CASE REPORT
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Primary pericardial mesothelioma presenting as constrictive pericarditis

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ABSTRACT

Primary pericardial mesothelioma is an extremely rare and lethal cardiac tumor. We report an autopsy case of a primary pericardial mesothelioma in a 52-year-old man. He developed dyspnea, cough, low-grade fever and night sweats approximately 3 months before last admission. Initially, he was evaluated at a hospital in another city, without a firm diagnosis. Due to progressive symptoms and the development of lower-extremity edema, he presented at our hospital in September 2005. The physical examination at admission demonstrated signs of pericardial tamponade. Chest radiography revealed marked enlargement of the cardiac silhouette. Specimens of bloody pericardial fluid were positive for pericardial mesothelioma by cytologic examination. The general condition of the patient worsened very rapidly and he was transferred to the intensive care unit where he later died. Postmortem examination confirmed primary pericardial mesothelioma of the mixed/biphasic type with lymphatic metastasis in the right lung. By using immunohistochemical analysis for specific markers of mesothelioma and for differentiation of the mesothelioma from the lung adenocarcinoma, definitive diagnosis was established: primary pericdial mesothelioma.

KEY WORDS: *Pericardium; Mesothelioma; Pericarditis, Constrictive; Diagnosis; Autopsy; Immunohistochemistry; Cytology*

INTRODUCTION

Mesothelioma is a malignancy deriving from the serous epithelial cells of the mesothelium (1-5). The most frequent sites are pleura (60%-70%) and the peritoneum (30%-35%); mesothelioma of the pericardium is extremely rare; they account for 0.7% of all diagnosed malignant mesotheliomas (5-7). The factors contributing to the low incidence of its antemortem diagnosis include the paucity and non-specific nature of the clinical signs and symptoms. Diagnosis is most often made by cytological and histopathological examination (8-14). Even then, the diagnosis may not be readily apparent on morphology alone and one may need to resort to immunohistochemistry and ultrastructural examination. This paper presents the case of pericardial mesothelioma with emphasis on some aspects of its clinicopathological presentation that have complicated the diagnosis.

CASE REPORT

Clinical history

The patient, a 52-year-old man, developed dyspnea, cough, low-grade fever, and night sweating approximately 3 months prior to the last hospital admission. Initially, he was evaluated at a hospital in other city and with a diagnosis idiopathic constrictive pericarditis. Due to progressive symptoms and the development of nausea and vomiting, along with lower-extremity edema, he presented at our hospital in September of 2005. Chest radiography revealed marked enlargement of the cardiac silhouette. Echocardiography demonstrated a pericardial effusion with signs of tamponade. Smears from the pericardial fluid, taken during pericardiocentesis, showed increased cellularity with groups and clusters of cells with distinct mesothelial differentiation. Nuclei were enlarged with prominent nucleoli and there was evidence of binucleation. Mitotic figures were noted (Figure 1).

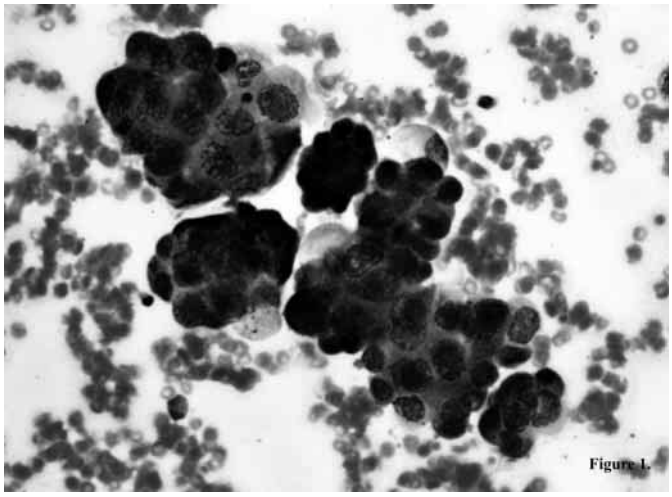

Figure 1. Cytologic characteristics of epithelial part of mesothelioma, May-Grünwald x 400

