Case Report:

Retroperitoneal synovial sarcoma presenting as paraneoplastic hypoglycaemia

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ABSTRACT

Synovial sarcoma is a well-recognized malignant mesenchymal neoplasm. Primary retroperitoneal synovial sarcoma is extremely rare and has poor prognosis. There are sparse reports in the literature on the secretory synovial sarcomas. In this report, we present the case of a patient with retroperitoneal synovial sarcoma who presented with recurrent attacks of hypoglycaemia.

Key words: *Synovial sarcoma, Retroperitoneum, Paraneoplastic hypoglycaemia*

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INTRODUCTION

Synovial sarcoma is a malignant mesenchymal neoplasm. It accounts for approximately 5%-10% of all soft tissue sarcomas; 85% to 95% of synovial sarcomas occur in the extremities near the large joints.[1] Only 5%-15% of synovial sarcomas affect the head and neck, mediastinum, abdominal wall, and retroperitoneum.[1,2] Primary retroperitoneal synovial sarcomas are very rare (about 1% of retroperitoneal tumours) and have poor prognosis.[1,2] We present the case of a patient with retroperitoneal synovial sarcoma who presented with recurrent attacks of hypoglycaemia.

CASE REPORT

A 56-year-old male presented with abnormal behaviour early in the morning since 6 months. Symptoms used to get relieved with intake of coffee. He was evaluated by a psychiatrist and was being treated. Later, the patient developed progressive abdominal distension with a dull-aching pain. He was evaluated by a physician and was found to have a large abdominal tumour and was referred for further workup to us. Patient was known to have hypertension and was receiving treatment for the same. There was no history of diabetes mellitus or previous surgery. On examination, the patient had diffusely distended abdomen with dilated veins over the abdominal wall and bilateral pedal oedema. Abdomen had a tense, cystic feel with no fluid thrill or shifting dullness being evident.

On evaluation, his fasting blood glucose during the episode of abnormal behaviour was found to be 45 mg/dL. Computed tomography (CT) of abdomen revealed a large lobulated predominantly cystic mass lesion with solid components measuring 37 × 30 × 28 cm in the central abdomen. No calcification was seen. The mass was displacing the left kidney and ureter anterolaterally. Intra-operatively, there was large retroperitoneal tumour occupying whole of abdomen infiltrating into the hilum of the left kidney and sigmoid mesocolon. No free fluid, enlarged lymph nodes or secondary deposits were evident in the peritoneum. It was suspected that hypoglycaemia could be due to

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paraneoplastic syndrome. Serum insulin, C-peptide and insulin like growth factor-I (IGF-I) levels were found to be 2.84 µIU/mL (reference range <30 µIU/mL);1.90 ng/mL (reference range 1.10-3.20 ng/mL); 120 ng/mL (reference range 106-398 ng/mL) respectively, suggestive of pattern observed in paraneoplastic syndrome. Serum insulin like growth factor-II (IGF-II) levels could not be tested due to non-availability of the test.

Excision of the tumour along with left kidney and sigmoid colon was done. Histopathological examination including immunohistochemistry (IHC) revealed a spindle cell tumour with solid and cystic areas (Figure 1). IHC showed that the cells were vimentin - positive (+++) (Figure 2), calretinin- negative, cytokeratin-focal positive (Figure 3) and S-100 protein negative. A diagnosis of primary retroperitoneal synovial sarcoma, monophasic spindle cell variant was made. Patient had good post-operative recovery. He received chemotherapy (doxorubicin 60 mg/m^2 once every 3 weeks) and is on regular follow-up. Also, blood glucose levels between 3 am and 8 am came to normal after surgery further confirming the fact that hypoglycaemia was due to paraneoplastic syndrome secondary to synovial sarcoma.

DISCUSSION

Synovial sarcoma is most prevalent in adolescents and young adults between 15 and 40 years of age.[3] A primary retroperitoneal sarcoma has been defined as a tumour arising in the retroperitoneal space originative from mesodermal structures exclusively of bony, renal, visceral, adrenal, and pancreatic tissues.[4] The potential origin of retroperitoneal synovial sarcoma is primitive pluripotent mesenchyme. Histopathologically there are two types of synovial sarcomas: biphasic and monophasic. Biphasic type is an admixture of epithelial cells and spindle cells. Monophasic type is composed of either only epithelial cells or spindle cells. The known poor prognostic factors are frequent mitotic figures (>10 or 15

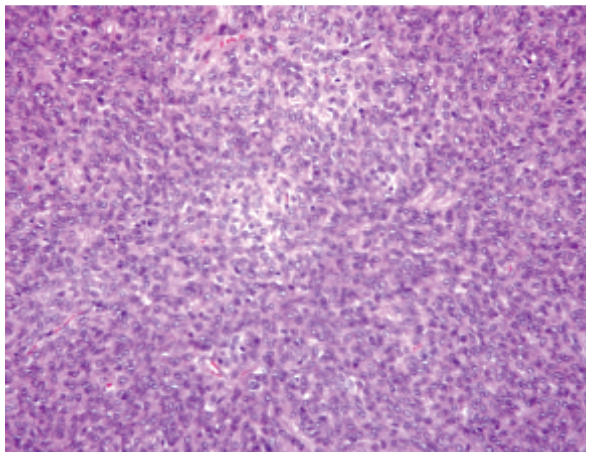

Figure 1: Photomicrograph showing pleomorphic plump to spindle cells arranged in criss- cross and whorly patterns (Haematoxylin and eosin, . 200)

