Superior vena caval syndrome and ipsilateral pleural effusion: A rare presentation of anterior mediastinal thymoma

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ABSTRACT

Incidence of thymic malignancies is very low. Thymoma, a tumor of thymus gland, is of epithelial origin and is most common anterior mediastinal tumor. In most cases, thymomas are localized and locally advanced thymomas may rarely present with superior vena caval obstruction (SVCO) and malignant pleural deposits. Microscopically, capsular invasion is noted in case of locally advanced thymomas, which behave like a malignant neoplasm. Complete surgical removal of the tumor along with intact capsule is the treatment modality of choice in case of localized tumors. Neoadjuvant radiotherapy (RT) and chemotherapy followed by surgical resection of residual tumor is useful in case of locally advanced tumors. RT is especially useful in case of SVCO to relieve the distressing respiratory symptoms. Here, we report a rare case of locally advanced thymoma, complicated by SVCO and ipsilateral pleural effusion in a 53-year-old male patient.

KEY WORDS: Pleural effusion, superior vena caval obstruction, thymoma

INTRODUCTION

Thymoma is of epithelial origin arising from the epithelium of thymus gland. Incidence of thymic malignancies is 2.5-3.2/10,00,000 population.[10] Thymoma comprises 20-25% of all mediastinal tumors and is most common anterior mediastinal tumor.[11] The tumour is rare in children, peak age of occurrence is between 40 and 60 years, with equal gender predilection.[10] Two-third to three-quarter cases are benign in nature and do not show gross or microscopic invasion of surrounding structures. Capsular invasion is surrogate marker of malignant nature of the thymomas, which is a rarity. Invasive thymomas show local invasion, local recurrence following removal and rarely lymphatic and hematogenous spread. Pleural seeding and obstruction of superior vena cava are two rare manifestations of local invasion of invasive thymoma. Here, we report a case of superior vena caval obstruction (SVCO) and ipsilateral pleural effusion due to malignant thymoma in 53-year-old male teacher.

CASE REPORT

This was a case report of a non-smoker, non-alcoholic 53-year-old male patient presented with gradually progressive breathlessness at rest and dry cough for last 8 months. He also complained low grade, intermittent fever in initial 2 months, which was resolved spontaneously. Recently, he noticed a swelling of face, neck and arm for last 1 month which was gradually progressing and aggravated on lying down position. Cough and shortness of breath were increased in severity in lying down position. He also complained dysphagia, but no hoarseness of voice, hemoptysis and chest pain. The patient was normotensive and non-diabetic and had no past history of pulmonary tuberculosis. There was no history of altered sensorium, convulsion, nausea, visual disturbance and dizziness. History of significant weight loss and anorexia were present. Aspiration of red colored fluid from right pleural space was done and category I regimen of anti-tuberculous drugs (ATD) (rifampicin, isoniazid, pyrazinamide and ethambutol) was advised by local DOTS Clinic, before he was presenting to us. At that time, pleural fluid analysis revealed lymphocyte predominant, exudative fluid with high adenosine deaminase (ADA) value. Ziehl Neelen stain and Papanicolaou stain were negative for acid fast bacilli and malignant cells respectively.

On general survey, clubbing was present, but no pallor, icterus, peripheral lymphadenopathy, cyanosis and
edema were present. Swelling of face, neck and upper extremities of both sides were noticed along with facial plethora, bilateral conjunctival suffusion and edema and engorged, non-pulsatile neck veins on both sides without positive abdomino-jugular reflux. All findings were more pronounced on raising the hands over the head. His axillary temperature was 97°F, respiratory rate 24 breaths/min, pulse rate 110 beats/min, blood pressure 110/80 mmHg and SpO₂ 82% at room air. The patient preferred upright posture without forward bending. Purpuric spot or other manifestations of bleeding disorders or coagulopathy were absent.