This cytological finding was strongly suggestive of malignant pericardial mesothelioma. The second admission, 2 weeks after the first, revealed an apparently ill patient with a blood

pressure of 110/70 mmHg and a pulse rate of 120/min. Examination of the cardiovascular system revealed feeble heart sounds all over. Examination of the respiratory system showed decreased breath sounds over the right lung. The pleura of both lungs was normal. Other systems showed no significant findings. The general condition of the patient worsened very rapidly and he died after admission into the intensive care unit.

Postmortem examination

The heart revealed diffuse involvement of the epicardium by a gray-white fleshy tumor having a maximal thickness of 18 mm at the base of the heart. The tumor essentially encased the heart. In general, there was a distinct border between the tumor and the underlying myocardium, but areas of obvious subepicardial fatty tissue infiltration were observed. Within the mediastinum, the tumor was confined by the parietal pericardium. Metastases were found in hilar lymph nodes of the right lung. Diffuse intralymphatic metastases in the right lung have, together with chronic passive congestion and more centrally located pulmonary hemorrhage, conspicuously produced the increase in weight of the right lung (1700 g). Acute venous emboli, arisen in thrombi within the femoral veins, were present throughout large pulmonary artery branches within the parenchyma of the right lung. Embolic obstruction of these arteries resulted in more centrally pulmonary hemorrhage.

Histopathological findings

The general histologic appearance of the tumor consisted of variably sized nodules of the mixed/biphasic type. The epithelial component consists of tubules, papillae, cords, and nests of infiltrating polygonal cells that incited a desmoplastic stromal response. The sarcomatoid component comprised of spindle shaped cells displaying nuclear atypia and prominent nucleoli; mitotic index varied with location, but areas containing greater than 5 mitoses per 10 high-power fields were present. Diffuse intralymphatic metastases were observed in the right lung.

Immunohistochemical studies

This study revealed both strong cytokeratin positivity in the epithelial component (Figure 2a) and vimentin positivity in the sarcomatoid component of mesothelioma (Figure 2b); metastatic epithelial component, discovered inside hilar lymph nodes and intrapulmonary lymphatics, was positive to keratin (Figure 3a) and negative to vimentin (Figure 3b). Cancer embryonic antigen (CEA), marker for lung adenocarcinoma, was also negative. These imunohistochemical results confirmed the histological diagnosis. Definitive diagnosis was: pericardial epithelial mesothelioma.

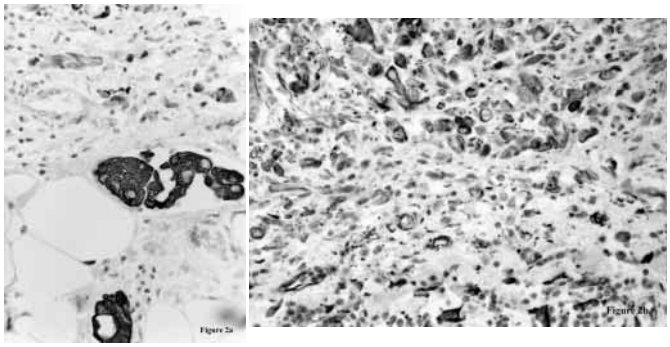

Figure 2. a. Marked presence of cytokeratin (AE1, AE3), LSAB2x400, b. Biphasic type of mesothelioma: diffusely positive reaction for vimentin, LSAB2x400

DISCUSSION

Primary heart mesothelioma accounts for about 2%-3 % of all cardiac and pericardial primary tumors and about 1% of all mesotheliomas (1,15-17): it is the third tumor after angiosarcoma (33%) and rhabdomyosarcoma (20%). Exposure to asbestos is correlated with the onset of pleural and peritoneal mesothelioma; however, the role of asbestos in the etiology of pericardial mesothelioma is unclear (16).

