

Case Report

***De novo* adrenal malignant peripheral nerve sheath tumor in a young female. An orphan disease**

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ABSTRACT

Tumors arising from the adrenal gland are not uncommon. Most of these are benign diseases. Most malignancies of the adrenal gland are carcinomas and usually diagnosed at an advanced stage with a guarded prognosis. Malignant Peripheral Nerve Sheath Tumor (MPNST) of the adrenal gland is an extremely rare pathology, mostly seen amongst patients with Von Recklinghausen's disease. Only eight cases of MPNST of the adrenal gland have been reported in the literature till date with only one case reported to be arising De Novo. Differentiation of this entity from other tumors of the adrenal gland becomes imperative in view of the various diagnostic and therapeutic implications. Moreover, the tumor size and pattern of expression for certain immunohistochemical markers may serve as independent predictors of aggressiveness. Herein we present the case of a 14 years old female who presented with a large right adrenal gland malignant peripheral nerve sheath tumor. With the nature of clinical presentation of this tumor, it is easy for the surgeon to be confused with any other adrenal tumor that tends to be benign. Differentiation of this entity from other soft tissue sarcomas and gastrointestinal stromal tumor of the adrenal gland becomes imperative in view of various diagnostic and therapeutic implications.

Keywords: Adrenal tumors, MPNST, Rare tumors, Orphan disease, Pheochromocytoma, Ganglioneuroma, Adrenal adenoma, Adrenal carcinoma

INTRODUCTION

Malignant Peripheral Nerve Sheath Tumor (MPNST) of the adrenal gland is an extremely rare pathology. Mostly seen in patients with Von Recklinghausen's disease and in association with pheochromocytoma. Only eight cases of MPNST of the adrenal gland have been reported in the literature till date with only one case reported to be arising De Novo. Moreover, the tumor size and pattern of expression for certain immunohistochemical markers may serve as independent predictors of aggressiveness. Herein we report the case of a 14 years old female who presented with a large right adrenal gland malignant peripheral nerve sheath tumor. It is the second

documented case of De Novo origin of MPNST in an adrenal gland.

Most tumors of the adrenals are benign and need only surgical resection. Malignant diseases are relatively uncommon and mostly present in an advanced stage with a guarded prognosis. MPNST is a rare form of sarcoma that arises from the soft tissue around nerves. Most malignant peripheral nerve sheath tumors arise from the nerve plexuses that distribute nerves into the limbs.¹ Neural crest cell origin of adrenal medulla imposes the risk of development of neuroendocrine tumors in the suprarenal space. Differentiation of this entity from other soft tissue sarcomas and gastrointestinal stromal tumor of

the adrenal gland becomes imperative in view of various diagnostic and therapeutic implications.

CASE REPORT

We present a case of a 14 year old female who presented with dull aching pain in the right hypochondrium and a vague mass for two months. There was no history of Headache, Palpitations, Diaphoresis, Flushing, or any mass effect.

On examination

Patient was average build with an unremarkable general examination. Per abdominal examination revealed no tenderness but a vague lump of size 6 x 6 cm in the right hypochondrium that moved very little with respiration. It was not bimanually palpable, nor was it ballotable. Per rectal examination was within normal limits.

Radiological investigations

Ultrasound examination showed a heterogeneous mass lesion of size 6 x 6 cm in the right supra renal position with minimal vascularity and the right kidney was morphologically normal. CT scan suggested a heterogenously enhancing mass lesion with central necrosis. The mass was found to abut the right lobe of liver and hepatic flexure. The tumor had displaced the inferior vena cava antero-medially (Figure 1).



Figure 1: CT abdomen showing the tumor with its relations to adjoining viscera.

Intervention

Patient was explored under general anaesthesia by a midline approach and the tumor resected enbloc with no injury to adjoining adhered structures. The tumor was

found to be adhered to the adjoining portion of IVC. However resection was done without any vascular injury. Patient was discharged on 12th post-operative day without any complications and is doing well after 2 months of follow up (Figure 2 and 3).



Figure 2: Intraoperative view of the tumor and surrounding viscera.

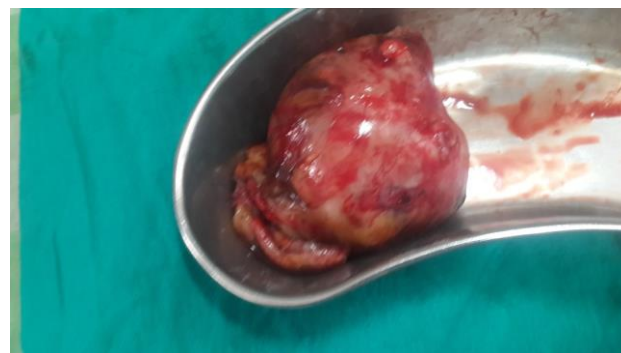


Figure 3: Enbloc resection of the tumor.

Pathological analysis

The entire adrenal gland was replaced by the tumor, which measured 12 x 10 x 8 cm; the capsular surface was smooth and tan-white with patchy areas of haemorrhage. The cut surface was tan-white, fleshy with intervening yellowish gelatinous areas. Focal small areas of haemorrhages and necrosis were present.