On examination of respiratory system, there was restricted movement and fullness of right side of the chest with engorged, tortuous veins over the anterior and lateral chest wall and also over anterior abdominal wall. Accessory muscles of respiration were grossly working and intercostal suction was present. Trachea was shifted to left and apex beat was at the 1 cm lateral to left mid-clavicular line in 5th intercostal space. Measurement of chest expansion was 3 cm. Direction of venous blood flow was from above downwards. On percussion, there was stony dullness from 3rd intercostal space downwards along the right mid-clavicular line, from 4th intercostal space downwards along mid-axillary line and from 6th intercostals space downwards on the back. Sternal percussion was dull (anterior D’Espine sign was positive). On left side, resonance note was noted; Traube’s space was tympanitic which was present in 6th and 7th intercostals spaces. On auscultation, diminished vesicular breath sounds were audible over right infraclavicular, axillary, lower interscapular areas, breath sounds were absent over right mammary, infra-axillary and infra-scapular areas. On left side, normal vesicular breath sound was audible in all areas. Bronchial breath sound was noted in upper interscapular area, below the fourth thoracic spine (posterior D’Espine sign was positive). No added sounds were audible in any areas. Vocal resonance was diminished over all areas of right side, except suprascapular and upper interscapular areas. Examination of abdomen revealed no organomegaly, ascites, tenderness and lymphadenopathy. Examination of other systems revealed no abnormality.

Complete hemogram and blood biochemistry were normal. Chest X-ray (postero-anterior view) showed right sided pleural effusion with right para-tracheal mass lesion. Sputum for acid fast bacilli and malignant cells were negative. Spirometry showed restrictive defect. Arterial blood gas analysis showed partial pressure of oxygen 56 mm Hg and that of carbon dioxide 42 mm Hg with bicarbonate value 23 mEq/L. Contrast enhanced computed tomography (CECT) scan of thorax showed anterior mediastinal mass with ipsilateral pleural effusion [Figure 1]. Pleural fluid analysis revealed lymphocytic predominant (95%), exudative red colored fluid with raised values of lactate dehydrogenase (LDH - 1654 IU/L) and ADA (271.9 IU/L). Total cell count was 2,000/cmm. Papanicolaou stain showed predominance of atypical lymphoid cells mixed with few lymphocytes and reactive mesothelial cells. Gram stain and Ziehl Neelsen stain were negative. Pyogenic and mycobacterial culture showed no growth. Closed pleural biopsy was inconclusive. Serum LDH, uric acid and alpha-fetoprotein values were normal. CT-guided fine needle aspiration cytology taken from the mediastinal mass showed high cellularity comprised of monotonous population of small cells having round to slightly irregular nuclei and very scanty cytoplasm arranged mostly in discrete pattern and occasion aggregates in background of blood, favoring the possibilities of lymphoma or small cell carcinoma of lung. CT-guided tru-cut biopsy taken from the mediastinal mass revealed a growth composed of plump epithelial cells having pale eosinophilic cytoplasm and oval nuclei, which show vague rosette formations accompanied by small lymphoid infiltrates. Scanty hyalinized stroma was also found [Figure 2]. This picture was suggestive of thymoma. On immunohistochemistry, it showed positivity for CD20, CD3 and negativity for CD15, keratin and epithelial membrane antigen.
was found that scattered small lymphoid cells were positive for CD3 and 80% tumor cells were positive for Ki-67 and pan-cytokeratin, but negative for CD20 [Figure 3]. Ultrasound of whole abdomen revealed no abnormality. CECT brain showed no metastatic deposits. Hence, Final diagnosis was anterior mediastinal thymoma (World Health Organization type B1) complicated with SVCO and ipsilateral pleural effusion, hence as per thymoma staging system of Masaoka and Koga, our case was stage IVa.[3,4] After the diagnosis, he had a rapidly downhill clinical course due to progressively increasing dyspnea as a result of rapidly increasing pleural effusion and increase in the severity of superior vena caval compression. Ultimately, the patient succumbed to his illness before starting chemo-radiotherapy (RT).

