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A Case of Giant Cell Myocarditis and Malignant Thymoma: A Postmortem Diagnosis by Needle Biopsy

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Summary: This paper reports a case of fulminant giant cell myocarditis arising in association with a malignant thymoma causing death in a 46-year-old woman. Although the diagnosis was suspected in life, postmortem examination was required for confirmation of giant cell myocarditis. Consent was obtained only for percutaneous needle biopsy of the heart. In order to respect the family's wishes and harvest sufficient diagnostic myocardium, a simple needle-based biopsy technique was devised. A bone marrow trephine needle was attached to a 20 ml syringe and, with suction, multiple passes were used to fill 15 tissue cassettes. The cores were placed immediately in formalin and B5 fixatives. High-quality tissue preservation was obtained without crush artefact. Immunohistochemical studies of the biopsy tissue confirmed that the giant cells were of macrophage derivation.

Key words: thymoma, myocarditis, giant cell

Introduction

Giant cell myocarditis is a rapidly progressive, almost uniformly fatal condition of unknown etiology. In addition to its primary form, giant cell myocarditis has been associated with numerous diseases, including granulomatous, autoimmune, infectious, and neoplastic conditions. Since the turn of the century, only 14 cases of an association between thymoma and giant cell myocarditis have been reported. Here we report the case of a patient with malignant thymoma and giant cell myocarditis. Although giant cell myocarditis was suspected clinically, postmortem examination was needed to confirm the diagnosis. The patient's family, reluctant to consent to a full autopsy, agreed to percutaneous postmortem needle biopsy. In order to respect the family's wishes and harvest sufficient diagnostic myocardium, we devised a simple needle-based biopsy technique. A bone marrow trephine needle was attached to a 20 ml syringe and, with suction, multiple passes were used to fill 15 tissue cassettes. Excellent quality histology with no artifact was obtained showing severe and extensive giant cell myocarditis with fibrinous pericarditis. Immunohistochemical analysis of the biopsies showed the giant cells to be of histiocytic origin.

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Case Presentation

A 48-year-old woman was admitted to a local hospital for the evaluation of 2 weeks of progressive shortness of breath. She had no past history of cardiovascular disease, and initial evaluation revealed pulmonary edema with a left pleural effusion, mild elevation of creatine phosphokinase-MB, and an ejection fraction of 20% by echocardiography. Her hospital course was complicated by ventricular tachycardia, treated with lidocaine, and she was subsequently transferred to our hospital for further evaluation and treatment.

The patient had a past medical history remarkable for recurrent thymoma, originally diagnosed in 1981 when she presented with a mediastinal mass. The tumor was resected in 1981 and required further debulking and radiation therapy when it recurred in 1983. The radiation treatments totaled 4500 rads to the upper mediastinum, including part of the right atrium. In 1984 she was found to have liver metastases and was given two cycles of chemotherapy with cytoxan and cisplatin. Four months prior to the present hospital admission, a computed tomography scan of the chest showed tumor mass anterior to the heart, in the liver, and in the right upper lobe (Fig. 1).

On physical examination she was afebrile, her pulse was 83, respiratory rate was 16, and her blood pressure was 84/ Doppler. She was awake and cognizant. She had jugular venous distension and her lungs were clear. Her cardiac examination revealed a diffuse and laterally displaced cardiac impulse, and an S3 gallop. There was no murmer or rub. Abdomen was without masses or hepatomegaly, and her extremities were cool with diminished pulses.

An electrocardiogram showed sinus rhythm at 70 beats/min with low voltage throughout, left anterior fascicular block, and anteroseptal ST-segment elevation. Right heart catheterization revealed a right atrial pressure of 16, pulmonary artery pressure of 24/13, pulmonary capillary wedge pressure of 13, and cardiac output of 1.7 l/min. Coronary angiography revealed no obstructive lesions. An echocardiogram showed severe biventricular dysfunction with a left ventricular ejection fraction of 15%, markedly elevated filling pressures, and thrombus in both the right ventricle and left atrium. An extracardiac mass was noted outside the main pulmonary artery and did not appear to cause obstruction.

