously (Figure 1b). Chest x-ray showed a significant increase in cardiac size since the earlier study (Figure 2b). Repeat echocardiography showed a small pericardial effusion and a large mass compressing the left ventricle (Figure 3b). Magnetic resonance imaging (MRI) of the chest revealed a 6 cm x 14 cm intrapericardial mass compressing the left ventricle (LV), left atrium (LA) and right ventricle (RV) (Figures 4a, 4b).

A cardiothoracic surgical consultant decided to defer surgical treatment of the mass until after delivery by caesarian section under general anesthesia with perioperative, invasive, hemodynamic monitoring. The intracardiac pressure (mmHg) were right atrial mean=24; right ventricle=30/24; pulmonary artery =30/24, and pulmonary atrial wedge mean =22 mm of Hg–all consistent with cardiac-tamponade physiology.

The patient had an uneventful caesarian section. However, urine output fell and the cardiac index ranging between 1.4 - 1.8 L/min/m^2 postoperatively. Intra-

venous fluids and a renal-dose-dopamine infusion were started. Urine output improved slowly, and blood pressure remained stable with elevated cardiac filling pressures. Because of persistently low cardiac output, the patient was taken to the operating room for thoracotomy and possible resection of the pericardial mass. The mass was found to be large, gelatinous, and unresectable. The patient had cardiac arrest during the procedure and could not be resuscitated. Autopsy and histopathologic examination confirmed the diagnosis of myxosarcoma originating from the left ventricular myocardium (Figures 5a, 5b).

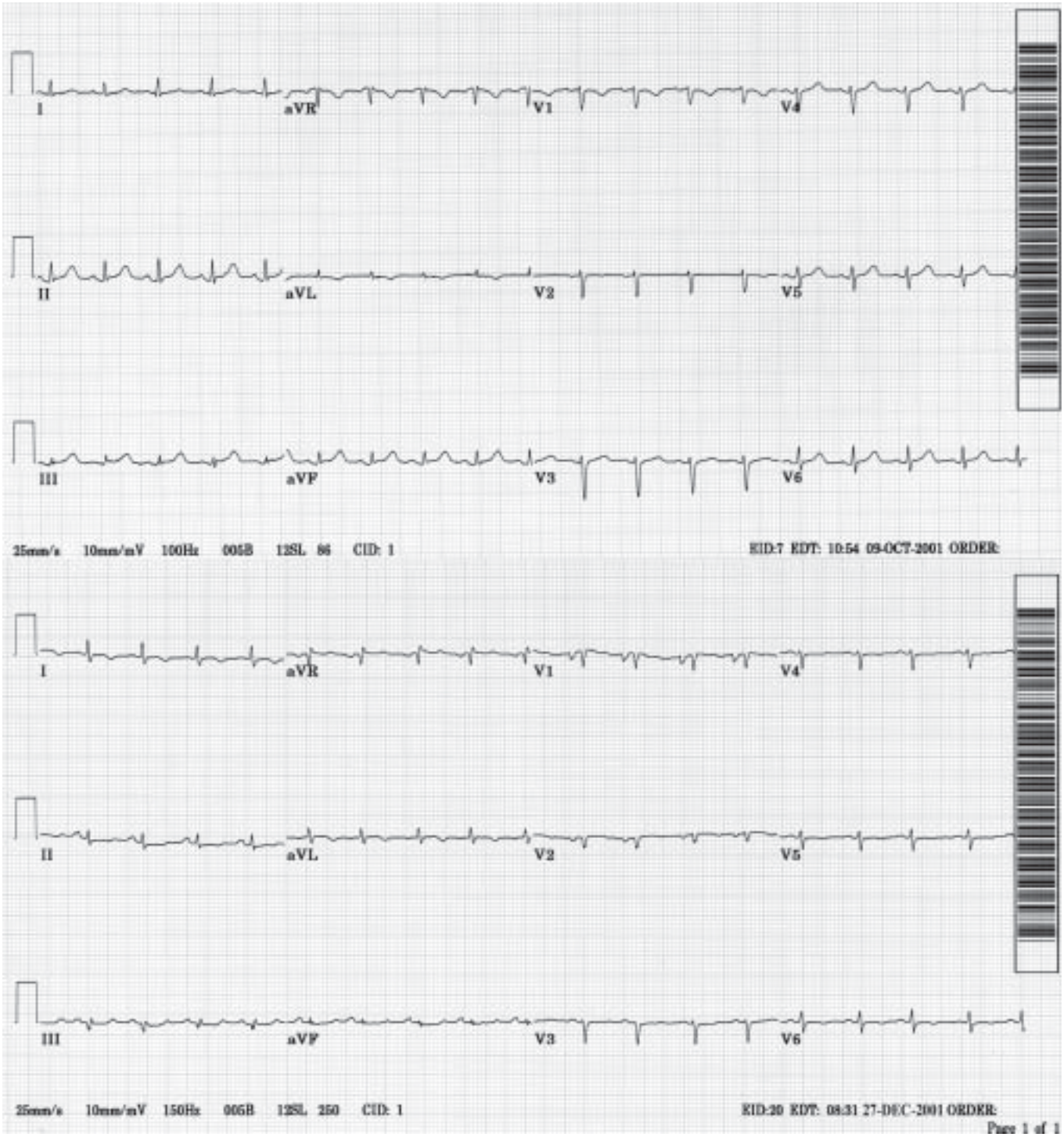

Figure 1a. EKG (October 2001) showing sinus tachycardia, low voltage, and minimal ST-segment elevation in leads II, III, aVF, V_6 (top); and **Figure 1b.** EKG (December 2001) showing sinus tachycardia, low voltage, left atrial enlargement, and widespread, non-specific ST-T changes (bottom).

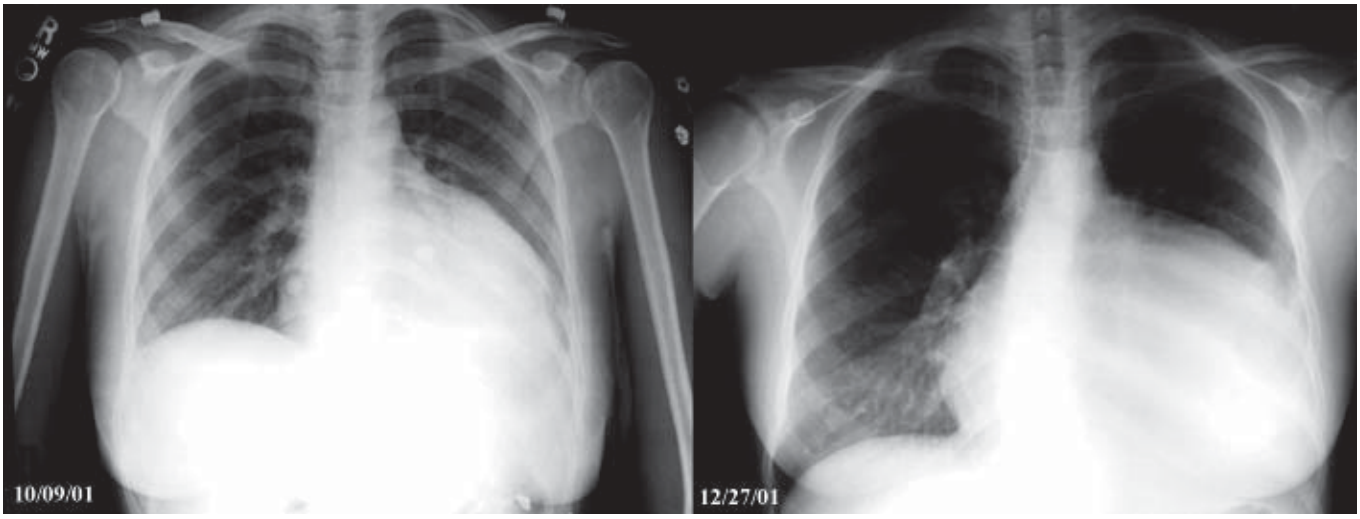

Figure 2a. Chest x-ray (October, 2001) showing moderately, generalized cardiomegaly (left); and **Figure 2b.** Repeat x-ray (December 2001) showing a significant increase in cardiac size (right).

Primary cardiac tumors are rare. Approximately a quarter of all primary cardiac tumors exhibit some features of malignancy or behave malignantly.[6-7] Most malignant primary cardiac tumors are either sarcomas (95%) or lymphomas (5%).[6-7] In order of decreasing frequency, malignant primary cardiac sarcomas are angiosarcoma, rhabdomyosarcoma, myxosarcoma, undifferentiated sarcoma, osteosarcoma, fibrosarcoma, liposarcoma, leiomyosarcoma, reticulum cell sarcoma, synovial sarcoma, neurofibrosarcoma and malignant fibrous histiocytoma.[5, 6, 8-14] The histopathologic diagnosis in our patient was cardiac myxosarcoma arising from the left ventricle. This is unusual, since most of the myxosarcomas arise from the left atrium, although right ventricular tumors also have been described.[3] To our knowledge, myxosarcomas arising from the left ventricle have not been described.

