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CASE REPORT

A CASE OF MULTIPLE SOLITARY FIBROUS TUMOR OF THE PLEURA ASSOCIATED WITH SEVERE HYPOGLYCEMIA: DOEGE-POTTER SYNDROME

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ABSTRACT

Solitary fibrous tumor of the pleura is a rare primary intrathoracic tumor that arises from mesenchymal tissue underlying the mesothelial layer of the pleura. It usually has an indolent clinical course. The hypoglycemia that accompanies SFTP was first described by Doege and Potter independently in 1930, hence the eponym Doege-Potter syndrome. The incidence of Doege-Potter syndromeis reported to be about 4%. In this report, we present a typical case of Doege-Potter syndrome that was cured through complete surgical resection.

Keywords: *Solitary Fibrous Tumors; Hypoglycemia, Doege-potter syndrome*

INTRODUCTION

Solitary fibrous tumor of the pleura (SFTP) is a rare, slow-growing tumor that accounts for about 5% of all pleural neoplasms (1). About 80% of SFTPs are benign, and about 50% appear as an asymptomatic mass, which may be discovered in a routine chest X-ray. Symptoms include cough and chest pain, fatigue, weight loss, dyspnea, and fever (2). More rarely hemoptysis, hypertrophic pulmonary osteoathropathy, and hypoglycemia may occur (3). Hypoglycemia occurs in 2-4% of cases (4).The hypoglycemia that accompanies SFTP was first described by Doege and Potter independently in 1930, which explains the eponym Doege-Potter syndrome (DPS). We report herein a rare case of DPS in a patient with multiple solitary fibrous tumors of the pleura.

CASE SUMMARY

A 41 year old male patient presented to us with a chief complaint of shortness of breath of five months duration. The shortness of breath was initially during exertion and later progressed to even at rest. It was exacerbated by lying supine and relieved by sitting up. He also had two months history of recurrent episodes of brief loss of consciousness associated with palpitation and sweating. Otherwise he had no history of cough, chest pain, fever, or weight loss. He was operated 12 years back for biopsy confirmed vascular leiomyoma of the mediastinum and improved. He was relatively well until his current presentation.

Physical examination revealed decreased air entry and dullness over the anterior, lateral, and posterior lower two-thirds of the right chest. Laboratory investigations revealed normal hematologic and chemistry panel except repeatedly low levels of serum glucose level (<50mg/dl). Serum tumor markers like alpha feto-protein (AFP) and carcinoembronyic antigen (CEA) were in the normal range. We were not able to check serum insulin-like growth factor II (IGF-II) level due to unavailability of the test in the hospital. Bronchoscopy showed extrinsically compressed right middle lobe and anterior segment of right upper lobe with endobronchial biopsy suggesting small cell lung cancer.

Chest X-ray showed dense radio opacity in the lower two -thirds of the right hemichest with modest mediastinal widening (Figure 1a). Chest computed tomography (CT) revealed multiple well rounded masses in the right hemithorax and left side of the anterior mediastinum with right smallloculated pleural effusion and chronic internal jugular thrombosis (Figure 1b). CT guided biopsy of the mass showed spindle cells without any specific pattern and suggested solitary fibrous tumor. Imaging studies of the head and abdomen were normal.

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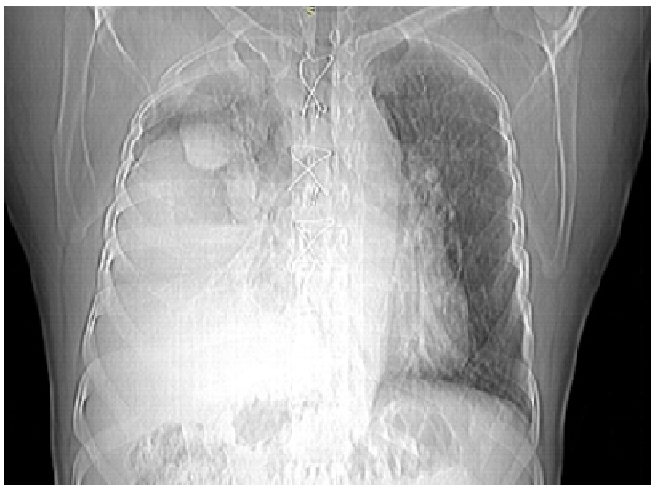

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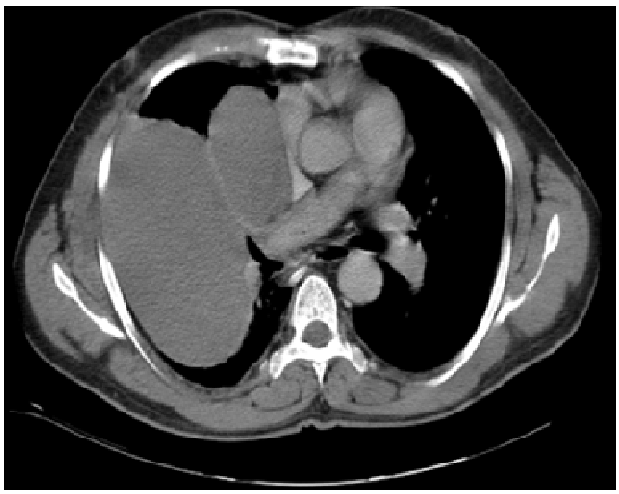