On Day 2 of her hospital stay, the patient had frequent episodes of ventricular tachycardia, requiring lidocaine, cardioversion, and amiodarone. She remained hypotensive and required dopamine for blood pressure support. Laboratory data revealed multiorgan system failure. Intravenous T4 was given for abnormal thyroid function tests and steroids for possible giant cell myocarditis, neither providing clinical improvement. Mechanical ventilation was instituted for respiratory distress, and on Day 5 of her hospital stay the patient expired.

Pathology

The autopsy was performed using a bone marrow trephine needle attached to a 20 ml syringe. From a single puncture site on the anterior chest wall, tissue was sampled from multiple directions and depths, sampling the entire heart and pericardium. After each pass, myocardial tissue was placed in formalin for 24 h and in B5 for 3 h. Fifteen tissue cassettes were filled. From the blocks, H and E sections were cut and reviewed along with gram, acid-fast, and methenamine silver stains for microorganisms. Immunohistochemistry was performed on one formalin-fixed and one B5-fixed block for leukocyte common antigen, the histiocyte marker KP1, the cardiac myocyte marker desmin, and proliferation markers MIB1 and PCNA.

Microscopic examination showed giant cell myocarditis with > 50% loss of myocardium. A hemorrhagic pericardial effusion was also present. The inflammatory infiltrate was comprised of numerous multinucleated giant cells, histiocytes, lymphocytes, and occasional polymorphonuclear cells (Fig. 2). The infiltrate appeared to track between groups of muscle fibers. Immunohistochemical studies revealed the giant cells stained with KP1 and not with desmin, indicating the histiocytic origin of these cells (Figs. 3, 4). Stains for microorganisms were negative. The proliferation markers showed no nuclear staining of myocytes or giant cells. In some of the biopsies, most of the myocardium was replaced by the infiltrate with early signs of fibrosis and granulation tissue. Other sections showed epicardial fat with adjacent inflammation, fibrosis, hemorrhage, and fibrin deposition. There was no evidence of cardiac infiltration by thymoma. The final diagnosis was giant cell myocarditis with organizing fibrinous pericarditis.

Discussion

Needle biopsy examinations may be ideal when the patient's or family's wishes are for limited autopsies, or when the postmortem involves potentially infectious material. The unequivocal determination of the exact cause of death is, however, not always possible when the postmortem is limited to needle biopsy. Wellman reviewed 394 cases in 1969, and more

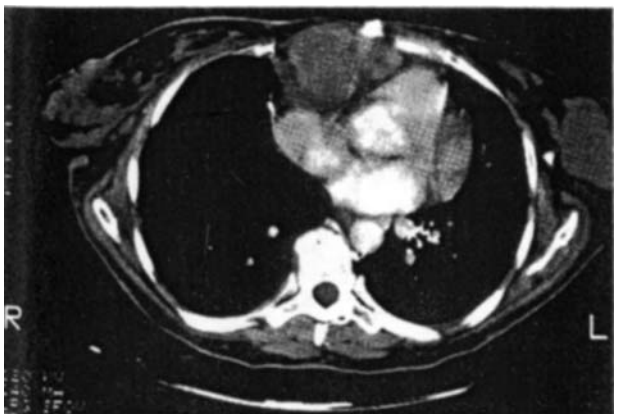

FIG. 1 A chest computed tomography scan performed at a local hospital 4 months before the current admission to assess tumor progression. The scan demonstrates a somewhat heterogeneous mass in the anterior mediastinum, distorting the cardiac contour and invading the chest wall.

