Primary mediastinal choriocarcinoma

Sir,

Primary choriocarcinoma of the mediastinum occurs in both sexes, but is extremely rare. Patients with mediastinal choriocarcinoma are mostly young men. The prognosis of primary mediastinal choriocarcinoma is still very poor despite the introduction of combination chemotherapy including cisplatin. We hereby report a case of primary mediastinal pure choriocarcinoma in a woman who had a poor outcome in spite of aggressive surgery and combination chemotherapy.

A 37-year-old housewife presented to the hospital with complaints of chest pain, hemoptysis and gradually progressing dyspnea (MRC Grade III) of four months duration. There was no history of exposure to any occupational or inorganic dusts. The chest pain was dull aching and mainly localized in retrosternal region. She was also having irritant nature of continuous cough with mucoid expectoration. There was minimal hemoptysis of recent onset. Examination revealed averagely built lady with BMI of 20, and no clubbing and lymphadenopathy. Respiratory system examination revealed diminished movements and breath sounds on the left hemithorax. Chest radiograph revealed a uniform density homogenous opacity in the lower left hemithorax with obliteration of the left cardiac border and costophrenic angle. There was no shift of the mediastinum [Figure 1]. CT scan of the thorax revealed two large well-defined heterogenous density masses in the anterior mediastinum at different levels without any communication to each other. There were some areas of necrosis within the mass. The masses were extending up to the pleural surface with minimal pleural effusion, but there was no infiltration of chest wall. There was no involvement of the mediastinal lymph nodes [Figures 2a and b]. Abdominal ultrasonography did not reveal any organomegaly. Routine blood investigations were within normal limits. Fibreoptic bronchoscopy did not reveal any abnormality. Bronchial washings and bronchial brush biopsy were inconclusive. Trans-thoracic tru-cut biopsy of the mass revealed masses of clear cells with vesicular nuclei surrounded by rims of syncytial dark cells presenting irregularly sized nuclei; but the diagnosis was indeterminate. As the diagnosis was inconclusive, the patient was taken up for thoracotomy with excision of the tumor. Intra-operatively it was observed that there were two large firm masses in the anterior mediastinum on the left side with invasion of the great vessels. The masses were extending up to the chest wall. Hence, debulking of the tumors was done to the extent possible. On gross examination, there were two separate tumors that were large, capsulated, and having extensive hemorrhage on cut section. There were few areas of necrosis. Histologically, it showed that there were dual cell populations which were consisting of cytотrophoblastic cells with uniform, round nuclei, clear cytoplasm, and prominent nucleoli, and second group consisted of large, multinucleated syncytiotrophoblastic

Figure 1: Chest radiograph showing complete homogenous opacification of left hemithorax

Figure 2a: CT scan of the thorax showing well defined non-homogenous density mass with central necrosis in lower part of mediastinum

Figure 2b: Coronal section of the CT thorax showing two well defined masses with central necrosis at different levels in the mediastinum
cells with bizarre nuclei, prominent nucleoli and they had abundant eosinophilic cytoplasm [Figure 3]. Immunohistochemically, the tumor cells were strong cytokeratin positive and showed beta-human chorionic gonadotropin (HCG) positivity [Figures 4 and 5]. The human chorionic gonadotropin titer was 66,496 IU/ml on the 16th hospital day. Post-operatively, she received combination chemotherapy consisting of Etoposide, Cisplatinum and Bleomycin after one week of surgical resection. But the patient continued to be symptomatic and her condition deteriorated. She was given second cycle of combination chemotherapy on 22nd day. Her condition worsened over a period of next one month and she expired subsequently on 48th hospital day.

