

Case Report:

A rare case of malignant solitary fibrous tumour of pleura with Doege-Potter syndrome

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ABSTRACT

Solitary fibrous tumour of pleura (SFTP) is a rare tumor contributing to less than 5% of all pleural tumours and about 10% - 30% of these tumours show features of malignancy. Occurrence of hypoglycaemia with solitary fibrous tumour is an unusual paraneoplastic syndrome designated as Doege-Potter syndrome which can occur both in benign and malignant tumours. Very few cases of solitary fibrous tumour with Doege-Potter syndrome are documented in world literature and only a couple of cases are documented in Indian literature so far. We, report here an interesting case of 40-year-old male who presented with a short history of weakness in left upper and lower limbs following an ischaemic stroke; breathlessness, productive cough, seizures and repeated episodes of loss of consciousness. Laboratory investigation revealed normal serum C-peptide level (1.04 ng/mL) and his blood sugar level was observed to be low varying from 25 mg/dL to 47 mg/dL. Computed tomography (CT) of lung and pleura showed a large mass in right hemithorax for which he underwent right hemithoracotomy. Histopathological examination of the resected thoracotomy specimen along with immunohistochemical analysis confirmed the diagnosis of malignant solitary fibrous tumour of pleura. Basing on the clinical, histopathological and immunohistochemical examination findings, the case was finally diagnosed as malignant solitary fibrous tumour of pleura with Doege-Potter syndrome. The clinico-pathological features and therapeutic management of such rare syndrome are being discussed here.

Key words: Solitary fibrous tumour, Carcinoma, Hypoglycaemia

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INTRODUCTION

Solitary fibrous tumour of pleura (SFTP) otherwise known as localized fibrous tumour is a rare mesenchymal tumour of pleura contributing to less than 5% of all pleural tumours.¹ The tumour is presumed to be of fibroblastic origin and usually arises from submesothelial mesenchymal cells. Occurrence of hypoglycaemia along with solitary fibrous tumour (SFT) is known as Doege-Potter syndrome (DPS) which is a rare paraneoplastic syndrome associated with 5% of SFTs. This hypoglycaemia is designated as non-islet cell tumour hypoglycaemia (NICTH) which is more

commonly associated with mesenchymal tumours, fibrosarcomas, carcinoids, myelomas, lymphomas, hepatocellular and colorectal carcinomas. It occurs due to overproduction of incompletely processed insulin-like growth factor (IGF) II which leads to stimulation of insulin receptor and increased glucose utilization.^{2,3} There are only a couple of reports in Indian literature depicting benign giant solitary fibrous tumour located in pleura and mesentery associated with hypoglycaemia.^{4,5} Here, we report a case of malignant solitary fibrous tumour associated with Doege-Potter syndrome.

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CASE REPORT

A 40-year-old male presented with history of weakness in left upper and lower limb since 6 months following ischaemic stroke with infarct on right-side that was ascertained by computed tomography (CT) of the brain, breathlessness with productive cough and seizure for 2 months. There was history of several episodes of loss of consciousness; each episode lasting for 10-15 minutes following which there was spontaneous regain of consciousness.

There was no history of diabetes mellitus. He was known to have hypertension, epilepsy and was receiving treatment for the same. Laboratory investigations revealed mild anaemia. During his stay in hospital he had repeated attacks of hypoglycaemia with blood sugar levels varying from 25 to 47 mg/dL over a period of 1 week. His serum C-peptide levels were found to be 1.04 ng/ml (Chemiluminescence method, Path Care lab. Pvt Ltd, Hyderabad, India). CT of lung and pleura revealed a large well defined expansile mass measuring 16 x 11.3 cm occupying the entire right hemithorax at middle and lower lobes with areas of calcification and necrosis. The mediastinum was shifted to left and there was mild right pleural effusion. CT brain showed focal hypodense area in left frontal lobe, periventricular deep white matter suggestive of ischaemia due to small vessel disease. CT imaging findings and preliminary histopathological examination of trucut biopsy of tumor were suggestive of solitary fibrous tumour of pleura (SFTP). The differential diagnoses considered were (i) pleural mesenchymal tumour; (ii) large cell carcinoma of lung; (iii) monophasic synovial sarcoma; and (iv) (E-GIST). Right-sided thoracotomy was done. Intra-operatively a solid, firm to hard, multilobular mass of 15.0 x 10.0 cm size was found in lower zone of right hemithorax pushing the diaphragm down abutting pericardium and lung. The tumour was

observed to be arising from pleura with the pedicle identified from posterior chest wall near 10th rib. As the tumour was large it could not be resected *in toto*; hence, it was removed in pieces. There was tumour spillage but capsule was intact. Near total excision of tumour was done and the resected specimen was sent for histopathological examination. His post operative period was uneventful and blood sugars were found to be within normal levels.