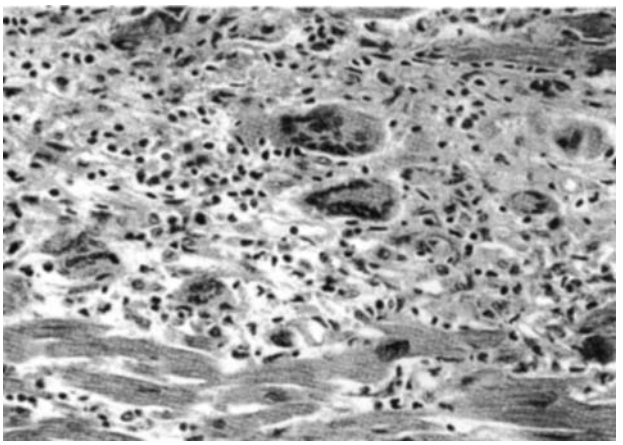

FIG. 2 Section of the heart showing an infiltrate of inflammatory cells, including giant cells, replacing the myocardium. Residual myocardial fibers are seen in the lower part of the figure. H and E, ×455.

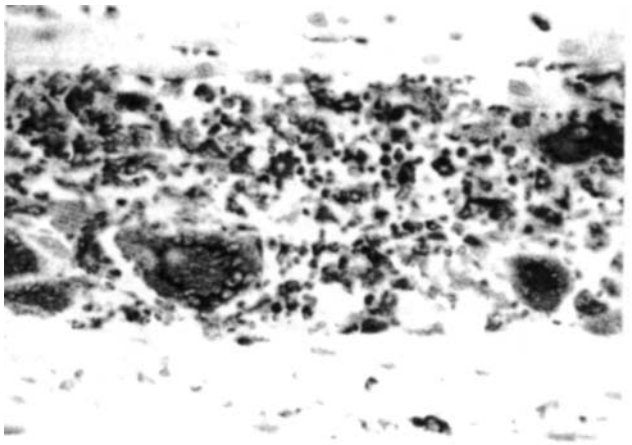

FIG. 3 This section is stained for KP1, a macrophage marker. The giant cells and many of the inflammatory cells give a positive reaction, indicating their derivation from macrophages. ×650.

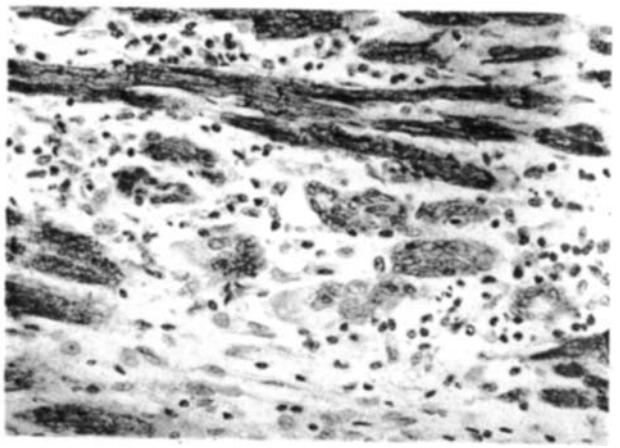

FIG. 4 This is an immunohistochemical stain for desmin, which has strong affinity for myocardial fibers. The inflammatory and giant cells are negative. ×455.

recently Foroudi *et al.* compared the use of Tru-cut biopsy needles with a conventional open autopsy in a series of 21 cases.[1,2] In the series by Foroudi *et al.*, the cause of death in 1 of the 21 cases of needle autopsy was found to be incorrect when compared with the open autopsy. In their series, it was possible to determine the cause of death correctly in 43% of the cases. Not all organs can be sampled with equal ease. For example, liver tissue can be collected between 92 and 100% of the time, while kidney is sampled only 9.5–34% of the time. The reliability of tissue sampling may be improved by the use of the bone marrow trephine needle, which can penetrate deep into any body cavity and produces very good quality tissue with little crush artefact. Correlation with antemortem diagnostic imaging should also facilitate tissue sampling postmortem.

Myocardial disease in patients with myasthenia gravis has been noted since the turn of the century. Early reports of pathologic findings associated with myasthenia gravis were summarized by Rottino *et al.*[3] Weigert noted microscopic cardiac involvement in a case of thymic tumor in 1901.[4] In the following two decades, several reports of cardiac involvement in patients with myasthenia gravis or thymic tumor were made.[5–8] The cardiac findings were primarily lymphorrhages, focal collections of lymphocytes, similar to those found in skeletal muscle in patients with myasthenia gravis. Although this finding is distinct from giant cell myocarditis, it helped to develop an appreciation of cardiac involvement in myasthenia.