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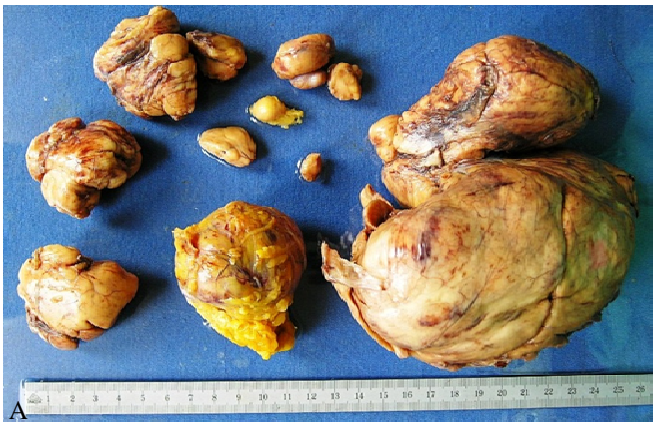
Figure 1(a) Plain chest radiography showed a large opacity in the right hemithorax.
(b) Contrast enhanced CT of the chest revealed multiple homogenously enhancing masses in the anterior mediastinum and the right hemithorax, the largest measuring 10cm.

With the radiologic, histopathologic and clinical impression of fibrous tumor of the pleura the patient was subjected to surgery. The approach was through right lateral muscle sparing thoracotomy. The intra-op finding was multiple lobulated and well circumscribed mass lesions (Figure 2a) in both pleural cavities and on the chest wall under the costal pleura with collapsed right middle lobe.

The left anterior mass was difficult to access hence left for resection after one month. And the specimens were sent for histopathology. The histopathology showed features consistent with solitary fibrous tumor of the pleura (Figure 2, a-d).



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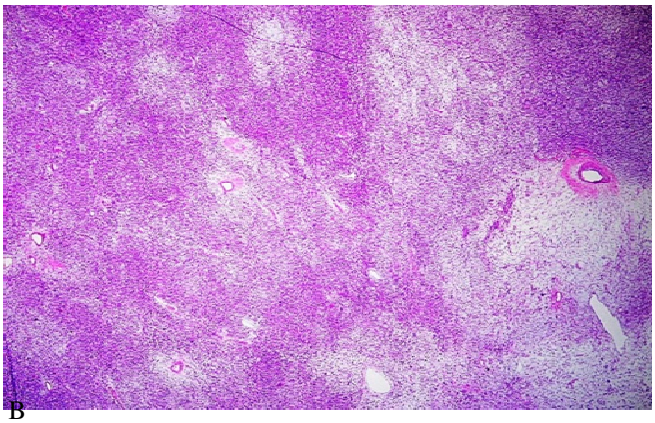

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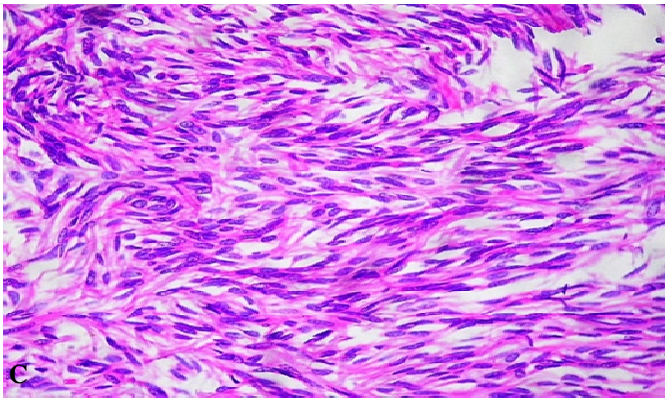

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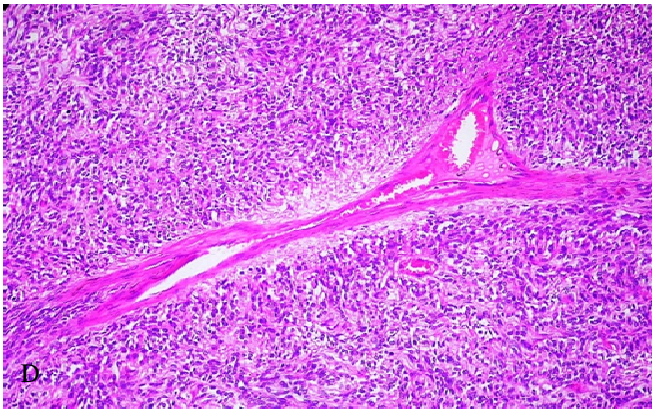

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Fig 2(a-d): Morphologic features of the resected mass. Grossly all the lesions are well delineated and firm (2a). Histologically the tumors are similar. Highly cellular areas alternate with less cellular zones (2b). The tumor cells show regular oval nuclei with coarse chromatin, but without nucleoli and mitotic figures (2c). Many vessels are hemangiopericytoma-like (staghorn), with some hyalinized wall (2d).