The term *myxosarcoma* currently is not used in standard classifications of soft-tissue tumors.[15] Pathologists restrict the use of the term *myxosarcoma* to cardiac tumors that are myxoid in all areas sampled, without cellular or vascular patterns diagnostic of other sarcomas.[3] Myxosarcoma and cardiac myxoma are sometimes considered to represent opposite ends of a biologic spectrum, because both are characterized by an accumulation of proteoglycans and because both typically are located in the left atrium. Myxosarcomas are gelatinous, multi-lobed tumors that are usually sessile endocardial growths. Although they may be grossly indistinguishable from myxoma, they are more likely to be multiple

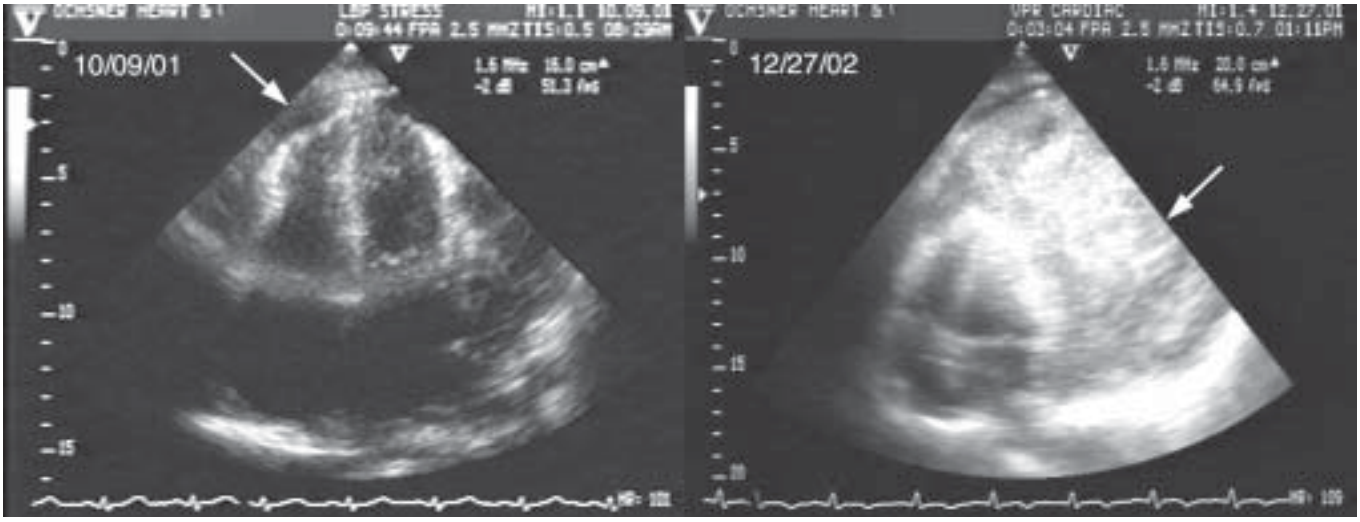

Figure 3a. Two-dimensional echocardiogram, four-chamber view (October, 2001) showing smallpericardial effusion (arrow) (left); and **Figure 3b.** Repeat two-dimensional echocardiogram (December 2001) showing small pericardial effusion and a huge mass (arrow)compressing the left ventricle and left atrium (right).

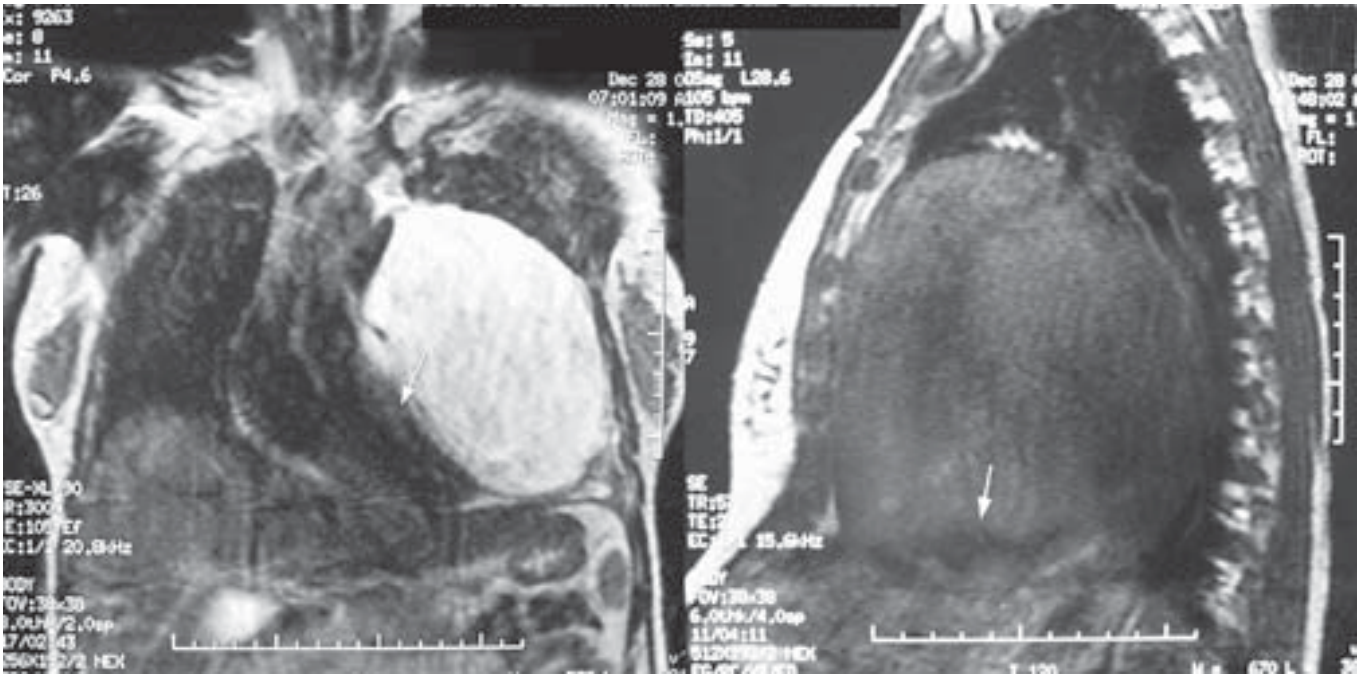

Figure 4a. Magnetic resonance image of the chest (T2 sagital section) showing a large mass compressing the left ventricle, left atrium, and right ventricle (arrow) (left); and **Figure 4b.** MRI of the chest (T1 coronal section) showing a large mass compressing the left ventricle (arrow) (right).

or to infiltrate the myocardium.

Partly due to the lack of specific histopathologic criteria for the diagnosis of myxosarcoma, only seven cases have been described in the literature.[3] Myxosarcomas are predominantly seen in women, and the age of presentation has ranged from 28 to 56 years.[3] The size and location of the tumor determines the symptoms. Pain, although absent with many sarcomas, is highly specific for them; its presence almost excludes the diagnosis of a benign tumor.[9] Dyspnea, pericardial effusion, right-sided heart failure, and syncope are also commonly seen with sarcomas.[16]

Echocardiography and MRI combined allow precise location of the tumor. In our patient, despite repeated echocardiography, the diagnosis could not be reached early in her course. Possible explanations include the infiltrating nature of the tumor, its origin from the left ventricular myocardium, and possible late aggressive growth just prior to diagnosis. From our experience in this case, we suggest earlier use of MRI in addition to echocardiography to delineate better the infiltrative type of sarcoma, especially in patients with recurrent chest pain.

Complete resection is the preferred treatment for a primary cardiac sarcoma. However, the frequently extensive nature of the sarcoma when first discovered al-

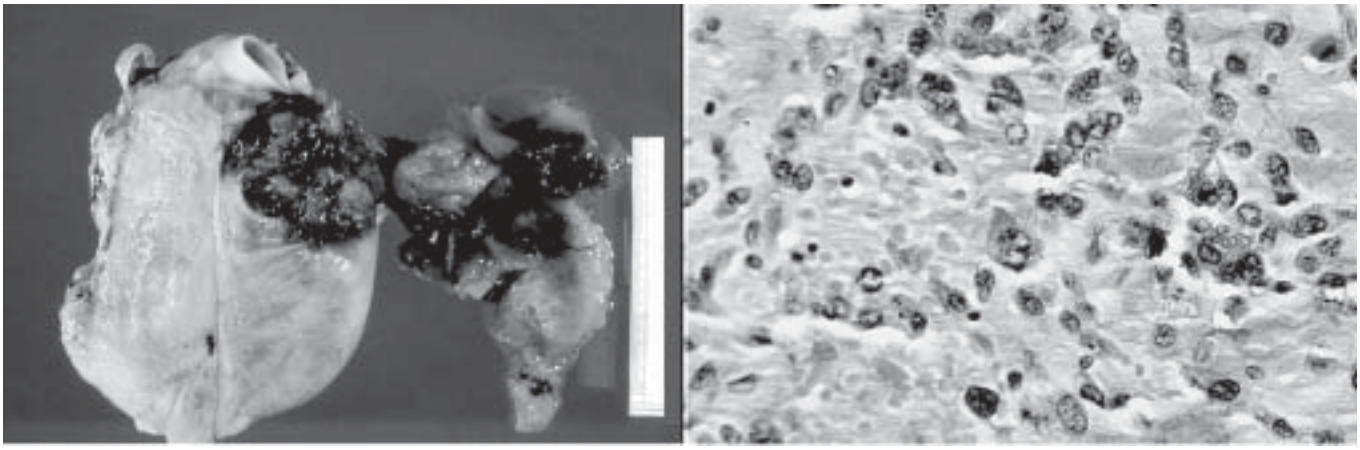

Figure 5a. The heart autopsy. Approximately 1000 grams of myxosarcoma filled the pericardial space and tamponaded the heart. Tumor seen here spilling through cut in pericardial sac (left); and **Figure 5b.** High grade myxoid sarcoma with multiple mitotic figures (right). Hematoxlin and Eosin, original magnification X 250.

