murmur, clinical evidence suggesting recurrent arterial embolization, absence of signs of infection, and negative blood cultures. Other clinical clues include the presence of a coagulopathy and right heart catheterization.

Echocardiography is a powerful tool which is able to assist in the antemortem diagnosis of the condition. Estevez and Corya described the serial M-mode echocardiographic features of NBTE of the mitral valve in a patient in whom the diagnosis was confirmed at surgery. Siegel et al. reported on a patient in whom two-dimensional echocardiography demonstrated the presence of a cluster of freely mobile vegetations associated with the tricuspid valve. Although they had strong circumstantial evidence that these lesions represented NBTE, there was no direct autopsy proof.

Our study is unique in that it is the first report of the two-dimensional echocardiographic features of NBTE with direct autopsy validation. The microscopic hallmark of these lesions is the absence of an inflammatory cell response, thus distinguishing these lesions from those accompanying acute and subacute bacterial endocarditis. The specific features on two-dimensional echocardiography which were seen were a well-defined diffuse thickening of the valve cusps with additional localized nodularity and the absence of significant limitation of cusp opening. The other conditions which can cause this picture include valvular degeneration with or without associated calcium deposition, and cardiac amyloidosis. By contrast, the vegetations of infective endocarditis typically appear "shaggy" and ill-defined, may be mobile, may be massive, and may be associated with evidence of destruction of the valve.

Increased awareness of the clinical importance of NBTE, together with a knowledge of the clinical settings in which the disease occurs and the appropriate use of echocardiography, particularly the spatially oriented two-dimensional technique, should permit more frequent diagnoses of the condition during life. This will open the way for studies directed at determining the pathogenesis of the process, and ultimately, effective therapeutic measures.

ACKNOWLEDGMENTS: We gratefully acknowledge the assistance of Suzanne Ellis and Linda Inman.

REFERENCES


Intracardiac Sarcoma Diagnosed by Left Ventricular Endomyocardial Biopsy*

Frederick H. Hausheer, M.S., M.D.; Richard A. Josephson, M.S., M.D.; Louise B. Crochou, M.D.; David Weisman, M.D.; Jeffrey A. Brinker, M.D., and Harlan F. Weisman, M.D.

Endomyocardial biopsy often provides information useful in the diagnosis and management of various myocardial diseases. Typical clinical situations include assessment of cardiac transplant rejection, anthracycline cardiotoxicity, and myocarditis. Seldom does a biopsy yield an unequivocal diagnosis. We present a case of high grade (undifferentiated) primary cardiac sarcoma diagnosed via percutaneous left ventricular endomyocardial biopsy which illustrates several advantages of this technique.

CASE REPORT

The patient was a 45-year-old white man in excellent health until ten months prior to admission when he was found to have stage IIIA nodular sclerosing Hodgkin's disease. He completed a subsequent course of mantle and periortic radiation therapy without complications. The cardiac structures were shielded below the level of the mitral valve. He was in clinical remission following completion of radiation therapy until the day of admission, when he presented with features of cardiac tamponade following a syncopal episode. Admission physical examination results were significant for pulsus paradoxus of 20 mm Hg, Kussmaul's sign, and a mid-diastolic high-pitched sound compatible with a mitral valve opening snap. A large pericardial effusion and a mass involving the left atrium, posterior mitral valve leaflet, and left ventricular free wall (Fig 1) were observed on initial echocardiographic evaluation. Echocardiographic features were considered to be most consistent with neoplastic process, and atypical for myxoma, thrombus, or vegetation. Possible etiologies of the intracardiac abnormality included recurrent Hodgkin's disease, non-Hodgkin's lymphoma, sarcoma, marantic endocarditis, or (fastidious) culture-negative endocarditis.

Pericardiocentesis was performed with subsequent catheter drainage yielding 650 ml of exudative bloody pericardial fluid. Pericardial fluid cytology study results were negative for malignant cells.

*From the Department of Medical Oncology, The Johns Hopkins Oncology Center, and the Division of Cardiology, Department of Medicine, The Johns Hopkins Medical Institutions, Baltimore.
†American Cancer Society Regular Clinical Fellow.
‡Medical Staff Fellow, National Institute of Aging, National Institutes of Health.
Reprint requests: Dr. Hausheer, Medical Oncology, Johns Hopkins Hospital, Baltimore 21205
cells. Hemodynamic status stabilized following the procedure. Diagnostic thoracocentesis with pleural biopsy, bone marrow aspirate and biopsy, and computerized tomographic examination of the chest, abdomen, and pelvis were negative for malignancy or infection.

Left and right cardiac catheterization and selective coronary arteriography revealed pericardial constrict; insig; significant mitral stenosis, significant mitral regurgitation, and neovascularization originating from both the left circumflex and right coronary arteries in the basal region of the left ventricle, corresponding to the mass lesion seen on echocardiography (Fig 2). Due to the uncertain histologic nature of the mass, percutaneous catheter-guided biopsy of the left ventricular free wall was performed. A high grade (undifferentiated) spindle cell sarcoma was documented by histopathologic studies from the left endomycocardial biopsy specimen (Fig 3).

Discussion

This patient's presentation and course raised several difficult issues. An atypically located primary cardiac tumor was considered, though it was believed to be too early for radiation-induced primary sarcoma or non-Hodgkin's lymphoma. Since the cardiac structures had been relatively spared from irradiation, consideration was given to the unusual possibility of "marginal miss" intracardiac recurrence of Hodgkin's disease. A tissue diagnosis was needed to formulate an optimal treatment approach. After completion of an extensive evaluation, left ventricular endomycocardial biopsy was successful in providing a tissue diagnosis without complication.