A choriocarcinoma in the mediastinum, without a detectable primary in the gonads or metastatic disease in the retroperitoneal lymph nodes, is termed a primary choriocarcinoma of the mediastinum. Primary choriocarcinoma of the mediastinum occurs in both sexes, but is extremely rare. It is commoner in man and is most often seen in the second and third decades of life. Only few cases are reported in the literature, due to which the proper therapeutic options are limited in such cases. The present case was a 37 year old woman, in whom it is a rare presentation. The origin of choriocarcinoma is unknown, but many theories have been proposed. The primitive germ cell theory has received the wide acceptance. These cells may arise in the covering mesothelium of the primitive gonad or may arise from the yolk sac endoderm, normally migrating along the urogenital ridge coming to rest in the gonad. In cases of primary mediastinal choriocarcinoma, arrest of the germ cell somewhere along the path may have occurred. These cells may remain dormant until puberty or later sex life when some stimulus might cause them to mature and develop into a tumor mass.

Primary mediastinal choriocarcinoma is characteristically seen in young caucasian men presenting with the symptom triad of cough, gynecomastia and chest pain. Gynecomastia is present in two-thirds, while cough and chest pain appear to be uniform. In woman it is a rarest presentation. Half of the patients are in the third decade and 29% over 30 years of age. Gynecomastia is related to the production of chorionic gonadotropin. Circulating gonadotropin stimulates the Leydig cells to produce testosterone and estrogen. This estrogen production may be the determining factor in the mammary gland hypertrophy so often seen. Our case was a young woman of child bearing age group. Moran and Suster has reported 8 cases of primary mediastinal choriocarcinomas in males whose mean age was 42 years. Clinically they had dyspnea, chest pain, cough, and superior vena cava syndrome; one patient also had gynecomastia. The a-chain of HCG, which shares with TSH an almost identical polypeptide sequence, causes hyperplasia of the thyroid follicles resulting in a clinical and histological picture akin to thyrotoxicosis. The development of biochemical and clinical thyrotoxicosis depends upon the duration of the choriocarcinoma and the levels of HCG. Primary mediastinal choriocarcinoma presents in the anterior mediastinum roentgenographically as a noncavitating well-defined mass with extremely rapid growth. In our case, there were two different masses at
different levels on left side with no communication to each other. Differential diagnosis includes in order of frequency: Teratomas, thymomas, lymphomas and others less common lesions in the anterior mediastinum. Immunohistochemical staining can establish the diagnosis of choriocarcinomas, which displays strong positivity of the syncytiotrophoblastic cells with both HCG and CAM 5.2, but it was uniformly negative for the other antigens tested.[10]

A noteworthy feature of mediastinal choriocarcinoma is that it has a distinctly poorer prognosis than its testicular counterpart.[11] No successful protocol has been proposed for this disease. Surgery is of little value due to the rapid growth and invasive nature of the tumor.[5] Deep radiation therapy has been tried in different case report series to prolong the survival. Earlier studies had tried methotrexate, chlorambucil and cyclophosphamide but had poorer outcome. Hence now days newer drugs are being tried in mediastinal choriocarcinoma – Etoposide, Cisplatin and Bleomycin. This combination has shown some promise in improving survival, and Kathuria and Jblokow[12] has reported survival up to two years after surgery and chemotherapy in mediastinal choriocarcinoma. In our case patient underwent surgery with removal of both the tumors, but there were lot of adhesions to the underlying structures. Hence complete removal of tumor was not possible. Post-operatively she received combination chemotherapy with etoposide, cisplatin and bleomycin. But after two cycles of chemotherapy her condition deteriorated and she expired due to the aggressive nature of the tumor. In Moron and Suster[1] series also, all the 8 patients died within 1-two months after chemotherapy. As the numbers of the cases reported are very few, it is not possible to advocate a definite chemotherapeutic combination. The newer chemotherapeutic agents should be tried in these patients to improve the survival in such cases.

In summary, primary mediastinal choriocarcinoma is an aggressive tumor that is associated with poor survival. Surgical resection of the tumor and post-chemotherapy forms the mainstay of the therapy at present. Establishment of more effective chemotherapy regimen is necessary for this condition.

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