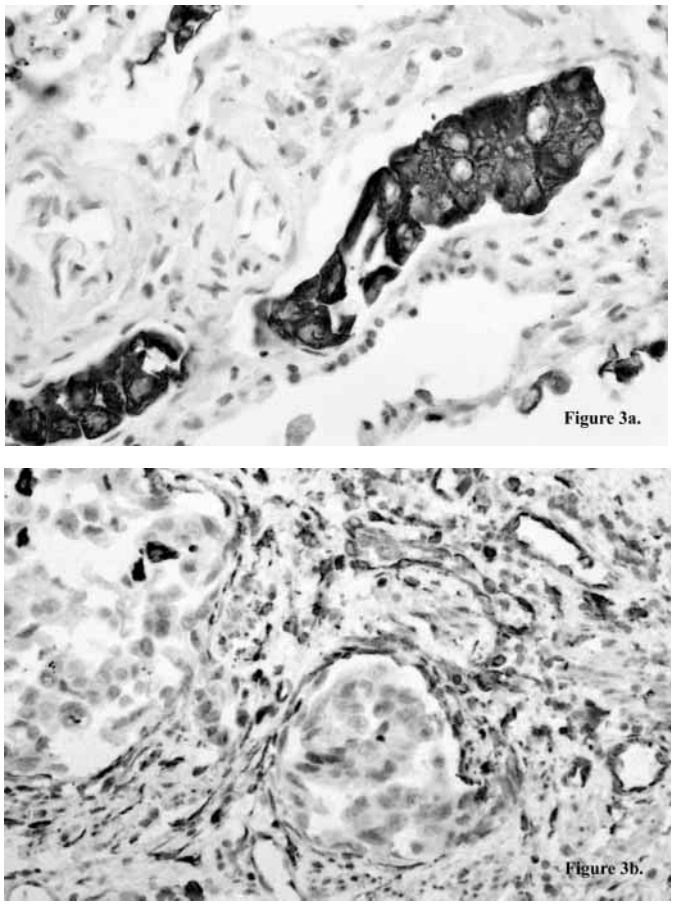

Figure 3. a. Epithelial part of mesothelioma: marked presence of cytokeratine (AE1, AE3), LSAB2x400, b. Lymphatic metastasis in the lung: negative exression of vimentin in epithelial part of mesothelioma, LSAB2x400

Although a wide age range is affected, over half of the cases occur in the 5th to 7th decade of life. Presenting signs and symptoms are nonspecific and are related mostly to the compromise of cardiac function caused by tumor mass, effusion or both. This nonspecificity may lead to diagnostic consideration or treatment of other disease states associated with pericardial effusion such as rheumatic fever, metastatic disease, dissecting aortic aneurysm, viral syndrome, and tuberculosis (1,5,10).

The diagnosis is made on the basis of cytological examination, ultrasound, or CT-guided biopsy. Only in 10%-20% of cases, diagnosis can be made before the death of the patient. Features that indicate the presence of malignancy are: infiltration of deep tissues, atypical cytoplasm, necrosis, and confluent forms. Immunohistochemistry is useful for the differential diagnosis, but it is necessary to obtain additional information (anamnestic, clinical or radiological). Mesothelioma cells stain positive for cytokeratin, vimentin (for sarcomatoid or biphasic type), epithelial membrane antigen (EMA) and calretin, and negative for CEA, CD-15, and S-100 (9). Pericardial mesothelioma infiltrates the myocardial and mediastinal structures. Metastases are present in about 25%-45% of the cases and involve the regional lymph nodes, lungs, and kidneys. Several studies have shown the efficacy of surgery, radiotherapy, and chemotherapy, but the results are modest and provide no significant difference in prognosis, which remains poor (the median survival is about six months from diagnosis) (5,16). The most frequent causes of death are cardiac tamponade, vena cava occlusion, and congestive heart failure (11,12,17).

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