Pathologic Quiz Case

A Patient With Down Syndrome Presenting With "Idiopathic" Pericarditis

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A 26-year-old white man with Down syndrome presented with a 2-week history of exertional shortness of breath, orthopnea, paroxysmal nocturnal dyspnea, and dry cough. He also had an episode of right-sided chest pain, which was aggravated by breathing. He denied fever, chills, and swelling of the legs. Physical examination revealed tachycardia, hypotension, and diminished breath sounds. Chest radiography revealed a markedly enlarged cardiac silhouette and right-sided pleural effusion, which was drained. A computed tomography scan of the chest revealed irregularities in the myocardium. A spiral computed tomography scan was negative for pulmonary embolism. Two-dimensional echocardiographic examination revealed pericardial effusion with cardiac tamponade. Ejection fraction was 54%. Cardiac catheterization did not indicate equalization of diastolic pressure. A pericardial window was created, and pericardial biopsy revealed mild chronic inflammation. Pericardial fluid cytology was negative for malignant cells. Antibodies to Coxsackie viruses A and B, *Mycoplasma*, *Legionella*, and *Chlamydia* produced negative results. Culture of the blood, urine, and pericardium were negative for pathogenic organisms. A few days after hospitalization, the patient developed respiratory failure, which required intubation. He then developed ventricular fibrillation that did not respond to resuscitation, and he died. Permission for autopsy was obtained. Dissection of the mediastinum revealed a tan tumor encircling the heart and the great vessels, with extension to the myocardium (Figure 1, arrows). Lungs and pleura were not involved. The tumor was composed of solid sheets of spindle cells with large pleomorphic, hyperchromatic nuclei and prominent nucleoli (Figure 2). Mitotic activity was high. The lesion was infiltrating in the parietal pericardium and epicardium and partially infiltrating in the myocardium. A desmoplastic reaction was noted. Electron microscopic examination revealed long and brushy microvilli (Figure 2, inset). Tumor cells were positive for cytokeratin (Figure 3), vimentin, and HBME-1 (Figure 4) and negative for carcinoembryonic antigen.

What is your diagnosis?

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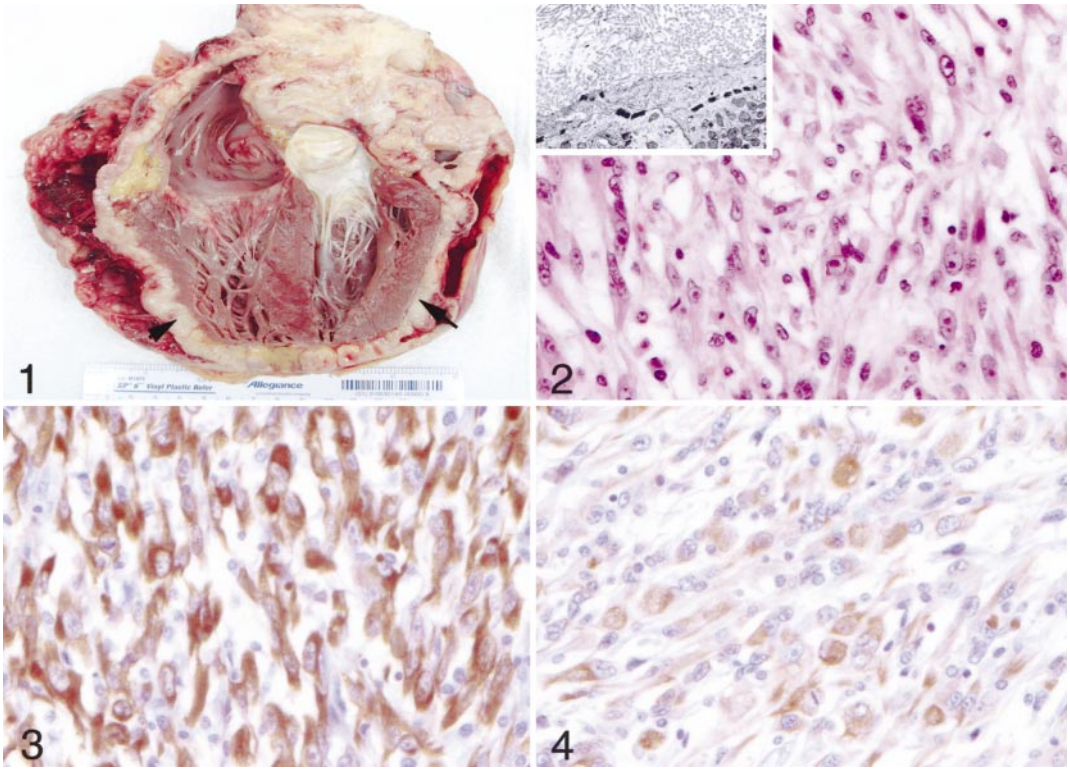