When lymphorrhages or granulomatous myocarditis were discovered in patients with thymoma, the clinical course was typically indolent and the cause of death was often not related to myocarditis.[3,9] However, when thymoma was associated with giant cell myocarditis, the clinical course was uniformly one of fulminant myocarditis with death ensuing from heart failure or ventricular arrhythmias.[10] A review of the English language literature resulted in 14 previously reported cases of giant cell myocarditis occurring with thymoma (Table I). All reported cases occurred in women between the ages of 31 and 76. All of the clinical courses described underwent rapid deterioration characterized by severe congestive heart failure, and supraventricular and ventricular arrhythmias. Nine patients died of rapidly progressive heart failure. Once symptoms of worsening heart failure arose, death occurred within several hours to several weeks. Intractable ventricular tachycardia and sudden death occurred in two of the patients. Due to the fulminant nature of giant cell myocarditis, diagnosis is often made postmortem. Successful treatment has been reported with combination immunosuppressive therapy including prednisone, azathioprine, and cyclosporine,[24,25] and with cardiac transplantation.[10]

Conclusion

We have reported the case of a 48-year-old woman with a history of recurrent thymoma who presented with ventricular

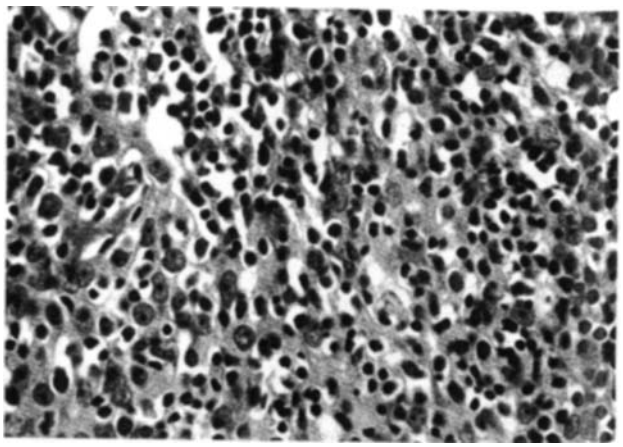

FIG. 5 A section of the malignant thymoma, showing atypical epithelial cells, with a prominent infiltrate of lymphocytes. H and E, ×650.

TABLE I Reported occurrence of giant cell myocarditis and thymoma

First author/year (Ref. No.)	Myasthenia gravis	Myositis	Presentation
Rottino/1942 (3)	+	−	54 yoF with CHF
Mendelow/1954 (11)	+	−	37 yoF with ant. mediastinal mass
Rowland/1955 (12)	+	+	31 yoF with CHF
Waller/1956 (13)	−	+	64 yoF with CHF
Langston/1959 (14)	−	+	75 yoF with CHF
Funkhouser/1961 (15)	+	−	53 yoF with CHF
McCrae/1963 (16)	+	−	
Rundle/1963 (17)	−	+	60 yoF with CHF
Klein/1966 (18)	+	+	69 yoF
Burke/1969 (19)	+	+	47 yoF with CHF
Davies/1975 (20)	−	−	72 yoF, sudden death
Johns Hopkins Hosp/1977 (21)	+	+	32 yoF, cardiogenic shock
deJongste/1986 (22)	+	−	VT
Butany/1991 (23)	−	+	

Abbreviations: + = present, − = not present, yoF = year-old female, CHF = congestive heart failure, VT = ventricular tachycardia.

arrhythmias and congestive heart failure. The patient's family did not consent to a full postmortem examination, but did allow a needle biopsy examination of the heart. Use of the bone marrow trephine needle yielded high-quality tissue for microscopic analysis with no crush artefact, permitting the easy diagnosis of fulminant giant cell myocarditis. Histologic staining confirmed the histiocytic origin of the multinucleated giant cells. This case of a rare condition that would otherwise have eluded diagnosis illustrates the utility of the needle biopsy postmortem study. The needle biopsy technique may be particularly useful when issues of consent or safety make a full autopsy unfeasible.

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