CASE REPORT

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Common Presentation with Uncommon Diagnosis: Multifocal Epithelioid Hemangioendothelioma

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ABSTRACT

A young female patient presenting with recurrent hemoptysis, neck swelling, and mediastinal mass mimicking lymphadenopathy was admitted to the Institute of Post Graduate Medical Education and Research and SSKM hospital, Kolkata, India. Clinical features, radiological studies, fibre optic bronchoscopy, and fine needle aspiration cytology from the neck swelling created a diagnostic dilemma until surgical resection and immunohistochemistry reports confirmed the diagnosis of multifocal epithelioid hemangioendothelioma, a rare vascular tumor with intermediate malignancy potential. Because it is a slow-progressing disease and due to the non-availability of standard chemotherapy, the patient, and her legal guardian, opted for palliative care only. She was asymptomatic for four years but again presented with hemoptysis, reappearance of the neck swelling on the same side, and a mediastinal mass compressing the superior vena cava and right pulmonary artery. This report describes the diagnostic problems and therapeutic challenges in the management of this rare tumor over a four-year follow-up period. The clinical course emphasizes the highly unpredictable nature of this tumor.

Epithelioid hemangioendothelioma (EHE) is a rare vascular tumor with an estimated prevalence of less than one in one million. It has an intermediate malignant potential and clinically behaves in an intermediate way between a benign hemangioma and a highly malignant angiosarcoma. It usually involves the liver, bone, lungs, skin, and other soft tissue.[1,2] Single organ involvement is more common than multi-organ involvement (64%).[2] Together the liver and lung (51%) were the most commonly involved organs in those who presented with multi-organ disease, as reported in a series of 264 patients of EHE.[2] The distribution of EHE involving soft tissue as described in a series of 49 cases are extremities (n=32), head and neck (n=6), mediastinum and trunk (n=4, each), genitals (n=2), and the retroperitoneum (n=1).

CASE REPORT

A 16-year-old, normotensive, non-diabetic, and non-atopic female patient presented with a dry cough with scanty mucoid expectoration. She also had a history of small bouts of hemoptysis. Additionally, she had a small swelling on the right side of her neck that had been present for about one year. There was no history of fever, weight loss, chest pain, shortness of breath on exertion, wheeze with seasonal variation, environmental smoke exposure, post-nasal drip, or heartburn. There was no history suggestive of connective tissue disease, nephritis, or menstrual abnormality. She had a single bout of hemoptysis moderate amount of two years prior and was treated with a six-month course of antitubercular drugs (ATD).

On examination, she was in good general health (BMI 23.4 kg/m^2) and afebrile. She had mild hepatosplenomegaly. There was a solitary neck swelling on the right side, which was 1.5 inches in diameter, firm, and non-tender. The swelling was not fixed to an underlying structure or overlying skin. There was no fluctuation or audible bruit over the swelling. Examination the remaining systems, including the respiratory system, revealed no abnormality. The blood biochemical parameters and hematological studies were all within normal limits. The posteroanterior view of the chest X-ray

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revealed a right paratracheal shadow with no parenchymal abnormality and contrast-enhanced computed tomography (CT) of the thorax revealed mediastinal lymphadenopathy and peripherally located non-homogenous opacity [Figure 1]. Ultrasonographic examination of the abdomen showed hepatosplenomegaly with multiple hypoechoic lesions in the liver. A lung function study and bronchoscopy examination were normal. Fine needle aspiration cytology (FNAC) from the neck swelling was done considering lymphoma, sarcoidosis, or disseminated tuberculosis (drug resistant) in the differential diagnosis. However, spindle cells were detected in the hemorrhagic smear raising the possibility of vascular malformation. CT guided FNAC of the parenchymal lesion revealed large atypical cells in a cluster with prominent nucleoli and scanty cytoplasm, which suggests a high possibility of non-small cell carcinoma or carcinoid lesion. However, the procedure was complicated by iatrogenic pneumothorax and massive life-threatening hemoptysis. The patient was resuscitated with intercostal tube drainage and was transfused five units of blood. Considering the intractable

