Primary Pericardial Mesothelioma in an Asbestos-exposed Patient with Previous Heart Surgery

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Abstract. *We present a case of primary pericardial mesothelioma occurring in an asbestos-exposed 67-year-old man who underwent four aortocoronary bypass grafting seven years prior to the onset of the mesothelioma. Primary pericardial mesothelioma is a rare tumor whose association with asbestos is more infrequent than that of the much more common pleural form. Factors other than asbestos that may play a role include genetic predisposition, immune impairment, infections, radiation, dietary factors, and recurrent serosal inflammation. We consider that, in the presented case, inflammation and healing resulting from pericardiotomy might have had a synergistic effect with asbestos in the pathogenesis of the tumor. To our knowledge, this is the first reported case of primary pericardial mesothelioma arising in a patient exposed to asbestos who previously underwent cardiac surgery.*

Primary pericardial mesothelioma is a rare tumor whose association with asbestos is more uncommon than that of the much more frequent pleural form. Factors other than asbestos that may play a role include genetic predisposition, immune impairment, infections, radiation, dietary factors, and recurrent serosal inflammation. We present a case of primary pericardial mesothelioma occurring in an asbestos-exposed patient following cardiac surgery, in which inflammation and repair subsequent to pericardiotomy might have had a synergistic effect with asbestos in the pathogenesis of the tumor.

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Case Report

In July 2008, a 67-year-old former plumber was admitted to the Cardiology Department for persistent chronic heart failure with increasing dyspnea and orthopnea. His clinical history was significant for an acute myocardial infarction involving both left and right ventricular walls which had occurred seven years before and had been treated with four aortocoronary bypass grafts. Physical examination revealed crepitant rales over 50% of lung fields, tachyarrhythmia, and dependent edema. Laboratory findings showed renal failure (creatinemia 1.9 mg/dl, uremia 110 mg/dl), increased C-reactive protein, erythrocyte sedimentation rate and white blood cell count, and slight elevation of CA 15.3 (28.1 U/ml, n.v. 0.25 U/ml); however, normal values of other tumor markers such as α-fetoprotein, carcinoembryonic antigen (CEA), and cancer antigen (CA) 19-9 were confirmed. Chest x-ray demonstrated bilateral pleural effusion, widespread interstitial involvement with reticular nodulation, and cardiomegaly. Thoracic CT scan demonstrated prominent pericardial effusion, irregular calcified thickenings of the pleura, partial collapse of the lower lung fields, and multiple parenchymal opacities associated with interstitial involvement with reticular nodulation (Figure 1). Echocardiography and transesophageal echography showed severe biventricular dysfunction, apical right ventricular thrombosis, and periapical and posterior pericardial thickening that was interpreted as pericardial effusion. A thoracentesis removed 500 ml of straw-colored fluid in which cytological examination revealed the presence of atypical mesothelial cells, occasionally clustered in papillary structures, highly suggestive of mesothelioma. The patient was transferred to the Department of Internal Medicine, where he underwent an additional thoracentesis, right thoracic drainage, and thoracoscopic talc poudrage. The patient self-discharged with the diagnosis of probable pleural mesothelioma, ischemic cardiopathy, heart failure NYHA class IV with severe biventricular systolic dysfunction, left ventricular thrombosis, and pericardial effusion. He subsequently died 40 days later.

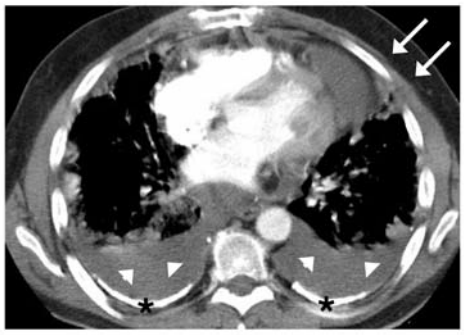

Figure 1. *Axial CT scan of the chest showing prominent pericardial effusion (arrows). Calcified pleural plaques (asterisks) and pleural effusion (arrowheads) are also evident.*

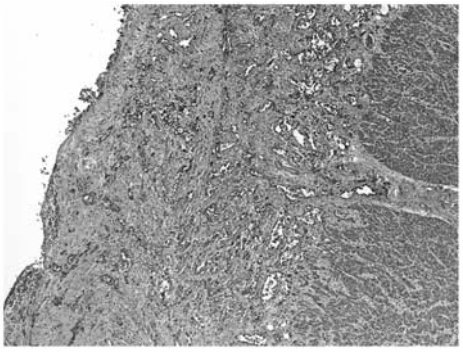

Figure 2. *Microphotograph showing malignant mesothelioma of epithelioid type originating from the epicardium and infiltrating the myocardium.*