most always makes this impossible. Both chemotherapy and radiation therapy have been used, usually without success.[5, 7, 17-18] Because these tumors are usually incompletely resectable at presentation, cardiac excision and transplantation have been tried with only occasional long-term survivors.[19-21] Such therapy demands exclusion of distant metatasis. A literature review reveals 28 patients who have undergone orthotopic heart transplant for inoperable primary cardiac tumors.[20] Of these tumors, seven were benign and 21 were malignant. Survival ranged from 8 to 105 months with a mean of 46 months without any recurrence of the tumor in the case of benign tumors. In contrast, in patients with malignant tumors, the orthotopic heart transplant results have been dismal. Thirteen of 21 patients had a recurrence of the tumor. Despite the modes of treatment described above, survival remains poor for primary cardiac sarcomas, with a one-year survival rate from the time of diagnosis of less than 25%.[22]

Myxosarcoma is a lethal tumor that grows rapidly. Early diagnosis is essential for best management. For early diagnosis, both echocardiography and MRI may be helpful, especially when a cardiac tumor is suspected as a cause of pericarditis, or for those patients with recurrent or persistent chest pain despite anti-inflammatory therapy for pericarditis.

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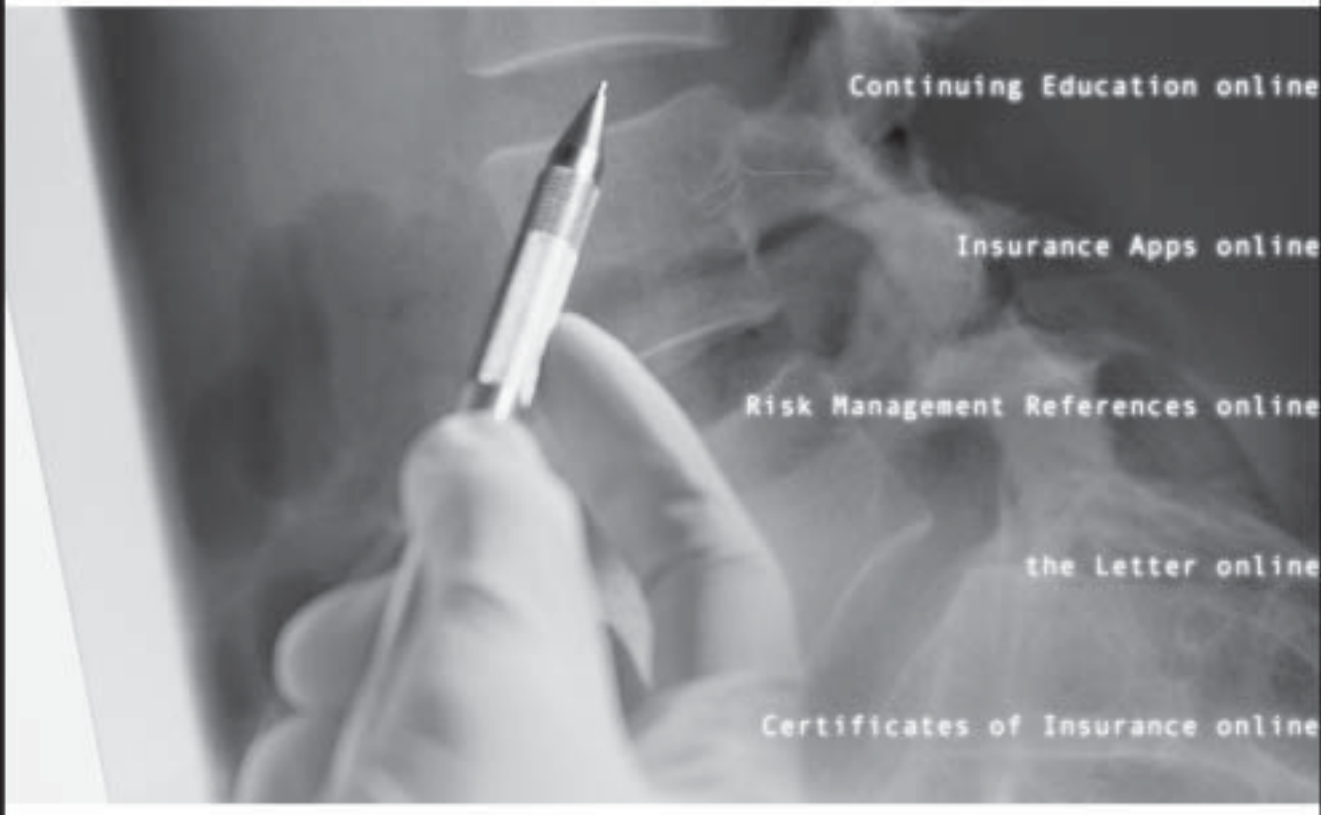

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Coronary-Calcium Screening to Improve Risk Stratification in Primary Prevention

Paolo Raggi, MD

Coronary artery disease is very prevalent in the United States where over 7 million people suffer from it, and more than 500,000 die from its complications annually. For the majority of individuals suffering an acute myocardial infarction, the event represents the first indication of the presence of underlying coronary atherosclerosis. Furthermore, due to the outward remodeling of arteries that slowly accumulate atheroma in their imtima (Glagov effect), sudden death or acute myocardial infarction may occur in the absence of obstructive luminal atherosclerotic plaque. Therefore, it might seem highly desirable to detect atherosclerosis in its early stages to implement effective preventive measures rather than apply delayed treatment. Yet, statistics from primary care and sub-specialty practices indicate that the preventive attitude of the majority of physicians is not sufficiently developed, and most training programs still struggle to implement strong educational curricula in this field. To these limitations, one may add that traditional risk factors help predict only about 60% to 65% of the risk, while many individuals continue to suffer events in the absence of established risk factors for atherosclerosis. In light of this knowledge, several tools have been developed to identify atherosclerotic disease in its pre-clinical stages in the hope of modifying its natural history. This review deals with the utilization of electron beam tomography for detection of coronary arterial calcium as an additional tool to risk stratify asymptomatic individuals.

Calcification of the coronary atherosclerotic plaque appears to be due to an active phenomenon of mineralization with deposition of hydroxyapatite and not a simple process of crystal precipitation.[1-3] It begins in the very early stages of atherosclerosis development and, although it is not clear whether it should be considered a repair process as opposed to being a part of the ongoing arterial wall damaging processes, it is an excellent marker of underlying disease.[4,5] Scientific publications over the past 10 years have established electron beam tomography (EBT) as the gold standard for identification and quantification of arterial calcium (Figure 1). Despite the lack of a site-by-site correlation between calcium and luminal stenosis, calcium scores calculated on images obtained with this technology accurately predict total atherosclerotic plaque burden.[6-8] Since the burden of disease is a more significant determinant of events than focal luminal stenosis, the assessment of disease burden with EBT constitutes a potentially useful approach to the identification of patients at risk of events. Nonetheless, the overuse and commercial propagation of such a sensitive imaging modality have raised substantial concern about the economic impact of preventive and therapeutic approaches driven by this technology.[9] Indeed, the identification of a large number of subjects with asymptomatic atherosclerosis that represents an as yet unrealized threat to their health may impose a large economic burden on our society. Besides the cost of imaging, a negative economic impact could derive from an inappropriate performance of unnecessary secondary testing as a result of the primary test results. Therefore, there are both a clear need to educate physicians on the proper application of plaque imaging and a need to develop standard criteria for the interpretation of imaging information to render it a fruitful risk-stratification tool.

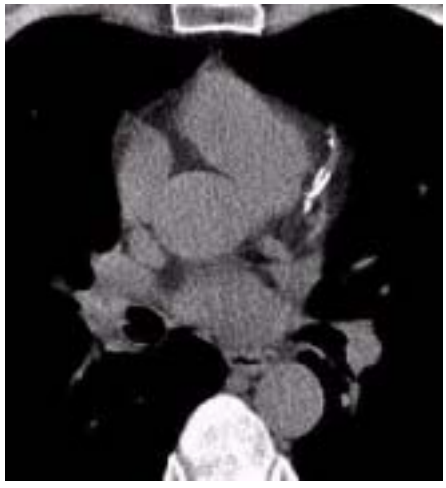

Figure 1. Moderate amount of calcium in the vessel wall in the mid-portion of the left anterior descending coronary artery on a screening electron beam tomography image.

PRIMARY PREVENTION

Risk stratification performed according to the recommended Framingham approach, combining multiple clinical markers such as age, hypertension, hyperlipidemia, smoking, and diabetes mellitus provides a good assessment of the median risk of coronary heart disease in a population.[10] However, it does not allow clear discernment of an individual's risk, and only about 60% to 70% of the variability in risk is predictable. The ability to utilize coronary-calcium screening in the setting of primary prevention requires the demonstration that it provides incremental value to risk prediction. A few published reports have addressed this important issue, and as will be discussed, more investigational data have been presented at scientific meetings.

