Primary pericardial mesothelioma – A rare entity

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Introduction

Primary mesotheliomas of the pericardium are rare neoplasms, accounting for 0.7% of all malignant mesotheliomas diagnosed. The factors contributing to the low incidence of its' ante mortem diagnosis include the paucity and non-specific nature of the clinical signs and symptoms. Diagnosis is most often made on the basis of cytology and histopathological examination. Even then, the diagnosis may not be readily apparent on morphology alone and one may need to resort to ancillary techniques such as immunohistochemistry and ultrastructural examination. In this article, we present a case of primary malignant pericardial mesothelioma, which was diagnosed on cytohistological examination, without the aid of specialized techniques.

Case Report

A 38-year-old male presented with history of breathlessness on exertion and cough since three months, which was increasing progressively. One such episode of sudden, severe breathlessness resulted in a hospital admission where a pericardial tap was done, which yielded three litres of haemorrhagic fluid. He was diagnosed as having massive tuberculous pericardial effusion with tamponade and treatment was started. His symptoms were exacerbated in spite of this and he was admitted at the St. John’s Medical College Hospital.

On admission, his pulse was 120/min, JVP was raised and his blood pressure was 100/70 mm Hg. Examination of the cardiovascular system revealed feeble heart sounds all over. There was however no thrill/murmur/pericardial knock. Examination of the respiratory system showed decreased breath sounds over the left inframammary area. Other systems showed no significant findings.

A chest radiograph showed significant cardiomegaly. A CT scan of the chest confirmed the cardiomegaly with thickened pericardium and a loculated pericardial effusion. (Fig. 1) The pleura and both lungs were normal. An ECG showed T-wave inversion in leads II, V4,5,6. Pulmonary function tests showed mild to moderate restriction. Cardiac catheterization showed evidence of a constrictive physiology and on pericardiocentesis 100 ml of haemorrhagic fluid was aspirated.

These findings were strongly suggestive of malignant pericardial mesothelioma necessitating surgery and subtotal pericardiectomy was done. It was observed at surgery that the pericardium was thickened, finely nodular with a layer of granulation tissue present over the epicardial surface, which also appeared highly vascular. Both pericardial surfaces were adherent to each other with locule formation. The pericardium was peeled off, loculi broken and fluid evacuated. Cytology, gross operative appearance and histopathology confirmed the diagnosis of malignant pericardial mesothelioma and are described separately in detail. Retrospective enquiry was negative for asbestos exposure. The post-operative period was uneventful and the patient was stable at discharge.

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Fig. 1. CT scan of the chest showing thickened pericardium with multiple loculations. There is no involvement of the pleura on either side.
Cytology

Smears from the pericardial fluid showed increased cellularity with groups and clusters of cells with distinct mesothelial differentiation. Peripheral knobbing was noted among clusters as also engulfing of one cell by another. At places, brush-border like periphery of the cytoplasmic margins were observed. Nuclei were enlarged with prominent nucleoli and there was evidence of binucleation. Mitotic figures were noted.

Gross Appearance

There were six flat pieces of tan coloured firm tissue ranging in size from 7x0.5x0.4 cm to 0.4x0.3x0.3 cm. The entire surface was studded with fine nodules ranging in size from 0.1 cm to 0.6 cm. One surface was congested. Adequate tissue was submitted for histology.

Histopathology

All sections showed fibrous tissue with an infiltrating neoplasm composed of epithelial cells arranged in solid nests, glands and a papillary pattern. The cells were cuboidal to polygonal with the nuclei displaying hyperchromasia, pleomorphism with prominent nucleoli and many mitotic figures. Some of the cell nests showed central necrosis and foci of calcification. Though showing an epithelial differentiation, the cells were seen to merge with the underlying stroma without a definite basement membrane. (Fig. 2) The surrounding fibrous tissue showed chronic inflammation. The Alcian blue stain at pH 2.5 showed positivity in many of the neoplastic cells that was abolished by predigestion with hyaluronidase, suggesting an acid mucin product, while the PAS stain was negative.

Immunohistochemistry showed expression of Vimentin by the tumor cells while pancytokeratin and desmin were negative.

With the combination of clinical, cytological and histological features, a final diagnosis of infiltrating epithelioid variant of malignant pericardial mesothelioma was made.

Discussion

Primary pericardial mesothelioma is a rare tumour, constituting 0.7% of all mesotheliomas diagnosed. By definition, the entity precludes the presence of tumor outside the pericardium, save for the finding of lymph node metastases. Earlier, a complete autopsy was mandatory to exclude an occult primary elsewhere, but with the advent of ancillary techniques, the diagnosis can be made even on biopsy samples.

Clinically, the patients present with dyspnea, chest pain and cough. Signs of cardiomegaly and pericardial effusion are generally present on chest radiograph and CT scan. Features of constrictive pericarditis, may be seen, as was noted in the present case. In such instances, cytological examination of the pericardial fluid assumes great importance, as is exemplified by our case. Increased levels of hyaluronic acid in the fluid are also said to be helpful in the diagnosis.

Though much has been written about the necessity for immunomarkers in diagnosis, occasionally, morphological appearances are characteristic enough to permit a definitive diagnosis, as in the present case.

On gross examination, mesotheliomas form firm, white, bulky nodules that fill the pericardial cavity. Microscopically, mesotheliomas of the pericardium are generally of the mixed/biphasic type. The epithelial component consists of tubules, papillae, cords and nests of infiltrating polygonal cells that incite a desmoplastic stromal response. The sarcomatoid component comprises of spindle shaped cells displaying nuclear atypia and prominent nucleoli, which was not seen in this instance. The presence of hyaluronic acid in the cells of mesothelioma by colloidal iron stain or Alcian blue stain at pH 2.5 has been used as a diagnostic parameter, which was seen in this case.

Immunohistochemically, mesotheliomas express High Molecular Weight (HMW) Cytokeratin, vimentin, Ephithelial Membrane antigen (EMA), Thrombomodulin, Calretinin and are negative for Carcino Embryonic antigen (CEA), B72.3 antigen and Leu-M1.