Gross examination of the resected specimen revealed multiple pieces of gray white tumor tissue together measuring 32.0 x 24.0 x 9.0 cm and weighing 2200 g; largest bit measured 15.0 x 13.0 x 6.5 cm. Cut-section showed gray white to gray brown solid, firm areas along with focal nodules, cystic spaces filled with mucin and haemorrhage. There were also pieces of pleural membranes which showed focal thickening and at places nodular tumor mass was adherent to it (Figures 1a and 1b). Multiple sections taken from the tumour showed microscopically a partially encapsulated tumour arranged in intersecting fascicles, diffuse sheets and at places exhibiting herringbone/storiform pattern. The tumour was moderately cellular and made up of oval to spindle cells with scanty eosinophilic cytoplasm having ill defined margin showing oval to spindle nuclei with clumped chromatin and mild to moderate nuclear atypia (Figures 2A and 2B). Stromal tissue showed dense band of collagenization (Figure 2C), focal myxoid change along with large areas of necrosis and haemorrhage. Many dilated and congested blood vessels were seen at places revealing staghorn or haemangiopericytoma like vasculature with evidence of perivascular fibrosis (Figure 2D). A number of mitotic figures 8-10/high power field were seen. Tumour was infiltrating into adjacent tissue. Histomorphologically, the tumour was diagnosed as malignant SFT with differential diagnosis of (i) monophasic synovial sarcoma; (ii) monophasic malignant mesothelioma; and immunohistochemistry

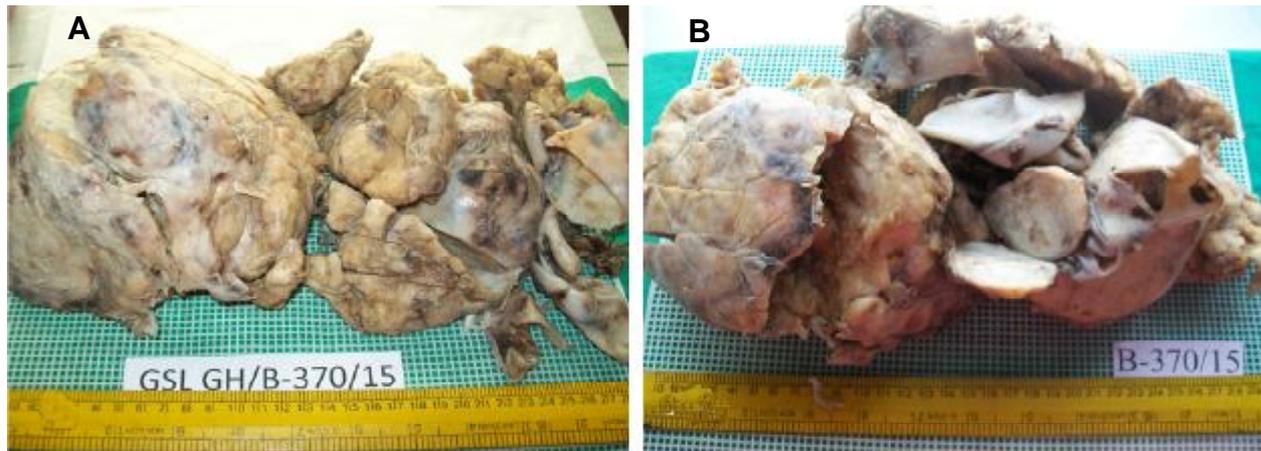


Figure 1: Gross specimen photograph (A) showing multiple pieces of resected tumour. Cut-sections of tumour showing solid nodular areas with focal haemorrhage, nodular masses adherent to pleura (B)