**DISCUSSION**

Most common cause of superior vena cava syndrome and malignant pleural effusion is lung cancer.[9] In this respect, these two presentations are rarely reported in association with thymoma. Histologically, thymomas are of three types: Epithelial type, where 80% of neoplastic cells are epithelially derived, Lymphocytic type, where 80% of neoplastic cells are lymphocytically derived and third one, mixed or lymphoepithelial type. Prognosis usually depends upon the clinical stage of the tumor.[8] However, aggressiveness of the thymoma also depends upon the appearance of the neoplastic epithelial cells and their numerical predominance over lymphocytes.[7] Hence, capsular invasion and adjacent structure involvement are more common in epithelial type and therefore malignant behavior. SVCO and malignant pleural effusion are more common in this type for the same reason. Nearly 40% of thymomas are asymptomatic, 40% patients have local compressive symptoms like SVCO and rest 20% has systemic manifestations.[11] Parathymic syndromes such as myasthenia gravis, pure red cell aplasia, hypogammaglobulinemia etc., may rarely be associated with thymomas,[7,9] which were absent in our case.

On the other hand, in majority, metastatic pleural seeding is characterized by exudative, lymphocyte predominant pleural effusion with low ADA level. Lymphocyte predominant, exudative pleural effusion with high ADA value (>60 IU/L) is seen in tuberculosis, complicated para-pneumonic effusion, empyema thoracis, rheumatoid arthritis, chronic lymphatic leukemia, mesothelioma and lymphoma.[9,10] After extensive search of the literature, we found that very few cases of malignant pleural deposits in thymomas are reported,[11,12] the pleural fluid was exudative and lymphocytic in all these cases, but they have remained silent regarding pleural ADA values. This may be due to the fact that unlike in a tuberculosis-prevalent country like India where ADA value is routinely advised in the evaluation of exudative pleural effusion to confirm or exclude tuberculosis, this may not be the routine practice in the developed countries. Hence, high ADA value is a unique feature of this case. Besides that huge anterior mediastinal mass (clinico-radiologically, in most of the time mistakenly diagnosed as mediastinal lymphadenopathy and variegated appearance indicating necrotizing lymph nodes of tuberculous origin) with lymphocyte predominant exudative pleural effusion with high ADA value frequently provoke the clinicians to start ATD (in fact, Category - I ATD was completed in this case before presenting to us), especially in tuberculosis endemic zones, like our country, but think twice, as misdiagnosis and wrong treatment may lead to adverse outcome. Hence, tissue diagnosis is essential in case of mediastinal mass before starting ATD.

Another interesting point is that combination of mediastinal mass simulating lymphadenopathy and lymphocyte predominant exudative pleural effusion with high ADA and lactate dehydrogenase values in most cases is diagnosed as lymphoma on histo-pathological examination. However, this combination without peripheral lymphadenopathy is unusual in lymphoma. Hence, in our case, absence of peripheral lymphadenopathy helps us to think about the diagnosis other than lymphoma.

Surgical removal of both the tumor and the entire surrounding gland is the primary treatment modality for localized disease.[13] Combined modality approach using RT, cytotoxic chemotherapy and surgical resection is very much effective in case of locally advanced tumor presenting with SVCO.[14] Neoadjuvant RT and chemotherapy lead to significant tumor regression and finally surgical resection of residual tumor results in complete recovery in significant number of the cases.[15] Local palliative RT (30 Gy in 10 fractions) is useful for relieving SVCO with distressing respiratory symptoms.[16] On the other hand, combination chemotherapy, comprising of cisplatin, doxorubicin, vincristine and cyclophosphamide, is helpful in treatment of pleural deposits.[16] In our case, unfortunately the patient succumbed to his illness before staring chemo-RT.
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