Microscopy showed a variably cellular spindle cell neoplasm with hyper- and paucicellular areas. The neoplastic cells were arranged in short and long interlacing fascicles (Figure 4). The tumor had a low mitotic count with 2-3 mitoses/10 HPF. Foci of necrosis

(approximately 20% of the tumor) and scattered inflammatory cells were identified. A battery of immunohistochemical stains were performed, which included smooth muscle actin (SMA), S100, desmin, CK (AE1/AE3), EMA, CD117, CD34, chromogranin, synaptophysin, HMB 45 and Ki-67. The tumor cells showed diffuse and strong immunoreactivity for S100 [Figure 5] and also for NSE (Figure 5). The tumor cells were negative for SMA, desmin, CK (AE1/AE3), EMA, CD117, CD34, chromogranin, synaptophysin and HMB 45. Based on the morphology and immunohistochemistry profile a diagnosis of MPNST was established.

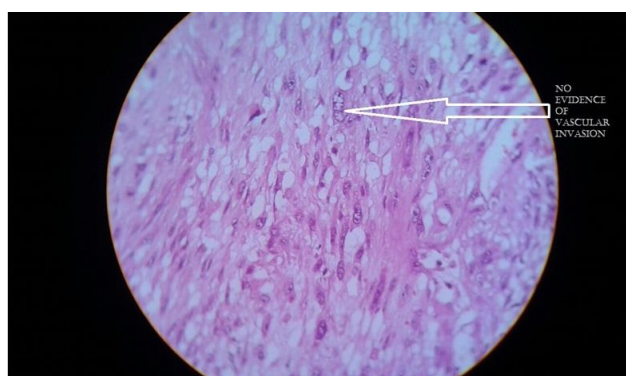


Figure 4: Light microscopy showing tumor cells.

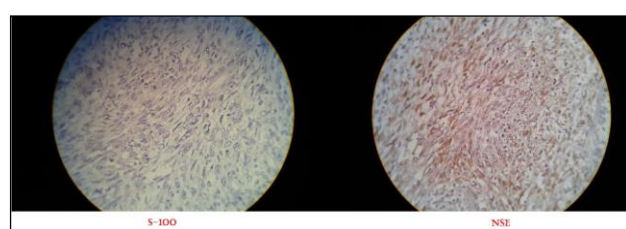


Figure 5: Immunohistochemistry of tumor cells showing S-100 and NSE positivity.

Response to treatment

No complications occurred during and after surgery and the patient was discharged on the 12th postoperative day. Patient is doing well after 2 months of surgery on follow up.

DISCUSSION

Soft tissue tumors involving the adrenal gland are relatively uncommon and primarily include benign mesenchymal neoplasms such as hemangioma, leiomyoma, schwannoma and neurofibroma while sarcomas are extremely rare. The various malignant mesenchymal tumor of the adrenal gland are angiosarcoma, leiomyosarcoma and MPNST. MPNSTs are reported to arise either *de novo* or in association with neurofibromatosis particularly in the spectrum of Neurofibromatosis type 1.² There are few cases of

MPNST of the adrenal gland reported arising within a ganglioneuroma, which are considered to be induced by radiation therapy.³ Reports of composite tumors with dominant pheochromocytoma and small elements of MPNST have been reported.⁴ Neoplasms with spindle cell morphology and low mitosis suggests a low grade sarcoma. Immunohistochemical studies with a panel of antibodies are useful to discriminate different spindle cell malignancies, highlighting heterogenous nature in case of composite tumor. The tumor cells of MPNST are usually positive for neural markers S-100, NSE, CD56, protein gene product 9.5 (PGP 9.5). In high grade MPNST, S-100 tends to be focally positive, unlike our case where diffuse S-100 activity was seen. The panel of antibodies that usually used to rule out differentials are Desmin, SMA, CD117, CD34, Inhibin, CK, EMA, HMB 45 and Chromogranin, Synaptophysin (Pheochromocytoma).

MPNST is a markedly aggressive tumor with high metastatic potential and poor prognosis. Majority of reported case developed metastasis or recurrence during follow up. PET-CT scan can be helpful for early detection of the same.

Zou et al., have described few predictive factors for development of metastasis and aggressiveness of the disease.⁵ Tumor size ≥ 10 cm, nuclear p53 positivity and lack of S-100 immunoreactivity in tumor cells are independent prognostic factor for aggressiveness. Considering the size of the tumor, the present patient falls into high risk category.⁶

MPNSTs are currently treated as other soft-tissue sarcomas, because they are too rare to perform trials with a sufficient number of patients. Overall survival with MPNSTs is poor, and the usual chemotherapy used for soft-tissue sarcomas does not improve the outcome. Recent advances in the molecular biology of MPNSTs may provide new targeted therapies.⁷

CONCLUSION

With a currently 'Orphan disease' status of Adrenal MPNST's, complete management of patients is not possible owing to the lack of scientific data. It is necessary for us Surgeon's to keep this diagnosis in mind in patients presenting with tumors of suprarenal origin, who do not demonstrate any evidence of hyperadrenalism and radiological findings are inconsistent with malignancy. Further research is advocated to delineate chemotherapy protocols to establish an appropriate management strategy for the disease.

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