At post-mortem examination, a lardaceous sleeve reaching 2 cm in maximum thickness at the ventricular apex encircled the right heart and infiltrated the pericardium with adherence of the heart to the posterior surface of the sternum. Post-pericardiotomy adhesions and diffuse epicardial sclerosis were also evident. Native coronary arteries were diffusely calcified and stenotic, and the anterior descending branch of the left coronary artery was completely obliterated, while the aortocoronary bypass grafts were patent. A wide posterior endomyocardial scar corresponding to the previous infarction was observed. There was conspicuous accumulation of fluid in the pleural space, and multiple diaphragmatic and parietal pleural plaques, some calcified, with the largest measuring about 9 cm. The visceral pleural surface was disseminated with numerous small neoplastic nodules that were also present in the pulmonary parenchyma. The quantification of asbestos bodies in the lung parenchyma, performed in accordance with the method of Smith and Naylor with slight modifications, revealed the presence of 1800 asbestos bodies per gram of dry lung tissue, consistent with an occupational exposure to asbestos. The histological picture was that of an epithelioid mesothelioma arising from the epicardium with deep invasion of the myocardium (Figure 2) and parietal infiltration of the coronary veins, and metastatic dissemination extensively involving the visceral pleura and the lung parenchyma. Immunohistochemically, the neoplastic cells were positive for cytokeratins 5/6, epithelial membrane antigen (cytoplasmic positivity with membrane enhancement), calretinin, weakly positive for vimentin, and negative for CEA and TTF-1.

Discussion

Mesothelioma of the pericardium is a rare tumor: fewer than 150 cases have been reported in the literature. It accounts for 0.7% of all malignant mesotheliomas, the majority of which originate from the pleural lining. The mean age of patients at presentation of pericardial mesothelioma is 46 years, with an age range of 2 to 78 years. The male to female ratio is nearly 2 to 1. The majority of patients with pericardial mesothelioma present with dyspnea, and cardiomegaly caused by pericardial effusion or solid tumor infiltration. Cardiac tamponade often develops during the course of the disease. Although effusion is the rule, the pericardial cavity may be obliterated by tumor, explaining the lack of fluid at pericardiocentesis in some cases. Echocardiography, CT and MR are the main diagnostic imaging techniques used. Echocardiography is generally effective in distinguishing solid tumor infiltration of the pericardium from effusion. Definitive diagnosis is based on cytologic examination of pericardial fluid, supported by the evaluation of biopsy samples which normally demonstrate typical histologic and immunohistochemical features (1, 2). Andersen and Hamsen's criteria to identify a primary pericardial mesothelioma require that there is no tumor present outside the pericardium with the exception of lymph node metastasis (3). With such certainty that such criteria are excessively restrictive, we concluded that the tumor was a pericardial primary on the basis of the extent of involvement of the pericardium compared to the pleura.

The association between malignant mesothelioma of the pleura and asbestos exposure is well known. It is currently believed that, like pleural mesotheliomas, at least some mesotheliomas of the pericardium are caused by asbestos (1). A case of pericardial mesothelioma that developed 15 years after pericardial dusting with asbestos and fiber glass as a treatment for angina pectoris has been described (4). The patient described in the present report lived in Monfalcone, a ship-building town in north-eastern Italy with a high incidence of mesothelioma. He had a history of asbestos exposure, confirmed by quantification of asbestos bodies in his lung parenchyma, indicating an occupational level of exposure. Nevertheless, the link with asbestos is weaker for

pericardial than for pleural mesothelioma. The proportion of women with pericardial mesothelioma is higher than that with pleural mesothelioma. In most cases of reported pericardial mesothelioma, no history of asbestos exposure is mentioned (1). Furthermore, cases of pericardial mesothelioma due to nonasbestos-related causes have been reported, including that of radiotherapy (5, 6).

An increasing body of evidence indicates that factors other than asbestos play a role in the pathogenesis of malignant mesothelioma, including genetic predisposition, immune impairment, infections, radiation, and dietary factors. Recurrent serosal inflammation has also been reported to represent a possible condition predisposing to malignant evolution. Mesothelioma generally develops on pleura affected by pleural plaques, which are the effect of recurrent inflammatory and repair processes occurring over decades (7). Moreover, cases of pleural mesothelioma secondary to chronic inflammation and old scars, observed after chronic empyema or therapeutic pneumothorax, have been described (8-10). The link between inflammation and cancer was first noticed by Virchow in 1863. Since this early observation, accumulating studies have supported that chronic inflammatory diseases are frequently associated with an increased risk of cancer. In a setting of chronic inflammation, the persistent tissue damage and cell proliferation as well as the enhanced production of reactive oxygen and nitrogen species contribute to a cancer-prone microenvironment. A variety of mediators, including cytokines, chemokines, and enzymes, may also facilitate cancer development via multiple signaling pathways (11).

In this case, inflammation and normal repair following pericardiotomy might have had a synergistic effect with asbestos in the pathogenesis of the tumor. To our knowledge, this is the first reported case of primary pericardial mesothelioma arising in a patient exposed to asbestos and previously subjected to cardiac surgery.

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