An obstacle to the acceptance of coronary calcium as a marker for risk of future events is the deeply rooted opinion that calcification of the atherosclerotic plaque may constitute an attempt to repair the arterial wall and that it might therefore be beneficial and not deleterious. If this were true, heavy calcification of the coronary tree should reduce the risk of hard coronary events and not increase it. Wayhs et al, however, clearly demonstrated that this opinion is incorrect. [11] In an observational study, they followed a cohort of 98 asymptomatic individuals with very high coronary calcium scores (score $\geq$ 1000) for an average of 17$\pm$11 months (range 4 to 36 months). The subjects in this study did not undergo any further test driven by the results of the EBT scan, mostly because of the uncertainty and lack of confidence of their primary care physicians in the information provided by calcium screening. Therefore this represented a true natural-history study of patients accidentally found to have large calcium scores. During the follow-up period the study subjects suffered 35 hard coronary events (myocardial infarction or death) at a yearly rate of 25%, with the majority of the recorded events occurring within the first 28 months of follow-up. Patients with hard events had significantly greater calcium scores than patients without events, while age and risk factor distribution did not differ. Of interest, the use of lipid lowering agents and beta-blockade was similar among the groups suffering and not suffering an event. The markedly elevated risk was statistically greater than that reported for historical symptomatic controls with severely abnormal results on a nuclear stress test. This study provided substantial evidence that extensive calcium in the coronary tree is a harbinger of a poor prognosis and should not be seen as protective against dramatic events. There are at least two explanations for these results: high calcium scores indicate the presence of extensive atherosclerotic plaque burden with the coexistence of disease in different developmental stages. While some plaques may be calcified, and indeed more stable than others, other plaques may contain a soft and inflamed core with high potential for rupture. On the other hand, high calcium scores have been shown to predict with good reliability the presence of luminal obstructive disease with all the possible attendant consequences, and these asymptomatic patients might indeed have had disseminated obstructive disease.

The report by Wayhs et al supports and confirms the concept that an extensive plaque burden, indicated by high calcium scores, poses a huge risk for events. However, the study did not address the question of whether calcium screening adds incremental prognostic information to risk factors. Such an approach was taken by Raggi et al in a recent publication.[12] The ability of coronary calcium and traditional risk factors to predict myocardial infarction and death was compared in a cohort of 676 individuals referred by primary care physicians for EBT calcium screening. Thirty hard events were recorded during a follow-up period of 3 years. Receiver-operator-characteristics (ROC) curves were used to ascertain the ability of the different methods (calcium screening vs. risk factors) to predict myocardial infarction or death. The area under the ROC curve for traditional risk factors was statistically smaller than that obtained using calcium scores adjusted for age and sex (Figure 2). Age and sex specific calcium scores were used to conform to a prior publication in which percentiles of calcium scores were shown to be more predictive of events than absolute calcium scores. [13] This notion is indeed similar to that expressed above regarding the importance and significance of an extensive plaque burden. A small absolute score in a young individual may not indicate the presence of obstructive lu-

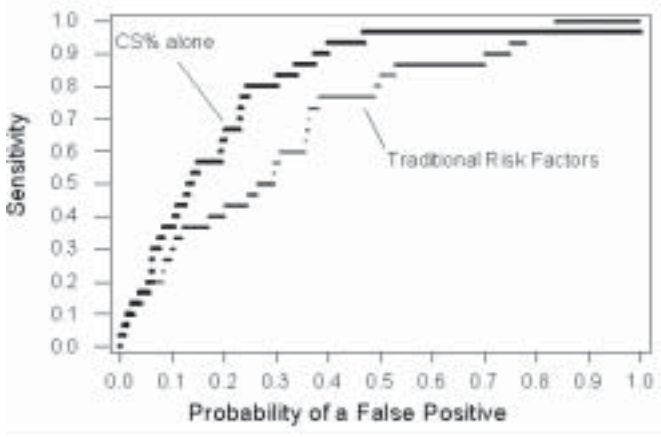

Figure 2. Receiver-operator-characteristics (ROC) curves to predict risk of hard events using traditional risk factors alone vs. calcium score percentiles (CS%) alone. The area under the curve of calcium score percentiles is statistically larger than the area under the risk-factors curve indicating a greater potential for event prediction.

minal disease, but it is most likely evidence of an accelerated atherosclerotic process with fresh and fragile plaques, prone to rupture, hidden behind small amounts of calcified disease. The second important finding in the study by Raggi et al was that the area under the ROC curve for prediction of a hard event became progressively larger as risk factors were added to age, and calcium score percentiles were added to age and risk factors.[12] This confirmed that coronary calcium added incremental prognostic information beyond that provided by simple chronological age and traditional factors.

Arad et al published two reports each involving over 1100 patients screened by EBT. They were followed for 19 months[14] and 36 months[15] respectively. These studies were criticized because of the enrollment of self-referred patients through calcium screening facilities and the reporting of a mixture of soft and hard events. Nonetheless, despite the diverse nature of the populations studied, the findings reported by Raggi et al[13] and by Arad et al[15] were comparable. In fact, the relative risk of events in the upper 2 quartiles of calcium scores ranged from 15 to 22 times that of patients in the lower quartiles. Again, in Arad's experience the area under the ROC curve for calcium scores was greater than that obtained employing risk factors alone. [14]

Finally, Wong et al followed 926 asymptomatic individuals for an average of 3.3 years after EBT screening for coronary calcium.[16] Patients in the upper 2 quartiles of calcium scores demonstrated 4.5- and 8.8-fold increases in the incidence of coronary events compared to those in the lowest quartile.

In all of the above-mentioned studies, very low calcium scores or absent coronary calcium predicted an extremely low risk of events (about 0.5% yearly). As a result of these publications, it is currently well accepted that absence of calcium on a screening EBT points to a very low risk of cardiovascular disease regardless of the presence of known risk factors.[9] Possible exceptions to this axiom are young heavy smokers. In these subjects, acute coronary syndromes may be precipitated by the formation of a thrombus over an area of endothelial erosion that does not necessarily contain an intimal calcified plaque. [13, 17-19]

The concept of coronary calcium as a marker of risk has found substantial opposition in the clinical and academic circles. Nonetheless, it is receiving increasing attention by those involved in the development of guidelines on risk reduction for atherosclerosis.[20] Indeed, it has been proposed that coronary calcium percentiles be applied to adjust, either increasing or decreasing it, the risk attributed to an individual on the basis of age. [20] This approach would then allow a physician to match the intensity of preventive efforts to the risk profile of the individual patient under consideration. Although research efforts should continue, these developments indicate that a better appreciation of the role and significance of coronary-calcium screening is developing.

EBT TO GUIDE MEDICAL THERAPY OF ATHEROSCLEROSIS

Another potentially useful application of EBT imaging is the monitoring of the effectiveness of therapy. Since atherosclerotic plaque calcification appears to be an active metabolic process resembling bone formation,[1-3] it seems reasonable to expect that such a process may be at least partially reversible through active catabolic pathways. A limited amount of research data support such expectation. Although it is not clear what stimuli initiate the plaque calcification process, oxidized lipids have been shown *in vitro* to induce osteoblastic transformation in vascular smooth muscle cells and to induce osteoclastic activities in bone cells in culture.[21-22] In addition, in experiments conducted in rhesus monkeys, statin therapy reduced the extent of calcification of atherosclerotic plaques previously induced by heavy cholesterol diets. [23]

Because calcification accompanies the development of new atherosclerotic disease, halting or reversing vascular calcification may be a useful indicator of the effectiveness of a selected therapy. In three studies, sequential EBT imaging was employed to follow the progression of coronary calcification in response to medical management of atherosclerosis. In a study by Callister et al, one year of aggressive treatment with statins (to a LDL level of <120mg/dl) caused a complete arrest of progression and even a minor reduction in coronary-calcium scores.[24] Withholding treatment or providing only moderately aggressive statin treatment (LDL>120 mg/dl) caused significant yearly progression of calcium scores of ~50% and 25% respectively.

In a study of 299 patients, sequential EBT scanning showed a range of annual calcium-score increases of 33% to 40% in untreated patients. In contrast, patients treated with statins displayed an average calcium score progression of 15% ($p<0.001$ for comparison with untreated patients).[25] More recently Achenbach et al[26] reported on 66 patients with coronary calcium on a screening EBT scan and a baseline LDL >130mg/dl. The subjects were not given any treatment, and a second EBT scan was performed after a follow-up of 14 months. During the ensuing year, treatment with cerivastatin 0.3mg/d was initiated, and a third and final scan was performed at the end of the follow-up period. There was a statistically significant difference in calcium score progression during the untreated period (25% median annual increase) compared to the treatment period (8.8% median annual increase). In 37 patients achieving LDL

levels <100 mg/dl with treatment the median calcium score change was –3.4% per year.

Ongoing trials will evaluate prospectively the role of EBT in assessing disease progression and the efficacy of different therapeutic modalities in halting or reversing atherosclerotic disease.[27] Obviously, the most compelling evidence of the utility of EBT as a method to assess disease progression will be provided by the demonstration that arresting arterial calcification lowers the risk of cardiovascular events, just as in the trials showing angiographic regression to be accompanied by lower risk.