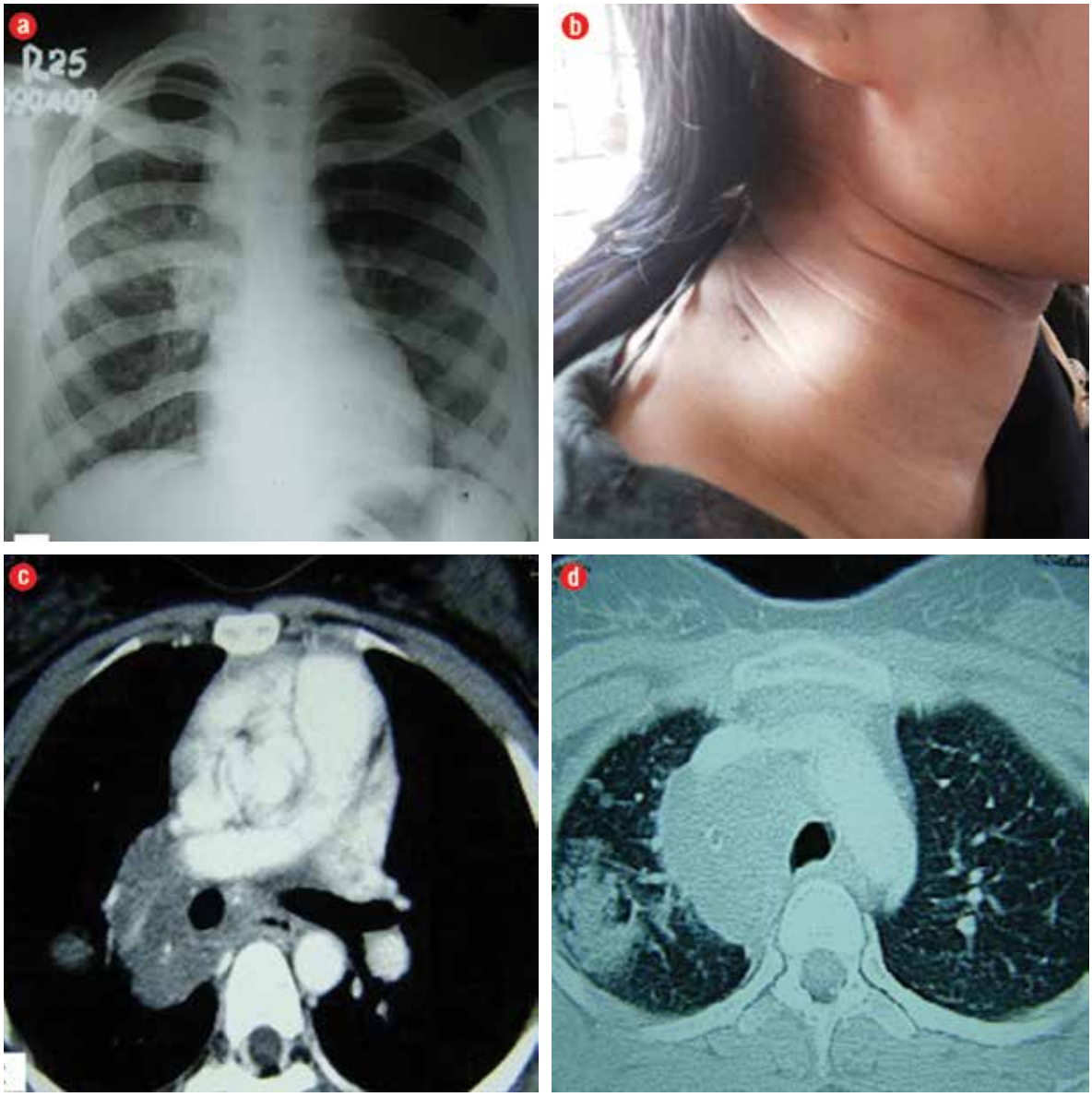

Figure 1: Clinical and radiological findings during initial presentation. **(a)** Chest X-ray posteroanterior view showed right paratracheal and hilar shadow. **(b)** Diffuse swelling of the right side of the neck. **(c)** Contrast-enhanced computed tomography (CT) of the thorax (mediastinal window) showing non-enhancing mass lesion in mediastinum with few calcified foci encircling the right main bronchus. **(d)** Contrast-enhanced thorax CT (lung window) showing parenchymal non-homogenous opacity involving the right upper lobe.