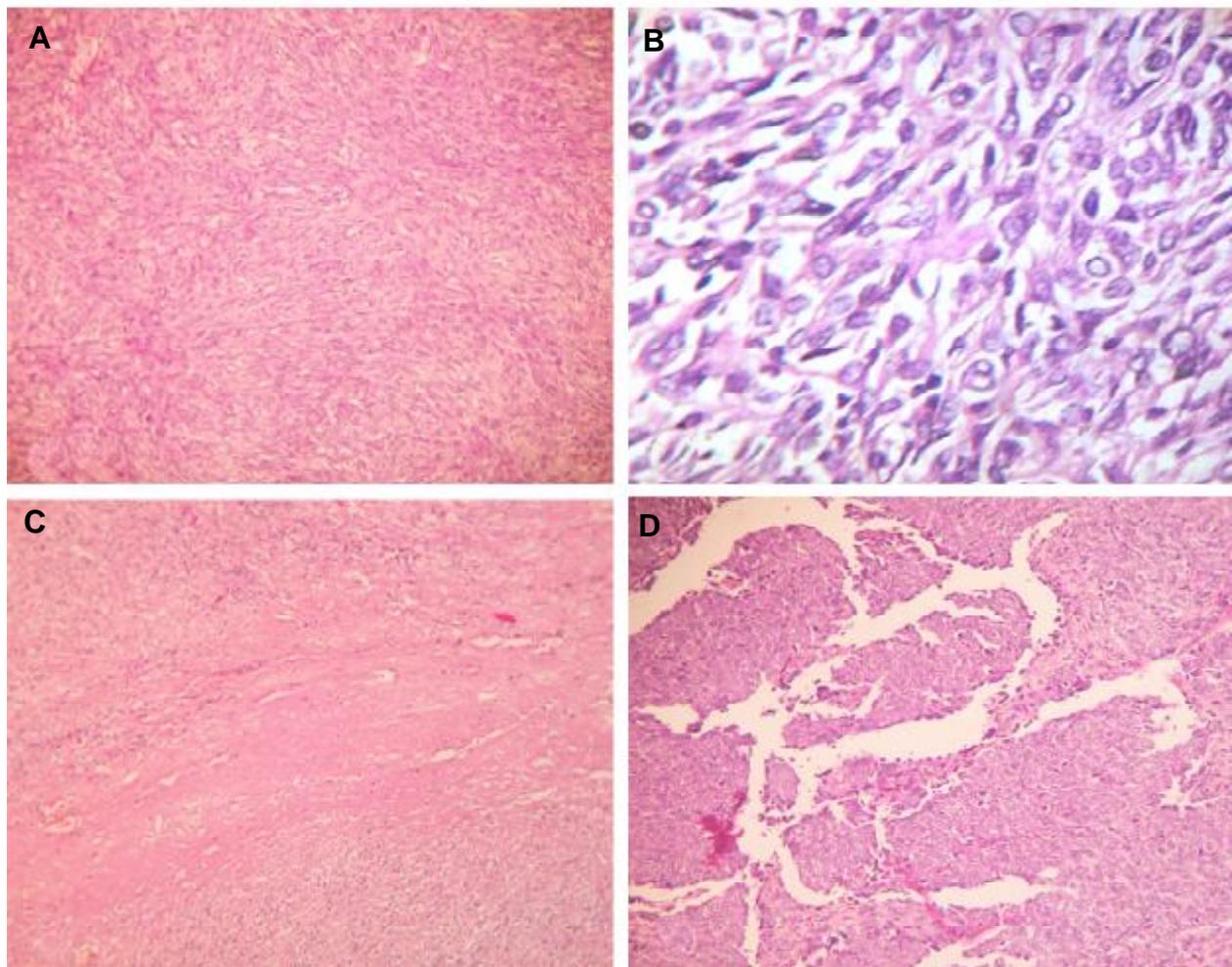


Figure 2: Photomicrographs showing cellular tumour arranged in intersecting fascicles showing storiform pattern (A) (Haematoxylin and eosin $\times 100$); oval to spindle shaped tumour cells exhibiting moderate nuclear atypia (B) (Haematoxylin and eosin $\times 400$); dense band of collagen in stroma (C) (Haematoxylin and eosin $\times 100$), staghorn like vasculature in stroma (D) (Haematoxylin and eosin $\times 100$)

(IHC) was advised. Immunohistochemical marker study revealed strong and diffuse positivity for vimentin (Figure 3A), patchy positivity for CD34 (Figure 3B) in tumour cells which was in favour of SFT. The tumour cells were negative for cytokeratin (CK), epithelial membrane antigen(EMA) and calretinin which excluded possibility of synovial sarcoma and malignant mesothelioma respectively. Hence, finally the case was offered the diagnosis of “malignant SFTP with Doege-Potter syndrome”. He was treated with 3 cycles of temozolamide as adjuvant chemotherapy which is a cell-cycle non-specific, non-classic alkylating agent and administered with a dose of 150 mg/m² per orally for 5 days every 28 days. His last follow-up was in April ,2015 when he was doing well without any further episodes of hypoglycaemia.