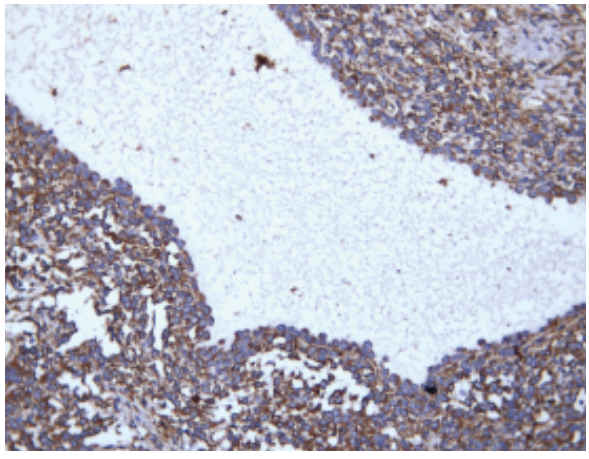

Figure 2: Photomicrograph showing tumour cells exhibiting intense cytoplasmic positivity for vimentin (Immunohistochemistry, . 200)

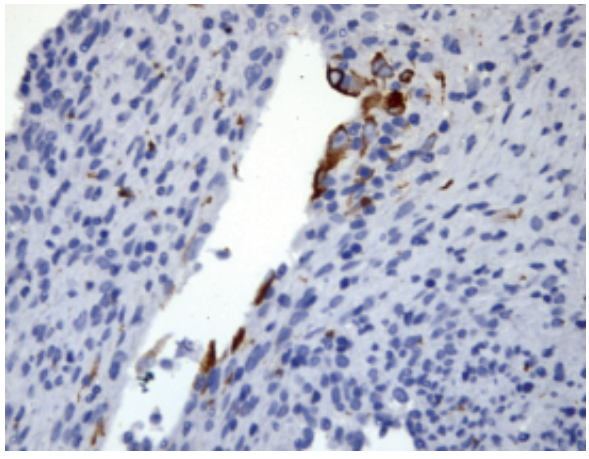

Figure 3: Photomicrograph cytoplasmic positivity for cytokeratin in some of the tumour cells (Immunohistochemistry, . 400)

mitoses per 10 high power field), extensive tumour necrosis and poorly differentiated (small cell) type. Favourable factors are young age of the patient (15 years or younger) and tumour size smaller than 5 cm, and distal rather than proximal location in the extremities.[5] Genetic alteration of significance in synovial sarcoma is t(X; 18) (p11.2; q11.2) on the genes SYT/SSX1 and SYT/SSX2.[6] Synovial sarcomas are IHC positive, at least focally, for cytokeratin, epithelial membrane antigen, vimentin, CD99 and calretinin. Some cases are focally positive for S-100 protein.[7]

CT and magnetic resonance imaging (MRI) are helpful in predicting resectability, detecting distant metastases, and evaluating response to treatment. Definite pre-operative diagnosis is made only on pathological characteristics of tumour on biopsy.[8]

Data suggest that the IGF-II/IGF-1R pathway is involved in the development and aggressiveness of synovial sarcomas.[9] Several types of soft tissue sarcomas are relatively often associated with hypoglycaemia due to the massive secretion of incompletely processed forms of pro-IGF-II, called 'big'-IGF-II. This form of paraneoplastic hypoglycaemia is called non-islet cell tumour-induced hypoglycaemia (NICTH). Solitary fibrous tumours are one of the most common mesenchymal tumours associated with hypoglycaemia. Other sarcomas are mesotheliomas, leiomyosarcomas and fibrosarcomas.[10] Tumours causing hypoglycaemia are usually large (diameter >10 cm).[11] They lead to hypoglycaemia as a result of excessive stimulation of the insulin receptor.

Surgical ablation remains the mainstay of management of retroperitoneal sarcomas, but complete resection rate is approximately 50%.[12] Post-operative margin status is the most important factor contributing to long term disease free survival. Post-operative radiotherapy should be considered following resection with microscopically positive margin or gross residual disease. Adjuvant chemotherapy following Ro resection is not proven. Chemotherapy with single or combination regimen is advised in advanced, unresectable or metastatic disease. A single institution study[13] of 100 patients treated with doxorubicin and/or ifosfamide showed a median survival of 22 months; single-agent doxorubicin or ifosfamide achieved responses in 25% of patients treated, but combination therapy achieved a response rate of 58%. The recurrence rate ranged from 28% to 36% even with adequate surgical and adjunctive therapies.[13] The reported 5-year survival rates of synovial sarcoma range from 25% to 51%.[4]

Retroperitoneal secretory synovial sarcomas are very rare. Even though the data suggests paraneoplastic hypoglycaemia can occur with tumours such as mesothelioma, haemangiopericytoma, fibrosarcoma, leiomyosarcoma, gastrointestinal stromal tumour (GIST), tumours of neuroendocrine and haematopoietic origin etc., occurrence of paraneoplastic syndrome, such as, hypoglycaemia with synovial sarcoma has not been reported. In our patient clinical and biochemical evidence of hypoglycaemic attacks which were relieved with the excision of the tumour could be documented.

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