DISCUSSION

Primary pleural tumors are histologically divided into two, one is the diffuse type and the other is localized. The diffuse form, considered to be malignant mesothelioma, accounts for 75-90 % of all cases and is associated with asbestos exposure, and well known for its rapidly fatal course (5). Localised (Solitary) fibrous tumors of the pleura are relatively rare benign tumors of the pleura accounting for 8% of benign pathologic diseases of the chest and 10% of pleural neoplasms and are said to have no relation with asbestos exposure. Malignant forms account for approximately12%of all localisedfibrous tumours of the pleura. They are rarely pedunculated and may arise from the visceral or parietal pleura (1). Theyoriginatesfrom the submesothelial mesenchymal tissues. Although SFTP is almost always defined as "solitary", there are few reports of synchronous multifocal tumors in the chest (6-9). Our case is one of these types.

These tumors present with various intrathoracic symptoms (dyspnea, chest pain, and cough) and extra thoracicPara neoplastic symptoms like hypertrophic pulmonary osteoathropathy and noniselet cell tumor hypoglycemia, known as Doege Potter syndrome (DPS), which are exceedingly rare yet important clinical features in terms ofdiagnosis and follow-up. Hypoglycemia associated with these tumors is a rare occurrence, accounting for about 4% of the cases. It is usually associated with slow growing large tumors. About 75% of patients presenting with SFTP and hypoglycemia have a tumor size of more than 10cm(10). In case of our patient one of the tumors were >10cm, but does not appear to be significantly associated with histologicalfeatures of malignancy.

Para neoplastichypoglycaemia results from secretion of an unprocessed or incomplete high molecular weight (HMW) form of insulin-like growth factor type II (IGF-II) (11). This HMW IGF-II is capable of activating insulinreceptor thereby inhibiting hepatic gluconeogenesis and increasing peripheral glucose uptake which results inhypoglycaemia (12). The HMW IGF-II is also capable of binding to IGF-I receptors leading to suppression of growth hormone by the pituitary, as well as reduction of insulin, IGF-I and IGF binding protein-3 by the pancreas (13).

Grossly these tumors are lobulated, well circumscribed sub pleural lesions, with glistering appearance on cross section. Microscopically, SFTP con-sists of ovoid or elongated spindle-shaped tumor cells with varying amounts of cytoplasm (4). An immunohistochemical study is a useful tool for differentiating SFTP from different mesenchymal tumors, sarcomatous mesothelioma, and sar-coma (3,4). Among the immunohistochemical markers, CD34 is very useful and characteristic, as it is often positive in most SFT cases and negative in most other pulmonary tumors. It is only the presence of cellular pleomorphism and mitosis, which differentiate benign from malignant tumors.

It is obvious from the good results reported in the literature that surgery is the treatment of choice for both malignant and benign pleural SFTs including those presenting with hypoglycaemia. Hypoglycaemia almost always completely resolve following surgical excision, usually with no complications, but the symptoms may recur with recurrence of the lesion (14).The local recurrence rate of pleural SFT following surgery is excellent for benign pleural SFT (recurrence rate 2% up to 8%) but varies widely for malignant pleural SFTs with a range of 14% for grossly pedunculated histologically malignant tumours, and up to 68% for sessile histologically malignant tumours, reflecting the importance of complete excision (15).

Most recurrences tend to occur within 24 months of initial resection but may happen even after more than 15-20 years. Therefore long-term follow-up is recommended due to varyingly high recurrence rates particularly for tumours that were difficult to completely excise and have histological features for aggressive or malignant behaviour (3). Hence they should be followed-up with periodic chest CT scans 6 monthly to yearly (16). Malignant transformation in recurrence of previously benign pleural SFT has been reported (2). Surgicalre-excision of the recurrences where possible and remains the preferred treatment (17).

Radiotherapy and chemotherapy have limited value in the curative treatment of pleural SFT because complete surgicalexcision is the best treatment. Nevertheless, radiotherapy and chemotherapy have been advocated for adjuvant treatment when resection is incomplete or impossible especially for histologically malignant tumours, as well as for recurrences (15). Long term survival rates for pleural SFT vary from 75% to 100% in various series (10,15).

In conclusion, DPS is an uncommon paraneoplastic phenomenon with SFTP. In this case, the patient had multiple SFTP. The diagnosis was based on clinical and histopathological pattern. No detailed association with IGF-II mediation was confirmed due to the lack of IGF-II measurements; but considering the large size of the multiple SFTP, and the normalized blood glucose level after the tumor resection, DPS was strongly considered. Although DPS is very rare, its possibility must be considered in cases of refractory non islet cell tumor hypoglycemia. In addition, early diag-nosis and surgical treatment must be performed and complete excision is said to be curative. Chemo-radiotherapy has limited place in those tumors which are not excised completely or histologically malignant lesions.

Consent: A verbal informed consent was obtained from the patient for publication of this Case Report and any accompanying radiologic and histopathology images.

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