Pathologic Diagnosis: Primary Pericardial Malignant Mesothelioma

Primary pericardial malignant mesothelioma is a neoplasm that arises from pericardial mesothelial cells or the more primitive submesothelial precursor cells. The tumor is limited to the pericardium only, with possible metastasis to the lymph nodes.[1] Pericardial mesothelioma is a rare tumor; approximately 200 cases have been reported worldwide. Only 0.7% of all mesotheliomas are pericardial, whereas 98% are pleural. The average age at onset ranges from 45 to 75 years, and the patient male-female ratio is 2:1.[2] An association with asbestos, as in cases of pleural mesothelioma, is hard to establish in a given case. The incidence of pericardial mesothelioma is increased in patients known to have been exposed to asbestos; however, often there is no history of asbestos exposure, as was the case for this patient. Exposure to other metallic fibers with high length-diameter ratios and long durability in tissue, such as crocidolite asbestos, erionite, and zeolite, increases the risk of pericardial mesothelioma.[2,3]

About 75% of affected patients present with dyspnea. Tamponade usually develops later, unlike in this case. Chest radiographs reveal cardiomegaly due to pericardial effusion or to solid tumor infiltration, which can obliterate the pericardial cavity. Extension to the carotids and epicardial coronary arteries may cause cerebral ischemia and myocardial infarction, respectively, whereas compression of the mediastinal vessels leads to superior vena cava syndrome.[4,5] Echocardiography can be used to distinguish pericardial mesothelioma from effusion.[6] Computed tomography scans and magnetic resonance images can be used to evaluate the involvement of the mediastinal lymph nodes and the mediastinal great vessels.[7] Hyaluronic acid concentrations in fluid derived from pericardiocentesis is usually more than 800 mg/L. Hyaluronic acid analysis was not performed in this case because mesothelioma was not in the differential diagnosis at the time of presentation.[8]

Grossly, pericardial mesothelioma forms tan, firm nodules or solid sheets that fill the pericardial cavity and encircle the heart and often encircle the great vessels, as in this patient. Deep invasion of the myocardium is rare. Tumor cut surfaces may have hemorrhage, necrosis, or cystic areas. Three histologic types of primary pericardial malignant mesothelioma have been described: epithelial, sarcomatoid, and mixed type. In epithelial pericardial mesothelioma, cells form tubules, papillary structures, and infiltrating cords that can induce desmoplastic response. Malignant epithelial cells have hyperchromatic large oval nuclei, prominent nucleoli, and abundant cytoplasm. The sarcomatoid mesothelioma has sheets of malignant spindle cells with features similar to those of the epithelial type. The case presented here most likely fits the sarcomatoid type. The mixed type (75% of cases) has both epithelial and sarcomatoid components. Malignant mesothelial cells have cytoplasmic vacuoles filled with hyaluronic acid, which stain positive with Alcian blue. Electronic microscopic examination reveals characteristic long microvilli, several times longer than wide. This tumor stains positive for cytokeratin (100% in epithelial type, 75% in sarcomatoid type). Epithelial membrane antigen is present in epithelial areas, whereas vimentin is present in sarcomatoid areas. HBME-1 antibody reaction with an unknown antigen on microvilli of mesothelioma cells is a useful immunostain. Tumors are also positive for thrombomodulin. Mesotheliomas generally do not express carcinoembryonic antigen, B72.3, and Leu-M1.[9,10]

A few mediastinal neoplasms may histologically resemble pericardial mesothelioma. Metastatic adenocarcinoma from the lungs, especially from the peripheral pulmonary adenocarcinoma, may resemble the epithelial pericardial mesothelioma. Mesothelioma usually encases the heart and is positive for vimentin and thrombomodulin and negative for diastase, carcinoembryonic antigen, Leu-M1, B72.3, Ber-EP4, MOC-31, blood group antigen ABH, Lewis-Y, and Lewis-X. Reactive mesothelial hyperplasia may be mistaken for sarcomatoid pericardial mesothelioma. Mesothelioma has infiltrating sheets of sarcomatoid cells with nuclear pleomorphism and hyperchromasia and lacks the benign picture of reactive mesothelial cells. Angiosarcoma may be histologically close, but usually it is positive for factor VIII and negative for cytokeratin. Synovial sarcoma is also in the differential, but it does not diffusely infiltrate the pericardium. Although both types of tumor are biphasic, glands in synovial sarcoma are branched and contain periodic acid–Schiff–positive diastase-resistant material. The sarcomatous cells in synovial sarcoma have finely stippled chromatin and inconspicuous nucleoli. Unclassified pericardial sarcoma and malignant fibrous tumor of the pericardium could be in the differential. However, those tumors do not have an epithelial component and are negative for cytokeratin.

Primary pericardial malignant mesothelioma is not curable. Pericardial resection is performed to prevent cardiac constriction, and sclerotic agents are used to prevent fluid accumulation. Radiation and chemotherapy have limited success. Prognosis is uniformly poor, and 50% of the patients die within 6 months.

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