DISCUSSION

SFTP is a rare mesenchymal tumour of pleura contributing to less than 5% of all pleural tumours.¹ The most common site of SFT is pleura but it can occur in various other extrapleural sites such as abdomen, kidney, pelvis, head and neck region.⁶ Clinically, these patients are mostly asymptomatic but symptoms of chest pain, breathlessness, cough, fever can be associated with. Nearly 10%-20% of such patients can present with paraneoplastic

syndrome like hypertrophic osteoarthropathy (Pierre-Marie-Bamberger syndrome) and upto 5% cases with refractory hypoglycaemia (Doege-Potter syndrome).^{5,7} Our patient had presented with complaints of dyspnoea, productive cough and repeated episodes of loss of consciousness due to hypoglycemia and CT chest revealed a tumour in the right hemithorax. He was not known to have diabetes mellitus, had a normal serum C- peptide level which excluded the possibility of insulinoma or insulin antibody mediated hypoglycemia.

Preoperative diagnosis of SFT basing on only fine needle aspiration cytology (FNAC) is difficult as there is often difficulty in distinguishing reactive mesothelial cells from well differentiated malignant cells due to lack of well defined cytologic criteria. Hence, it can lead to error in diagnosis. However, ultrasonography guided core needle biopsy combined with IHC analysis might be a safe and rapid method to provide a confirmatory diagnosis. Though SFT fibrous tumours are most often benign but 10% - 30% cases show features of malignancy. The criteria for malignancy is not yet standardized but as per the World Health Organization (WHO) classification of soft tissue tumours, it has been set as hypercellularity, focal moderate to

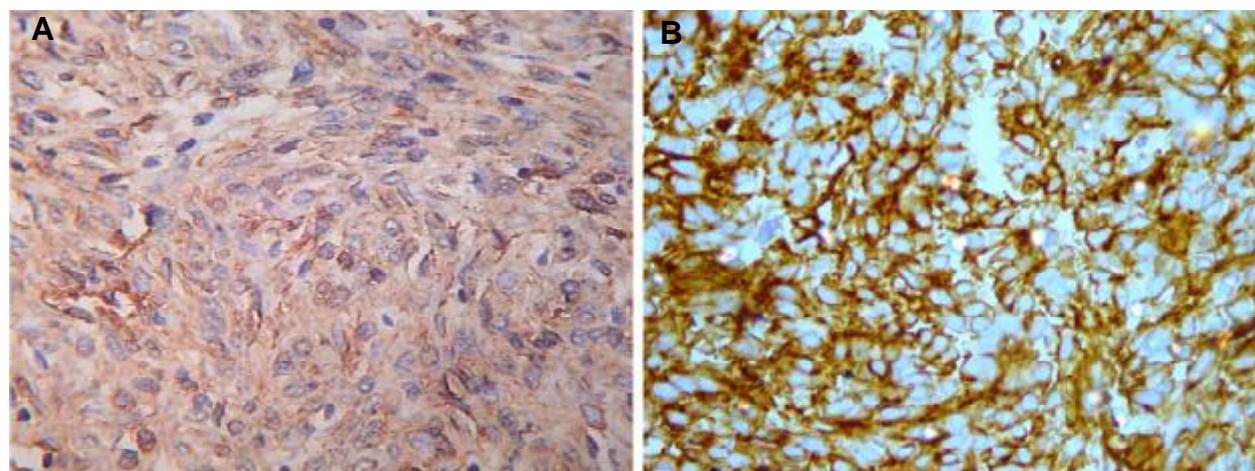


Figure 3: Immunohistochemistry Photomicrograph showing vimentin positivity (A) (× 400), CD34 positivity (B) in tumour cells (× 400)

marked cellular atypia, tumour necrosis, 4 or more mitoses/ 10 high power fields and infiltrative margin.⁸ Hence, FNAC can give a suspicion of malignancy but can not be confirmatory. In the present case, all of these features of malignancy were seen on histopathological examination of excised tumor. The tumor showed patchy positivity for CD34, strong and diffuse positivity for vimentin and negative for CK, EMA, calretinin. Thus, the case was finally diagnosed as malignant SFTP with Doege-Potter syndrome basing on the clinical, histopathological and immunohistochemical examination findings of the resected tumour. Extensive literature search revealed only two documented cases of benign SFT associated with Doege-Potter syndrome in Indian literature; one arising from pleura and the other one from mesentery.^{4,6} Not a single case of malignant SFTP with Doege-Potter syndrome has been so far reported in India, to the best of our knowledge.