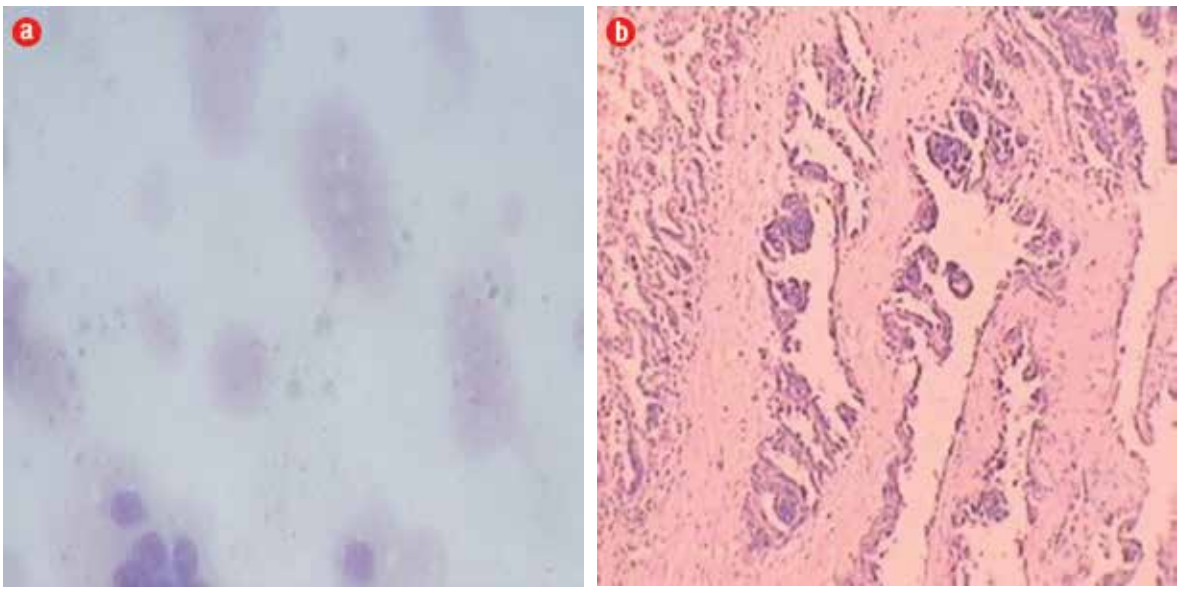

Figure 2: (a) Fine needle aspiration cytology of right supraclavicular swelling showing hemorrhagic smear with occasional spindle cells. **(b)** Histopathology section with hematoxyline and eosin stain showing proliferating endothelium and myxoid stroma, magnification = 40 ×.

hemoptysis and the fact that the patient was otherwise healthy and young, a multi-disciplinany decision was made for surgical intervention. A partial lobectomy of right upper and right middle lobe was performed. However, complete resection was not possible due to extensive adhesion to the surrounding structures.

The histopathological biopsy report of the excised cervical swelling showed a lesion with lobulated appearance where lobules showed the proliferation of blood vessels lined by plump endothelial cells with occasional mitotic figures suggestive of a vasoformative tumor [Figure 2]. The final diagnosis was confirmed to be hemangioendothelioma by immunohistochemistry study of the paraffin-embedded surgical tissue block, which was positive for CD31 and vimentin, and negative for CD34, cytokeratin (CK), epithelial membrane antigen (EMA), smooth muscle actin (SMA), desmin, HMB-45, WT-1, and calretinin. Because it is a slowly progressive disease and due to the non-availability of standard chemotherapy, the patient, and her legal guardian, opted for palliative care only. The patient was asymptomatic during the next four-years follow-up. However, she presented again with the reappearance of neck swelling on the same side and recurrent small bouts of hemoptysis. Contrast-enhanced-CT thorax showed a huge lobulated inhomogeneous enhanced mediastinal mass compressing the superior vena cava and right pulmonary artery along with multiple hypodense lesions in the liver and ascites [Figure 3]. She was discharged on supportive care.