CONCLUSIONS

Coronary artery-calcium screening is emerging as a useful tool to improve risk prediction for the individual patient and promises to become a helpful method to monitor noninvasively the effect of various therapies for atherosclerosis. Research must continue to confirm that coronary-calcium screening provides incremental prognostic value beyond traditional risk factors and to verify that this technology is cost-effective. Although some questions still remain, EBT stands poised to be integrated into regular clinical practice to improve existing deficiencies in the management of coronary artery disease.

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Descending Necrotizing Mediastinitis

Henry F. Tripp, MD; Kerry L. Paape, MD; and William H. St. Martin, MD

Descending necrotizing mediastinitis (DNM) is an infrequent clinical entity. DNM is the result of infection originating in the oropharyngeal regions and spreading along cervical fascial planes to cause mediastinal abscess and sepsis. Even with prompt recognition and treatment, the mortality and morbidity associated with DNM are appreciable. The opportunities for successful outcome are improved with liberal use of computed tomography, aggressive surgical therapy, and a multidisciplinary team approach. We report a case of DNM that illustrates how these principles were employed in the successful management of this rare and often fatal condition.

A 32-year-old man was transported from an offshore oil-drilling platform to the emergency department with fever and chills. The patient's complaints began 3 days before when he experienced an episode of epigastric distress followed by two episodes of retching. Subsequent to this he complained of a non-productive cough, pleuritic chest pain, and the onset of rigors, which caused him to seek medical attention. His past medical history was significant for hypertension, and his social history was notable for 15 pack-years of smoking and episodic binge drinking. On physical examination his blood pressure was 122/82 mmHg; his temperature was 101.9°F; his respiratory rate was 30/minute; and his heart rate was 110/minute. At the time of admission he had some tenderness in the right supraclavicular area and suprasternal notch. No neck masses, axillary, or cervical adenopathy were appreciated. At the time of admission his white blood cell count was 21,000/µL. An arterial blood gas sample revealed pH 7.49, PCO_2 25 mmHg, and PO_2 58 mmHg. Chest x-ray at the time of admission showed a linear infiltrate at the base of the right lung, and there was a prominent mediastinal shadow with an irregular contour above the right heart border. CT scan of the chest was performed revealing bilateral pleural effusions, greater on the left, and bibasilar atelectasis. There was evidence of mediastinal inflammation with diffuse edema involving the mediastinal fat and a small fluid collection in the right superior mediastinum (Figure 1). He was started on triple antibiotic coverage to include clindamycin, gentamicin, and piperacillin/tazobactam, as well as fluconazole prophylaxis. On the evening of admission he developed respiratory distress requiring intubation. Placement of a left chest tube revealed purulent fluid, raising concerns about esophageal perforation.

Esophagogastroscopy revealed a Mallory-Weiss tear of the gastroesophageal junction. Because of the history of retching, CT evidence of mediastinitis, and an abnormal esophagoscopy, plans were made for exploration of the left hemithorax. A left posterolateral thoracotomy revealed necrotic tissue and an abscess within the mediastinum. The esophagus was mobilized from the level of the gastroesophageal junction to the inferior pulmonary vein and was totally normal without evidence of induration or perforation. Large bore drains were placed in the mediastinal abscess. At the time of intubation there was noted to be asymmetry of the tonsillar pillars, and postoperatively a CT scan of

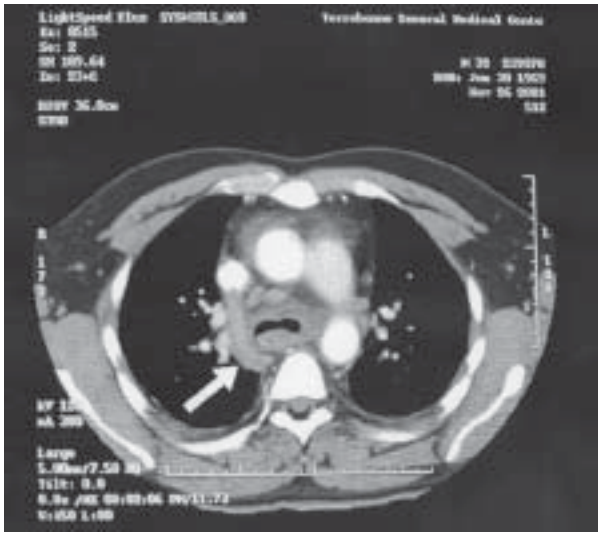

Figure 1. Contrast-enhanced CT scan of the chest at the level of the carina showing mediastinal edema (arrow).

the neck showed a right peritonsillar abscess with communication into the neck (Figure 2). The right peritonsillar abscess was incised and drained. Through a separate incision the carotid sheath was debrided and irrigated. A right-sided mediastinotomy through an anterior incision also was performed with drainage and irrigation of the mediastinal abscess. Over the next 24 hours the patient remained febrile and septic; another CT scan revealed fluid in the left paratracheal region and aortopulmonary window. Left mediastinotomy allowed debridement and drainage of this area, along with re-exploration of his neck incision. Previous cultures revealed Group C streptococcus and Fusobacterium *necrophorum*. His antibiotic therapy was modified, and parenteral nutrition was begun. Although he had developed adult respiratory distress syndrome (ARDS), his ventilator requirements stabilized, and his septic course subsided somewhat. However, 72 hours later he needed increased fluid, required multiple pressor agents and inotropes for hemodynamic support, and showed signs of multiple-organ failure.

Repeat imaging studies, including CT scan and echocardiography, revealed a large pericardial effusion (Figure 3). He underwent subxiphoid pericardial drainage, tracheostomy, and further debridement and drainage of his right neck and mediastinotomy incisions. Although he improved hemodynamically, fever and leucocytosis persisted, and repeat CT scan the following day showed further fluid in the right posterior mediastinum. Right posterolateral thoracotomy allowed drainage of the right paratracheal region. His condition gradually improved over the ensuing 6 days, and he required only one additional procedure, re-exploration of the neck abscess, during that time. Nearly 4 weeks after admission he was weaned from the ventilator and made rapid progress. He was discharged home within 2 weeks and has been doing well at subsequent follow-up.

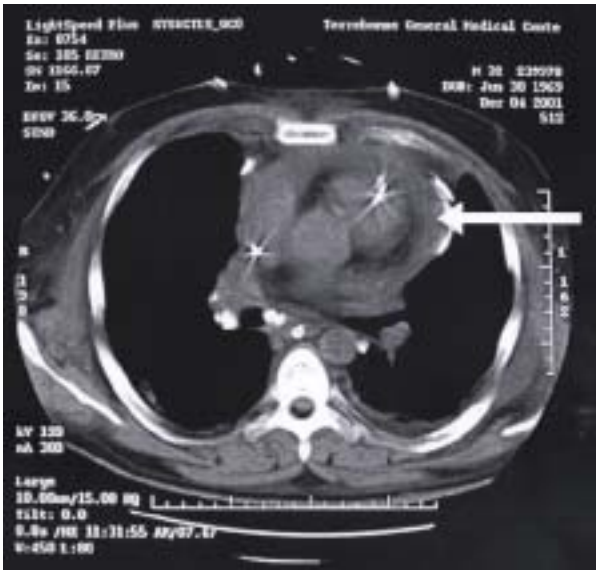

Figure 3. CT scan of the chest taken on hospital day 7. The level of the scan is just distal to the tracheal bifurcation, and a large pericardial fluid collection is seen (arrow).

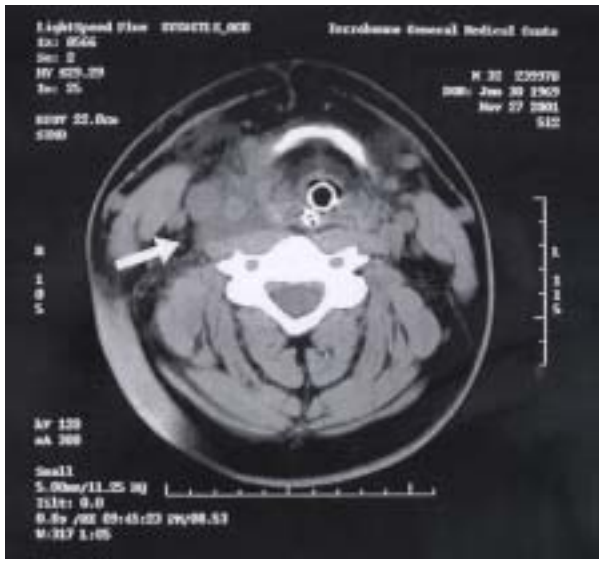

Figure 2. CT scan of the cervical region. Note the shift of the endotracheal tube to the left and the presence of fluid surrounding the right carotid artery and jugular vein (arrow).

DISCUSSION

Mediastinitis may result from complications of cardiac surgery, esophageal perforation, or ,more uncommonly, from infections arising in the oropharynx and spreading along cervical fascial plains into the mediastinum.[1,2] The latter mechanism is termed descending necrotizing mediastinitis (DNM) and presents a septic picture with symptoms referable to the source of the infection and to the chest. The diagnostic criteria for DNM were defined nearly 20 years ago and include 1) clinical evidence of severe oropharyngeal infection, 2) characteristic roentgenographic features of mediastinitis, 3) documentation of necrotizing mediastinal infection at operation or necropsy (or both), 4) and establishment of the relationship between DNM and the oropharyngeal infection.[7] The patient presented met all of these criteria.