It has been postulated that malignant SFT arises either *denovo* or in a pre-existing benign solitary fibrous tumour. The syndrome of hypoglycemia is usually associated with large tumour with high mitotic rate.⁹ The prognostic outcome of these tumours can be predicted by the risk stratification model based on age of the patient, size of the tumour and mitotic index.¹⁰ The metastatic potential of these tumours varies with the sites *i.e.*, malignant solitary fibrous SFTs have propensity to spread intrapleurally and mediastinal sites but rarely outside the thorax whereas abdominal tumours behave more aggressively having tendency for spreading to extraperitoneal as well as to distant sites.¹⁰ Considering the clinical and histopathological features, our case was categorized into high risk group who is at greater risk for metastasis and death. He has received 3 cycles of temozolamide and was asymptomatic without any further episode of hypoglycemia till his last follow-up.

We have reported this case to highlight the clinico-pathological features, biological behaviour as well as the therapeutic management of malignant solitary fibrous tumour of pleura which is rarely encountered in clinical practice. Though this case has been successfully treated by surgery and post operative chemotherapy; being at higher risk for recurrence and metastasis he requires regular follow- up examinations.

Solitary fibrous tumours are successfully treated with surgery. Completeness of initial resection can prevent recurrence and paraneoplastic syndromes usually disappear after complete resection. Since, these tumour show unpredictable biological behaviour, long term follow-up examinations are necessary for early detection of local recurrence or malignant transformation and metastasis.

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REFERENCES

1. Cardillo G, Carbone L, Carleo F, Masala N, Graziano P, Bray A, et al. Solitary fibrous tumour of the pleura: an analysis of 110 patients treated in a single institution. *Ann Thorac Surg* 2009;88:1632-7.
2. Service JF, Hirsch IB, Mulder JE. Non islet cell tumour hypoglycemia. Available at URL: www.uptodate.com/contents/non-islet-cell-tumor-hypoglycemia. Accessed on August 20,2016.
3. Marks V, Teale JD. Tumour producing hypoglycemia. *Endocr Relat Cancer* 1998;5:111-29.
4. Marla NJ, Swethadri GK, Naik CNR, Fernandes H, Chandrasekhar J. Giant solitary fibrous tumor of the pleura (SFTP) associated with paraneoplastic Doege-Potter syndrome. *Indian J Thorac Cardiovasc Surg* 2012;28:26-8.
5. Kuvda R, Monnappa V, Rao A. Giant solitary fibrous tumor of mesentery: A rare case. *J Can Res Ther* 2011;7:376-8.

6. Bishop JA, Rekhtman N, Chun J, Wakely PE, Ali SZ . Malignant solitary fibrous tumor- cytopathologic findings and differential diagnosis. *Cancer Cytopathol* 2010;118:83-9
7. Roy M, Burns MV, Overly DJ, Curd BT. Solitary fibrous tumor of the pleura with hypoglycemia: the Doege-Potter syndrome. *J Ky Med Assoc* 1992;90:557-60.
8. Guillou L, Fletcher JA, Fletcher CDM, Mandahl N. Extrapleural solitary fibrous tumor and hemangiopericytoma. In: Fletcher CDM, Unni KK, Mertens F, editors. *Pathology and Genetics of tumours of soft tissues and bone*. Lyon: IARC Press;2002:86.
9. Zafar H, Takimoto CH, Weiss G. Doege-Potter syndrome: hypoglycemia associated with malignant solitary fibrous tumor. *Med Oncol* 2003;20:403-8.
10. Demicco EG, Park MS, Araujo DM, Fox PS, Basett RL, Pollock RE et al. Solitary fibrous tumor: A clinicopathological study of 110 cases and proposed risk assessment model. *Modern Pathol* 2012:1298-306.