DISCUSSION

This is a unique case of EHE involving the mediastinum, lungs, liver, and soft tissue of the neck in a young female patient, who presented with recurrent hemoptysis and neck swelling. The disease is more commonly reported in the second and third decades of life and approximately equally in both males and females.[2,3] The tumor is frequently diagnosed as an incidental finding.[2,4] Hemoptysis is not a very common presenting complaint. It was reported in only six of 149 patients with EHE who were enrolled in worldwide internet registry over a five year period.[2] Mediastinal hemangioendothelioma is an extremely rare tumor. It usually arises from medium-sized or large veins (e.g., the superior vena cava, azygous vein, and left brachiocephalic vein). They may be diagnosed incidentally in asymptomatic patients with widened mediastinum or may present as superior vena cava syndrome or with features of compression of surrounding structures.[4,5] Pulmonary EHE usually presents as bilateral multiple discrete nodules in young females.[6]

The management of EHE is challenging because of the highly unpredictable clinical course and non-availability of a consensus statement on the

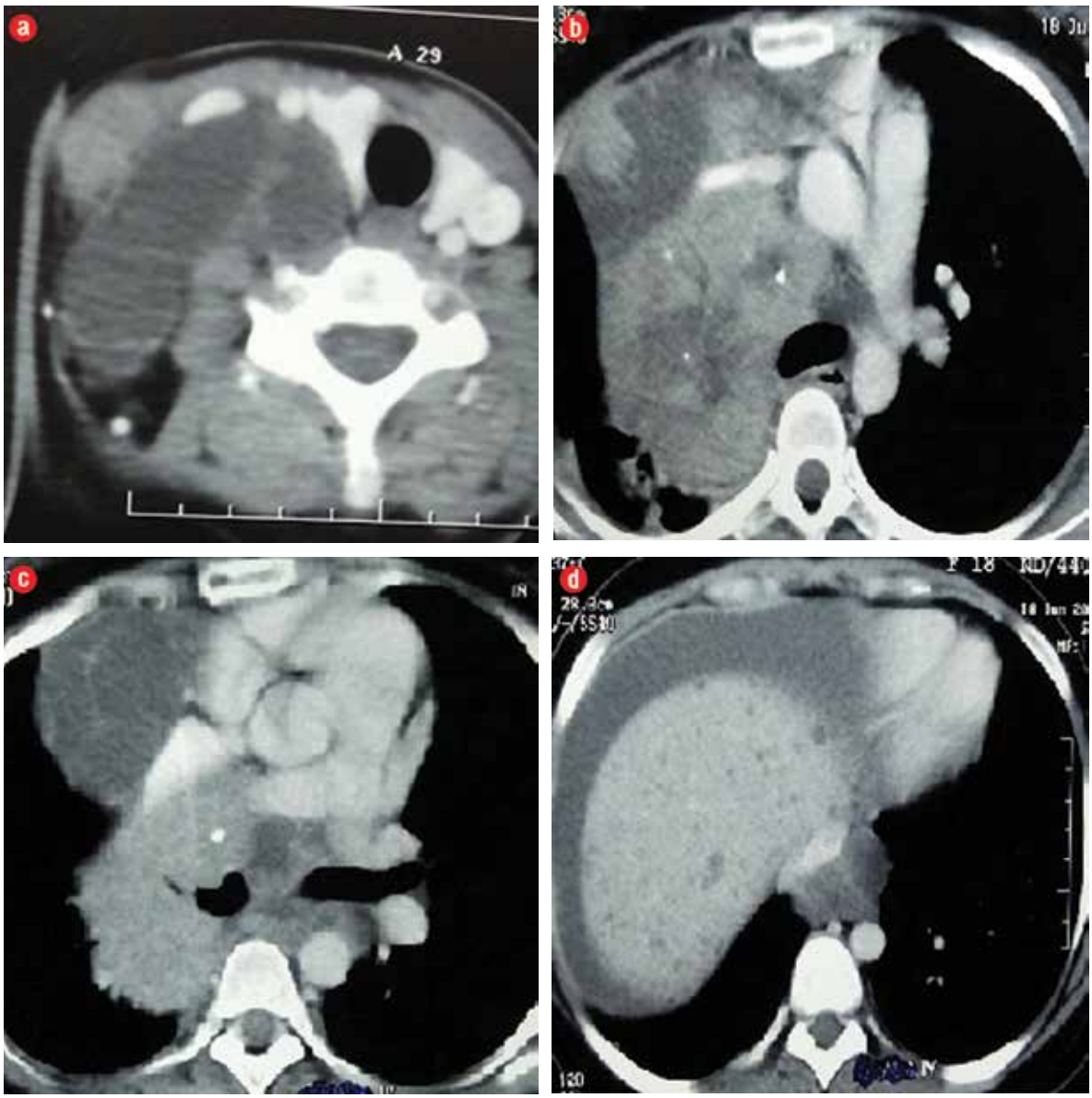

Figure 3: Computed tomography of the thorax after four years showing large lobulated inhomogeneous enhancing mass. **(a)** Extending to the right side of the neck. **(b)** Mediastinal mass lesion occupying retrosternal, prevascular, pretracheal, right paratracheal, precarinal, subcarinal, paraesophageal, right hilar, and infra hilar region. **(c)** Mediastinal mass lesion causing compression and displacement of proximal superior vena cava and right main pulmonary artery. **(d)** Multiple small hypodense lesions in the liver with ascites.

most effective treatment. To date, surgical resection is the most definite treatment option. However, a varied clinical response to follow-up chemotherapy or radiotherapy has been reported.[7] Several reports have shown a good partial response to combination chemotherapy with carboplatin, paclitaxel, and bevacizumab.