The inciting infection in DNM most often is dental in origin, although peritonsillar abscess (as in the case presented), retropharyngeal abscess, parotitis, cervical lymphadenitis, and trauma may all lead to this syndrome.[3,4] As in the case presentation, men in their third or fourth decades appear to be the patients most commonly affected, and the majority have been previously healthy.[3,5] A variety of aerobic and anaerobic organisms have been isolated in cases of DNM, consistent with the oropharyngeal origin of the inciting infection.[3] In the

case presented, Fusobacterium *necrophorum* was a primary isolate. This anaerobic, gram-negative bacillus, found in large numbers in the human mouth, produces several lytic toxins and has undergone increased recognition recently as a potential cause of necrotizing soft-tissue infections.[3,6] Clindamycin was continued in the antibiotic regimen because of its potential ability to halt toxin production.[9] The routes of spread of DNM are well defined and include the pretracheal planes anteriorly, the lateral pharyngeal planes in the mid-neck, and the retropharyngeal-retrovisceral planes posteriorly.[3] In our patient, the route of spread occurred through the carotid sheath. The carotid or perivascular space serves very infrequently as the route of spread for DNM infections, and has been given the eponym the Lincoln Highway after the east-west highway of the same name. [2,8]

Prompt diagnosis of DNM is necessary to initiate definitive therapy. Computed tomography has proven invaluable in establishing the diagnosis of DNM and should be considered the diagnostic test of choice when DNM is suspected.[2, 4-5] Empiric coverage with broad-spectrum antibiotics should be initiated as soon as the diagnosis is suspected and modified as appropriate culture and sensitivity data dictate. As with other necrotizing soft-tissue infections, early and aggressive surgical drainage and debridement are essential. [2-6] In one of the largest single-center series of DNM, Freeman et al collected data on 10 patients who were managed at their institution with liberal and frequent use of CT scanning and frequent, aggressive surgical therapy.[5] They compared this group with a historical cohort of 96 reported patients taken from a thirty-year period in the English-language literature. The historical group had mortality rates of 25% to 40%, depending on the decade the patients were reported. In the patients treated at their institution there were no deaths (p=0.05). They attributed this difference to their increased use of CT scanning (a mean of 6 +/- 4 scans per patient) and surgical interventions (transcervical procedures, mean of 4 +/- 1 per patient; transthoracic procedures, mean of 2 +/- 1 per patient), compared to the historical controls (CT scans, mean 2 +/- 1 per patient, p=0.02; transcervical procedures, mean 2 +/- 1 per patient, p=0.0001; transthoracic procedures, mean 0.7 +/- 0.3 per patient, p=0.003). They recommended CT scanning be performed as the initial diagnostic procedure, for any evidence of clinical deterioration, and empirically as surveillance studies at 48 to 72 hours after any operative drainage or debridement, and that surgical explorations be performed for any accumulations of fluid or air and after identification of an abscess in the neck, chest, or abdomen. We adopted this philosophy in the management of the patient presented, who underwent a total of five CT scans and nine surgical procedures (four transcervical and five transthoracic).

In addition to aggressive use of CT scanning and operative debridement, Freeman et al, champion a multispecialty approach to these very ill patients.[5] In addition to thoracic surgery, we enlisted consultants from otolaryngology, pulmonology, oral and maxillofacial surgery, as well as an infectious disease specialist, all of whom provided valuable insight and expertise allowing a successful outcome in the patient presented. It is only through the meaningful contributions of all team members that the best chance for a successful outcome in DNM may be realized.

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Pick Up from Sept/October 2002 Page 229

Argent Financial Group “Navigators”

Hospital Ethics Committees: Formation, Function, and Case Consultation

Thomas P. Gonsoulin, MD, MPS and Janis M. Taube, MSc

The objective of this paper is to present the concept of hospital ethics committees (HEC) with the hope of expanding awareness, knowledge, and use of such entities. HECs typically serve three functions—education, development of hospital policy, and ethical case consultation. In the last role, HECs aim to assist healthcare professionals and their patients achieve mutually acceptable decisions when dilemmas about care arise. The theory and practical methodology used by an HEC when processing a case are detailed. It is expected that a greater awareness of the functions and construction of an HEC will expand use of this service by health professionals and ultimately enhance patient care.

The first recorded recommendation for establishment of Hospital Ethics Committees (HECs) came from pediatrician Karen Teel in 1975 as a response to the "Johns Hopkins baby."[1] The latter was a Down's syndrome baby at the Johns Hopkins Medical School whose parents refused to consent to a surgical procedure that would have saved the life of the newborn. Stimulated in part by Dr. Teel's recommendation, the New Jersey Supreme Court endorsed the concept of ethics committees in their 1976 decision on the Karen Quinlan case.[1,2] Further impetus was provided by the President's Commission for the Study of Ethical Problems in Medicine and Biomedical and Behavioral Research in Appendix F of their report in 1983.[2] A model of the function and composition of HECs was included which was prepared for the American Society of Law and Medicine. Starting with the Quinlan case, judicial determinations regarding "right to die" have proliferated and have been a source of legal influence on HEC deliberations.[3] Today HECs typically have a multidisciplinary membership who aim to provide a formal forum for all parties involved to discuss ethical issues and explore options in cases requiring critical decision making. Many of these cases still center on end of life issues, and often focus on advanced directives (or lack of), pain management, and how to define "futile treatment." Cases typically emerge from patients' families having divided opinions over how much care to give terminally ill patients.

The number of hospitals with ethics committees and the number of consultations per committee have grown over the last two decades. In 1980 only 1% of hospitals in the United States had an ethics committee; by 1988 over 60% of large hospitals had formed a functional HEC.[4] In Louisiana, as of October 2000, approximately 60% of hospitals had some type of ethics committee (unpublished personal survey, TPG). Today five major hospitals in the New Orleans area alone have an active HEC. The reasons for this expansion are multifactorial and are thought to include recognition of the utility of an HEC by healthcare providers, increased awareness of the plurality of patient values, and conflicts engendered by the current economic climate in healthcare. Additionally, the Joint Commission of Accreditation of Healthcare Organizations began to require the existence of a specified process for dealing with ethical issues in accredited hospitals in the early 1990s.[4,5,6] For these same reasons, it can also be safely anticipated that the number of HECs in Louisiana and the USA as a whole will continue to grow and extend into urban, suburban, and rural settings. We present here an overview of the functions, construction, and principles of HECs, including how an ethical case is processed, with the hope of continuing to further awareness and use of an expanding service available to Louisiana health professionals.

COMPOSITION

While varying opinions exist about HEC composition, some generally accepted positions have emerged.[7,8] Most committees are multidisciplinary and are composed of physicians, nurses, hospital administrators, social workers, clergy, an attorney, and ideally someone with professional training in medical ethics. The inclusion of an attorney has created some debate par-

ticularly over whether a hospital attorney, whose major interest will be risk management, should be a member. Hospital board members and outside community representatives may also be included. Sexton and Thigpen[6] recommend that the composition of an HEC should reflect the diversity of cultures, socioeconomic status, and public opinion that exist in the community served by the institution.

FUNCTIONS

Three roles for the HEC have generally been recognized: education, policy development, and case consultation.[8-11]

Education

HECs have recognized roles in the education of healthcare professionals. The HEC must first ensure that its own members are current in bioethics and health law in order to provide high quality consultations. When an ethics committee is formed in a hospital, education of the committee members is the initial step. Ideally one or two years of training occurs before a new HEC begins case consultations.[4] The educational function of an HEC logically extends to the hospital staff, including physicians, nurses, and other personnel. Extension of educational opportunities to patients, families, and the general community is another appropriate role. Lectures, seminars, and in-service workshops are useful educational modalities. In teaching institutions, grand rounds is particularly useful for physicians in training.

Policy Development

The policy development of an HEC will vary with the institution. Certain issues, such as forgoing medical treatment including ventilators and artificial nutrition and hydration, brain-death definition, advanced directives, and do not resuscitate protocols all lend themselves to significant input from an HEC in the formulation of hospital policy. Similar to case consultations, the policy recommendations are advisory and not mandatory. Final approval of policy recommendations typically rest with the hospital's governing body. HECs lack administrative power but ideally, if functioning well, possess considerable moral power within the institution. Furthermore, as policy in critical care areas is established, the need for case consultation should decline, and the HEC can shift its focus to the continued education of the involved healthcare personnel. In the ever changing and expanding medical world, new ethical dilemmas will arise to create new challenges.

Case Consultation

There are different models for case consultation by an HEC. Case consultation can be performed by the entire HEC, by a small team of committee members, or by an individual who reports to the whole committee. Trade-offs exist between the diversity and range of perspectives offered by a group and the more timely reviews and recommendations provided by a smaller subcommittee or an individual. At Tulane, we use the subcommittee approach with two groups rotating monthly with the aim of providing a prompt response that reflects diverse viewpoints. Excluding the consultant model, case review typically includes the involved physicians, nurses, patient and/or family, subcommittee members, plus other support personnel as deemed appropriate. Case consultations often open up communication between interested parties plus lay out options and ethical preferences. Typically the attending physician presents a case summary and all of the interested parties are asked for input. The committee then discusses the case openly with one member finally summarizing the case; consensus is then sought among the group.[9-11] In the United States, the committee ethical opinions generated are typically advisory and not mandatory.

