Epithelioid hemangioendothelioma

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Abstract

Epithelioid Hemangioendothelioma (EH) is a rare, vasoformative vascular tumour, which displays intermediate clinical behaviour between that of hemangioma and angiosarcoma. We report a case of EH in a 30-year old female, with recurrent pericardial effusion, cough, shortness of breath, haemoptysis, and a negative malignancy workup of pericardial fluid aspiration cytology, and pericardial biopsy. The diagnosis of EH was established after open lung biopsy. Our patient had a malignant form of the disease, who had evidence of alveolar haemorrhage terminally. This is the first case being reported from Nepal. Chemotherapy was advised which she refused, and she died within five months of onset of symptoms.

Keywords: Epithelioid hemangioendothelioma; pulmonary; pericardial effusion.

Case Report

A 30-year old female, presented to our hospital with the chief complaints of chest pain, cough, shortness of breath and intermittent low grade temperature for two months. Physical examination was unremarkable. Investigation reports were as follows:

CBC Hb - 13.6g%

TC - 13,200/cumm

N-64%

L-34%

M-2%

ESR - 23mm/hr

RFT normal

LFT normal

Chest X-ray - Cardiomegaly

Echocardiography - pericardial effusion

Fig. 1

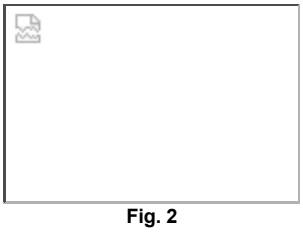

Fig. 2

Pericardiocentesis was done and 350 ml of haemorrhagic fluid was aspirated. Examination results were as follows:

Sugar - 4mmol/L

Protein - 46.0g/L

Cells - 700/cumm

polymorphs 40%

lymphocytes 60%

RBC - plenty

AFB smear - negative

Cytology - reactive mesothelial cells seen. No atypical cells seen.

The patient gave a past history of tuberculosis of lymph node (biopsy proved) in 1992, for which she had received antitubercular drugs for 9 months. With
a provisional diagnosis of tubercular pericardial effusion, we decided to treat the patient with the four drug regimen (HREZ) with prednisolone 30mg/day. Although she had initial improvement of symptoms,
she came for follow up in one month
and complained of cough, increasing breathlessness and malaise. Chest X-ray showed cardiomegaly (greater than the first film) and echocardiography revealed gross pericardial effusion. Pericardiotomy was done and 1 litre of haemorragic fluid was aspirated. The pericardial biopsy was reported as non-specific inflammation with plasma cells and lymphocyte infiltration. Areas of haemorrhage and blood clots
were seen. There was no evidence of tuberculosis or malignancy. Pericardial
fluid AFB culture sent from the first tap
was negative. The patient was discharged with advise to continue ATT. She was brought to hospital in three weeks with worsening cough, haemoptysis and dyspnea. She also had symptoms of anaemia. Chest X-ray done this time
showed multiple nodular opacities in both the lungs, suggestive of metastatic
lesions. CT scan of thorax also showed multiple nodular opacities in both the lung fields.

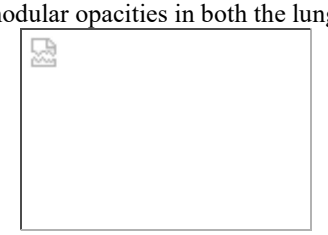

Fig. 3

Fig. 4

The results of other investigations were as follows:

CBC Hb - 5.8g%

TC - 7300/cumm

N-77%

L-23%

ESR - 43mm/hr

Plts. - 2,22000/cumm

Bone marrow aspirate - normocellular with erythroid hyperplasia and megaloblastic maturation.

Sputum cytology - no atypical cells seen

Bronchoscopy - normal

RA factor, ANF, DS-DNA, negative.

HIV - non reactive.

USG abdomen - normal

Clinical examination of the thyroid, breast and the pelvis were normal.

Diagnostic procedure

An open lung biopsy via left
thoracotomy was performed. Samples
were sent for pneumocystis carinii,
fungus stain and culture, AFB smear, which were all negative. The histopathology (following immunohistochemistry) reported the tumour cells to be reactive to
factor VIII and ulex europaeus. Cytokeratin, Epithelial membrane antigen, S-100
protein and Desmin were negative, thus establishing the diagnosis of epithelioid hemangioendothelioma.