[8] The tumor may undergo spontaneous regression or may remain stationary for a prolonged period. Okamura et al,[9] reported one such case with multiple bilateral pulmonary EHE surviving over 10 years without treatment though only two of the nodules increased in size and one of them showed activity in an 18-Fiuoro-deoxyglucose (FGD)-positron emission tomography (PET) scan. Certain pathological findings like tumor size over 3 cm, marked cellular atypia, mitotic activity (>1 mitosis per 10 high power fields), and necrosis and extensive spindling are associated with more aggressive disease. Some clinical presentations have been identified as poor predictors of survival in the male population such as presenting at middle age with hemoptysis, uncontained tumor growth and involvement of

three or more bones.[2] Even metastatic disease per se is not associated with poor survival.[2] Radiotherapy could be a less effective treatment option, only in the the presence of bone metastasis. However, opinion varies regarding the optimum dose and schedule of such therapy.[10] Since EHE is a relatively rare tumor condition, long-term follow-up studies are limited.

In our case, it is difficult to comment whether they were multicentric in origin or metastases from a primary lesion. Due to the origin of the tumor in the mediastinum, complete resection was not possible due to extensive invasion to vital structures. No follow-up chemotherapy was administered considering limited information regarding the most effective chemotherapy. However, the patient was asymptomatic for the next four years. Suddenly the tumor started growing at an accelerated rate and presented with huge mediastinal mass extending to the soft tissue of the neck and multiple metastasis in the liver and ascites. A similar situation was reported by Kim et al.[8] Their patient was put on chemotherapy two years after the initial diagnosis. There was no obvious benefit and treatment was ultimately terminated. However, our patient refused chemotherapy for the second time despite progression of the disease.

CONCLUSION

We often overdiagnose pulmonary tuberculosis in tuberculosis-endemic regions even in the era of the Revised National Tuberculosis Control Programme/Programmatic Management of Drug Resistant Tuberculosis (RNTCP/PMDT) program. The clinical course of EHE is unpredictable. Some asymptomatic patients may survive years without any treatment, whereas some may progress dramatically suddenly after apparent quiescence. There is an urgent need for developing a consensus report for management of this rare tumor as more cases are reported.

Disclosure
The authors declared no conflicts of interest.

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