HOW HECS PERFORM AN ETHICS CONSULTATION

HECs involved in ethics consultations should have a policy and procedures statement that includes: who can request a consultation, how the HEC is contacted, who responds to the request, how the consultation is conducted, who is to be included in the consultation, standardized methods for documentation, notification of affected persons, and protection of patient confidentiality.

Request for Ethics Consultation

Cases submitted to the HEC for consultation often require attention to both philosophical and interpersonal conflict. Reiter-Theil[12] identified four major categories of problems most often addressed by HECs: 1) conflict between ethical principles, such as what constitutes futile treatment at the end of life, 2) uncertainty as to the patient's wishes or best interests, 3) dissent between involved parties, and 4) dilemmas with non-compliant patients who may be perceived as being at risk of self-harm. Such issues have the potential to provoke ethical and interpersonal consternation amongst any of the involved parties. As a result, HECs typically allow anyone with a stake in the case to initiate a consult, including nursing staff, social workers, patients, and/or family members and hospital department heads. In practice, however, most case consultations are requested by the attending physician.

Contacting the HEC and Who Responds to the Request

The person initiating the ethics consultation is typically required to submit a written request to a central office, such as medial staff affairs. HECs usually have one member who is designated as the receiving entity for these consultation requests. This member will often screen the request for appropriateness, ensuring that some type of ethically related issue is being raised. Depending on the situation, a phone call may address the needs adequately.

A form is provided for the attending physician to complete which provides the patient's diagnosis, prognosis, and treatment options, as well as the ethical question being asked. At Tulane, after receipt of this information, our on-call team meets for the consultation at a time and place worked out by the central contact person.

Case Consultation

The consultation team interviews the attending physician, resident, patient and/or family, nursing staff, social workers, and any other appropriately interested parties in an attempt to identify pertinent issues and foster open communication. Some committees include the patient and/or family at the consultation; others review the findings with them later. Initially the clinical information is expanded. The natural history of each major disease process is reviewed and the probabilities of success of the varied treatment options are explored. Will they be effective and of benefit to the patient? Will the treatment options be physically, emotionally, fiscally burdensome? Further questions of special relevance are asked. Is the patient terminal? In the persistent vegetative state? Respirator dependent? Artificial hydration and nutrition dependent? Competent? If incompetent is there a morally and/or legally valid surrogate? The team works to identify the ethical issues and questions, aiming to separate these issues from other concerns such as treatment options and legal questions. The relevant persons and institutions are identified. An attempt is made to discover the attitudes, background, personal dynamics, values, and motivations of those involved. Are there conflicts among the decision makers? What is the patient's moral/religious heritage? Besides the patient, does anyone benefit personally from a particular decision? Who gets to make what decisions?

The initial analysis usually stems from the perspective of common morality, the wisdom of a culture's moral heritage. Here narratives of common heritage, religious codes, and professional codes play a role. In fact, some would use the narrative approach to frame the case deliberation.[5] Common experience and previous similar situations also contribute to the discussion. The four universal ethical principles of autonomy, beneficence, nonmalefeasance, and justice, so well discussed by Beauchamp and Childress in their text,[13] can be used by the committee to orient the ethical discussion. Autonomy refers to the principle by which persons are free to determine their own destiny, including healthcare decisions. Informed consent is a key component. Has the patient and/or family been adequately informed of the disease conditions and treatment options? Is the patient's right to choose being honored? Beneficence provides the primary goal and rationale of medical healthcare. It includes all forms of medical intervention and practice designed to benefit patients. Have the physician's recommendations and concerns been expressed and respected properly? Has the benefit/burden ratio of treatments been delineated? What are the obligations of the health professionals? Are there conflicts between principles, between obligations? How can they be resolved? As these questions and issues are sifted through, the consulting team tries to establish an atmosphere of trust and confidentiality. The consultation team works through all of these considerations and attempts to arrive at an ethically sound option(s) for the patient. It then seeks consensus among all of the involved parties.

An alternative methodology for case consultation is that of casuistry, as promulgated by Jonsen, Siegler, and Winslade.[14] Case analysis proceeds from four topics: medical indications, patient preferences, quality of life, and contextual features. Again the goal is to provide prudent counsel to healthcare professionals and their patients, striving for consensus in action.

Submitting Advice

When the deliberations have ended, the HEC reports its recommendations to the party who initiated the consultation, either through a note in the chart, a letter from the committee chair, or a verbal report. At Tulane, we aim to provide both the attending physician and family with a written consultation in a timely fashion, generally within 48 hours. The report typically includes documentation of the decisional process, available options, and the ethical reasons both for and against the decision of the ethics subcommittee. Lastly all consultations are included in the HEC records, and a summary of the consultation is documented in the patient's chart. The extent and format of the information written into the medical record may vary depending on local hospital requirements and regulations. At Tulane each subcommittee case consultation is then discussed at the monthly full committee meeting.

FUTURE OF HECS

The role that an HEC plays in a hospital depends not only on the climate of the institution but also on the age of the committee. New committees focus initially on education of its members, then of the hospital physicians and staff. As HECs mature, policies and procedures are instituted which are then reviewed periodically. When developed policies and procedures are in place, some ethical dilemmas can be anticipated and solved at the onset. It can be anticipated that advancements in technology will present new challenges and mandate continual review of policies. Is email an acceptable forum for ethics consultation? At least one institution utilizes that format for this purpose.[15] Does a new device influence policy on life-sustaining treatment and end of life issues? Once policies and procedures are instated, a main function of the HEC will be to educate hospital personnel. As a result, the demand for case consultation may diminish.

For those HECs involved in case consultation, the quality of a consultation depends on "the ability to provide a forum for open discussion of medical, moral and legal issues surrounding a difficult situation."[16] More concretely, we often attempt to evaluate services within a single HEC by asking questions such as: has confidentiality been addressed and maintained? Do the stakeholders have access to the process? Is the process being utilized? If not, why not? Has the availability, policies, and procedures of case review been adequately publicized to appropriate personnel, including patients and parents or guardians? Is there a lack of confidence in the process of case review by possible stakeholders such as physicians?

There is currently a movement to institute universal quality control measures that allow for the monitoring of outcomes, including impact on patient care, physician satisfaction, ability to affect institutional change, impact on healthcare costs, as well as the competence and methodology of providers of services.[5,12] This may allow for comparison between different HECs. Ethics consultations do not render themselves easily for appraisal. The individual ethical issues of each case that make it difficult to resolve also make it difficult to evaluate and, furthermore, to compare to other cases. As Charon and Montello note, "the endpoints are not 'clean', the desired outcomes are not identical across populations, and the ills being treated are hard to compare...More vexingly, the goals of ethics practices vary widely from case to case, except at the most abstract level of, say, preserving autonomy or supporting beneficence."[17]

Because of the uniqueness of each case addressed, it is difficult to compare cases within one HEC, and even harder to identify broad themes across HECs. However, one theme that most HECs deal with often is end-of-life, and this may lend itself to being the first step for cross-case and cross-HEC scrutiny. For example, if end-of-life issues are further categorized into neonatology, oncology, and intensive care and are documented, this categorization may aid in the sharing and evaluation of treatment at the end of life between different HECs.

As discussed, one well recognized current role of an HEC is to improve communication between patients and healthcare professionals, with the aim of improving patient care. Whenever problems are identified, addressing them becomes a priority, not only on a case by case basis, but certainly at the level of hospital policy. In the future, the comparison of cases across HECs has the potential to have a greater impact on clinical decision making, perhaps even at the level of state or national health policy. At a local level, the formation of a consortium of HECs to share common problems and to seek a common vision could benefit their respective institutions.

CONCLUSION

The number of hospital ethics committees in existence has grown substantially over the last 25 years. During this time HECs have evolved to serve the three major roles of education, policy development, and case consultation. They will no doubt continue to evolve as future challenges such as new diagnostic and therapeutic challenges present themselves. Physicians are encouraged to familiarize themselves with the services of their local HEC and to participate actively in the process. When all or some of these services are absent in a physician's local hospital, the development of an HEC or expansion of the capabilities of a pre-existing HEC are encouraged.

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A Call to Leadership

Donald J. Palmisano, MD, JD

Editor's Note: **Dr. Palmisano served as President of the Louisiana State Medical Society in 1984-1985. He has served as American Medical Association (AMA) Trustee since 1996, and in 2002 was elected President-Elect of the AMA. Dr. Palmisano gave the following campaign speech at the AMA's Annual Meeting in Chicago on June 15, 2002.**

Friends, Delegates, Leaders,

It has been an honor to serve as a Trustee for our great organization and for all of you for the past six years. Thank you.

Our AMA has three important challenges.

First, we must correct the impediments in our current healthcare system so that there are no threats to the patient-physician relationship and patient access to medical care. Danger is upon us and danger invites rescue. Rescue must fix the out-of-control tort system, the price controls that prevent physicians from privately contracting with patients, the oppressive costly unfunded mandates, and more. These threaten the economic viability of a practice. We need serious debate in Congress about changing the framework of health insurance: Let our vision of individual ownership of insurance policies, defined contribution, and a way to make it happen with refundable tax credits enter the contest of ideas. Rights and responsibility go hand-in-hand. We need to protect ethical science-based Medicine. Let's set priorities and **focus**!