The patient was advised chemotherapy which she refused, and died within two months due to progression of disease.

Discussion

Epithelioid Hemangioendothelioma is a unique vascular tumour occurring around medium and large sized vessels, particularly a vein in the soft tissues of mainly adults.[1] In such tumours, well defined vascular channels are inconspicuous, and the tumour cells are plump and often cuboidal, thus resembling epithelial cells. Identical tumours occur in other organs including the lungs, liver, bone, stomach pleura, heart, skin, lymph nodes and even brain and meninges. Dail and Liebow first reported epithelial hemangioendothelioma in the lung in 1975.[2] Considering the tumour to be epithelial in type, they coined the term intravascular bronchioalveolar tumour (IVBAT). Since their first report fewer than 50 cases have been reported worldwide, and this is the first case to be reported in Nepal to the best of our knowledge.[3] The endothelial nature of the neoplastic cells was later established by the identification of Weibel-Palade bodies in
the cytoplasm, and the demonstration of immunoreactivity for factor VIII related antigen. EH occurs over a wide age range, but it is most common in the middle aged adults; it is distinctly rare in children.

Pulmonary Epithelioid Hemangioendo-thelioma (PEH), has been reported in patients from 7 to 76 years of age with a female-male ration of 4:1.[4,5,6] Of the 20 cases described by Dail and his associates, 80% were females with an average age of
39 years. Tumours in the soft tissues are usually solitary, in contrast to the multi-centricity at other sites (Lung, Liver), which can be mistaken for metastasis.[7] Classically it presents as asymptomatic bilateral pulmonary nodules in a young woman[8,9] and is generally considered to be a low-grade malignant tumour with unpredictable behaviour.[8] Although the female prepon-derance raises the question of a hormonal influence, estrogen and progestion recep-tors have not been identified.[10] Most patients have a slowly progressive, indolent course and die of respiratory failure due to infiltration of tumour into the pulmonary interstitium.[9] The average survival for patients with lung lesions is 6.4 years.[4]
Our patient died within 5 months of onset
of symptoms and within 2 months of appearance of multiple pulmonary nodules. Terminally she developed hemoptysis
and chest X-ray suggested alveolar haemorrhage.

Fig. 5

There has been a single case report of alveolar haemorrhage with epithelioid hemangioendothelioma, where the patient also had the progressive form of the disease.[4] The rapidly progressive course and fatal outcome in our patient extends the clinical spectrum

of EH to include this more malignant, aggressive course. Significant morbidity may also result from pulmonary hypertension and right ventricular dysfunction[11], atelectasis and pulmonary vein thrombosis.[8] Features that portend a worse prognosis include the presence of clinical symptoms, extensive intravascular, pleural, and bronchiolar invasion, and peripheral lymphadenopathy. A spindle cell growth pattern and mitosis greater than 1/10 high power fields are predictive of malignant behaviour.[12] Unusual variants may present as a thickened pleural surface resembling malignant mesothelioma, an anterior mediastinal mass, or a solitary peripheral calcified nodule.[4]

Immunohistochemistry test results invariably demonstrate factor VIII-related antigen and Ulex europaeus lectin positivity. A proportion of cases (upto 50%) show positivity for cytokeratin. As opposed to epithelial tumours, EMA (epithelial membrane antigen) is usually negative. The keratin positivity most likely reflects the high filament content of the cell cytoplasm. Primitive intracytoplasmic lumen formation and Weibel-Palade bodies are the most helpful diagnostic features.

Our patient had an atypical presentation with pericardial effusion. Both pericardial fluid cytology and pericardial biopsy were negative for malignancy. Pericardial effusion has been reported in a 12-year old girl with EH, however, the malignancy status is not known.[3]

The treatment of EH is primarily surgical excisions. Both radiotherapy and various chemotherapeutic regimens have been tried but have not proved helpful.[4] The mortality is higher in lung lesions (65%), which have a greater tendencies to be multifocal, compared with 13% for soft tissue lesions.

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