Primary cardiac malignancies are rare. The reported incidence at autopsy ranges from 0.0017 to 0.25 percent, as compared to 1 to 22 percent for metastatic cardiac involvement. Sarcomas are the most common primary cardiac malignancies, and usually originate from the right side of the heart or pericardium. Patients with cardiac sarcomas present at an average age of 40 years, but can range from 10 months to 79 years. The clinical manifestations are usually subtle, but in some instances there may be dyspnea, elevated jugular venous pressure, edema, embolic phenomena, hypotension, or tamponade from effusion or neoplastic encasement.

There are no reported cases of left ventricular endomycocardial biopsy diagnosing primary cardiac malignancy. This method may be useful in situations where pathologic identification of left-sided cardiac abnormalities might significantly alter clinical management. Echocardiography, angiography, gated CT or magnetic resonance imaging scans are useful in evaluating the presence and extent of cardiac involvement, but none of these can establish a histopathologic diagnosis. Diagnosis of intracardiac mass lesions is one of the few contexts in which endomyocardial biopsy may be conclusive rather than suggestive of a diagnosis. This procedure offers less morbidity and mortality than thoracotomy with approximately the same risk as routine cardiac catheterization. An additional advantage of endomyocardial biopsy is that it may permit diagnosis in patients with high operative risk. It is important to note that this method obtains a small sample of tissue, which by virtue of possible sampling error may allow for misinterpretations of the neoplastic process. There is also a risk of systemic embolization of friable tumor tissue with subsequent infarction or metastases.

178 Intracardiac Sarcoma (Hausheer)
Primary and secondary cardiac malignancies generally portend a poor prognosis, but some metastatic tumors are now curable with specific therapy (eg, testicular cancer and lymphomas) and long-term palliation is achievable with many more. Since survival is improving in many oncologic disorders, the incidence of cardiac malignancy may rise and the use of methods such as echocardiography may increase antemortem recognition of this involvement. In cases with suspected cardiac involvement, it may be difficult to establish the diagnosis. Endomyocardial biopsy may be useful in such instances to diagnose and optimize management without the risk of thoracotomy. The relative diagnostic and treatment influence of this procedure will need clarification by further experience.

ACKNOWLEDGMENT: We greatly appreciate the diagnostic assistance and expertise of Dr. Francis Kuhajda regarding interpretation of the patient's cardiac biopsy histopathology specimens.

REFERENCES
1 Mason JW. Techniques for right and left ventricular endomyocardial biopsy. Am J Cardiol 1978;41:857-92
4 Straus R, Merlii R. Primary tumor of the heart. Arch Pathol 1945;39:74-78
7 Harvey WP. Clinical aspects of cardiac tumors. Am J Cardiol 1968;21:328-43

Amiodarone Pulmonary Toxicity Presenting as Bilateral Exudative Pleural Effusions*

Ricardo J. Gonzales-Rothi, M.D., F.C.C.P.;
Stephen E. Hannan, M.D.;* C. Ian Hood, M.B., Ch.B.;
and Daisy A. Franzini, M.D.

Therapy with the antiarrhythmic drug amiodarone has been associated with drug-related side effects. In addition to pulmonary fibrosing alveolitis, anecdotal reports have alluded to incidental pleural involvement associated with amiodarone. We describe an unusual manifestation of amiodarone-induced pulmonary toxicity in a patient with bilateral exudative pleural effusions and toxic involvement of other organs. We review amiodarone-associated pleural reactions reported in the literature.

Amiodarone (Cordarone, Wyeth Laboratories), is a powerful antiarrhythmic drug that has been associated with increasing multi-organ toxicity. Since the report by Rotmensch et al linking pneumonitis with amiodarone therapy, we have learned that amiodarone-related pulmonary abnormalities can be detected in many asymptomatic patients and can progress to significant pulmonary insufficiency. Pleural involvement associated with amiodarone treatment, infrequently described as an incidental radiographic finding, has not been clearly documented. We describe a patient whose amiodarone-induced exudative pleural effusions and pleuritis spontaneously resolved after withdrawal of amiodarone treatment.

CASE REPORT

A 62-year-old former 30 pack-year smoker with angiographically documented coronary artery disease and normal ventricular function developed sick sinus syndrome two years prior to admission, requiring a permanent atrioventricular sequential pacemaker. Nine months prior to admission he experienced symptomatic ventricular tachycardia. He was cardioverted and myocardial infarction was ruled out. Despite therapy with various combinations of conventional oral antiarrhythmic drugs, ventricular dysrhythmias persisted. These medications were discontinued and the patient began treatment with 1,600 mg oral amiodarone daily for two weeks, followed by 1,200 mg daily for eight weeks. His symptoms and dysrhythmias subsided. Ten weeks after starting amiodarone therapy he complained of fuzzy night vision, but result of an ophthalmologic examination was normal. Because of stable cardiac status, amiodarone dosage was reduced to 800 mg daily for the following ten weeks, when he gradually began experiencing malaise, halo vision, lethargy, anorexia, a 30-pound weight loss, nausea, vomiting, dry cough, and progressive dyspnea. He took no other

*From the Pulmonary Division, Veterans Administration Medical Center, and the Departments of Medicine and Pathology, University of Florida, Gainesville.
†Dr. Hannan is a Christmas Seal Fellow supported by the American Lung Association of Florida.
Reprint requests: Dr. Gonzales-Rothi, 111A Pulmonary Division, VA Medical Center, Gainesville, FL 32602

FIGURE 1. Posterior-anterior view of chest roentgenogram at the height of the patient's illness, after four months of amiodarone therapy. Pre-therapy film was normal (not shown). There is marked blunting of both costophrenic angles with pleural fluid which layered on lateral decubitus views (not shown). In addition there are bilateral fine interstitial markings in the lower lung fields.

CHEST / 82 / 1 / JULY, 1987 179