Second, the House of Medicine needs to speak with one voice. Yes, let's foster diversity of opinion, fair debate, and conclusions based on the facts. But once our decision is reached, let's go forth *united*. Just like the motto on our American currency: E Pluribus Unum – Out of many, one. Just like the gladiators in the Coliseum, as portrayed in the movie *Gladiator*, we need to stay together for any chance of survival. Good advice then and good advice now.

Third, we need to deal with the naysayers and critics who decry our efforts to protect and improve the greatness of American Medicine. These naysayers would shackle our freedoms and the liberty won by the courage and blood of the patriots who gave birth to this great Land of Liberty we call America. Let's cut the chains that inhibit innovation and quality care. Let's offer hope to future generations of healers and patients. A leader without hope ceases to be a leader. To do less dishonors our founding patriots as well as those who continue to defend our cherished heritage; and it would bring shame on us! We will be told it can't be done. We will be told all is lost.

Bold leadership challenges those assumptions and lights the path of achievement. Leadership is not giving up! A leader doesn't get discouraged but rather treats adversity as an opportunity to formulate a creative solution. The ultimate victory is all the sweeter.

We won't be intimidated by the naysayers who say it can't be done because history often proves they don't know what they are talking about.

Keep in mind these comments by naysayers: *"Man will never reach the moon regardless of all future scientific advances,"* Dr. Lee De Forest, inventor of the Audion tube and a father of radio. And he said that in 1967, two years before American Neil Armstrong stepped on the moon.

"Everything that can be invented has been invented." Charles H. Duell, U.S. Commissioner of Patents, 1899.

"Who the hell wants to hear actors talk?" Harry M. Warner, Warner Brothers, 1927.

And let me give you one more:

"There is absolutely no way this tort reform bill will ever pass the Louisiana Legislature. Labor is against it, the trial lawyers are against it, and I am against it." So said the Insurance Commissioner of Louisiana addressing me in 1975. And the validity of that statement? Despite the additional comments by some defense and plaintiff lawyers that the cap was unconstitutional, the bill passed and became Louisiana Act 817 of 1975. The Louisiana State Supreme Court subsequently ruled it constitutional and the United States Supreme Court said there was no federal question.

I say, "Phooey on naysayers". Well, you get the picture.

The point is, the skeptic often is wrong, and we can

prove them wrong by following the advice my dad always gave me: *Do your homework, have courage, and don't give up.* If we do this, nothing is impossible!

So I say, " Onward!" We can do it! Let our dreams echo through the corridors of time. Let our actions move us confidently in the direction of our shared vision. That is leadership!

It is worth repeating what Shakespeare wrote in *Julius Caesar*.

> There is a tide in the affairs of men,
> Which, taken at the flood, leads on to fortune;
> Omitted, all the voyage of their life
> Is bound in shallows and in miseries.
> On such a full sea are we now afloat,
> We must take the current when it serves,
> Or lose our ventures.

So let us be a "band of brothers" (and sisters, I would add!), as Shakespeare also advised in *Henry V*, and enter the field of battle together.

Yes, the tide is here in Congress and in American Medicine. We need to take the current to success…

And those that help and those that don't need only reflect on Shakespeare again.

You know me. I don't have all of the answers. But I have learned to listen and communicate, and I will work tirelessly with you and for you to reach our goals.

I thank you for the privilege to serve as a Trustee. Now I respectfully request your support and help for President-Elect. I stand ready to enter the arena as your representative.

Carpe Diem! Seize the day! Seize the future! Control your destiny!

And God bless America, the AMA, and each and every one of you!

Donald J. Palmisano, MD, JD is a Clinical Professor of Surgery and a Clinical Professor of Medical Jurisprudence at Tulane University School of Medicine in New Orleans, Louisiana.

Driving to the ER at Age Sixty-six

Ed Spudis, MD

Three AM for 100 degrees--
a privilege at age sixty-six?
So, where's the
interventional internist?
~No rash but a stiff neck. What
the tick said to *burgdorfi*?
~Did I earn these privileges quoting
the three W's--Wallenburg,
Waardenberg, and
Warten...something?
~Bond funds are less risky
and uncallable. HMOs are
crashing.
Hard rain.
~No tPA if he's slept 5 hours, 4?
~Clever clues from his shoe soles?
There's a McDonalds still
open. Later. And the First
comment to the med student
has to begin with,
"Like, you know..."

CALENDAR

January 2003

22-23 National Health Policy Conference
JW Marriott
Washington, DC Contact:202.292.6700.

February 2003

5-9 The American Academy of Orthopaedic Surgeons 70th Annual Meeting
Morial Convention Center
New Orleans, La. Contact: 847.823.7186

14 LSMS 125th Anniversary Dinner
Ritz Carlton
New Orleans, La. Contact: 800.375.9508

15 LSMS Leadership Conference
Ritz Carlton
Baton Rouge, La. Contact: 800.375.9508

LSMS MEETINGS

January 2003

1 New Year's Holiday
LSMS Offices Closed

7 Membership Committee Teleconference
5:00PM

11 Continuing Medical Education Committee Meeting
10:00AM

February 2003

No Events Currently Scheduled.

(Unless indicated otherwise, all meetings are held at the LSMS Headquarters.)

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Please let us know what you think about your *Journal of the Louisiana State Medical Society*. Answer the following questions and **fax your answers to 225.763.2332** by January 15, 2003. For more information, contact Jennifer P. Smith at 225.763.2308.

1. Of every 6 issues of the *Journal of the Louisiana State Medical Society (Journal)*, how many do you read or look through?

- ❑ 6 of 6 issues
- ❑ 5 of 6 issues
- ❑ 4 of 6 issues
- ❑ 3 of 6 issues
- ❑ 2 of 6 issues
- ❑ 1 of 6 issues
- ❑ 0 of 6 issues

2. Please select the one phrase which best describes how you read or look through an average issue of the *Journal*.

- ❑ Read cover to cover
- ❑ Read articles of interest and look through the rest
- ❑ Read table of contents and articles of interest only
- ❑ Skim or look through quickly

3. Do you want to continue/discontinue your subscription to the *Journal*?

❑ Continue ❑ Discontinue Name _____

4. What is your reading time for an average issue?

_____ minutes

5. The *Journal* is comprised of different types of articles. Please indicate your *usual* reading level for each type listed below:

	Always Read All	Read Some	Never Read
Case of the Month Articles (eg, ECG, Radiology, Cardiology, etc)	❑	❑	❑
CME Articles	❑	❑	❑
Feature Articles (Not CME)	❑	❑	❑
Advertisements	❑	❑	❑
Editorials (eg, President's Message, Editor's Editorial)	❑	❑	❑
Calendar of Events	❑	❑	❑

7. On a scale of 1 (low) to 5 (high), to what degree does the cover design influence your reading of a given issue of the *Journal*? (Please circle one.)

Low 1 2 3 4 5 High

8. How do you rate the majority of the scientific articles published in the *Journal*?

- ❑ Excellent
- ❑ Above Average
- ❑ Average
- ❑ Below Average
- ❑ Poor
- ❑ No comment

9. Regarding scientific articles, what subjects would you like to see included in the *Journal*?

_____

10. How do you rate the majority of the socioeconomic articles published in the *Journal*?

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- ❑ Average
- ❑ Below Average
- ❑ Poor
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_____

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13. Rank the overall content and appearance of the *Journal*.

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Good	❑	❑
Fair	❑	❑
Poor	❑	❑

14. Do you save the *Journal* for future reference?

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❑ Yes ❑ No

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- ❑ Yes, I prefer the information combined in one monthly publication.
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18. Please check your age group.

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19. Please feel free to provide comments or suggestion on the *Journal* in the space below.

Thank you for your thoughts and time. Please fax to 225.763.2332 by January 15, 2003.

Journal of the Louisiana State Medical Society
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To earn CME credit, read the articles on page 292 and 296 and answer the questions. Please mark your answers to the questions at the bottom of this page. Fill out the registration form (please print legibly or type) and mail or fax to the LSMS Educational and Research Foundation, 6767 Perkins Road, Suite 100, Baton Rouge, Louisiana, 70808; fax **225.763.2333**. To receive CME credit, forms must be postmarked or faxed no later than **December 31, 2003**. *Journal* CME activities are included in LSMS membership benefits. (Non-LSMS members must include a check in the amount of $25.00 per credit hour payable to LSMS Educational and Research Foundation.) Participants must attain a score of 75% to receive CME credit. A letter verifying your credit will be mailed to you within 30 days of receipt. For questions, contact the ERF at 225.763.8500.

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		Clinical Case					Cardiology Report				
		Strongly Agree				Strongly Disagree	Strongly Agree				Strongly Disagree
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a)	The content meets the stated learning objectives.	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
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	Clinical Case		Cardiology Report	
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Suggested topics: _____

Please mark your answers to the December 2002 CME questions below.

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2) True False
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4) a b c d e

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1) True False
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4) a b c d

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AUTHOR INDEX

I

J

K

L

M

N

O

P

S

T

V

W

Y

Z

SUBJECT INDEX

D

E

F

G

H

I

L

M

N

O

P

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