Case Report

Malignant peripheral nerve sheath tumor with divergent differentiation

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ABSTRACT

A malignant peripheral nerve sheath tumor (MPNST) is an uncommon spindle cell sarcoma accounting for approximately 5% of all soft tissue sarcomas. A 55-year-old female with a right suprarenal tumor showed MPNST with additional foci of epithelioid, rhabdomyoblastic, osteogenic and lipogenic differentiation. Although the capacity of MPNST to undergo epithelioid, rhabdomyoblastic, osteogenic and very rarely lipogenic differentiation is reported in literature, the occurrence of all these differentiation in one case has not been described in literature before. To the best of our knowledge, this is only the second MPNST case with lipomatous differentiation.

KEY WORDS: Divergent differentiation, epithelioid MPNST, malignant triton tumor, malignant peripheral nerve sheath tumor

INTRODUCTION

A malignant peripheral nerve sheath tumor (MPNST) is a spindle cell sarcoma arising from Schwann cells or within neurofibromas. MPNST accounts for approximately 5% of all soft tissue sarcomas.[1] About half of these tumors arise denovo and the other half has a strong association with Type 1 Von Recklinghausen's disease. The capacity of peripheral nerve sheath sarcomas to exhibit other than Schwannian or fibroblastic differentiation was first reported by Garre in 1892.[2] We report an unusual case of MPNST with epithelioid, rhabdomyoblastic, osteogenic and lipogenic differentiation.

CLINICAL SUMMARY

A 55-year-old female presented with a gradually enlarging abdominal mass of 2 years duration associated with pain for the past 6 months. On examination, a firm irregular mass was seen in the right lumbar region. There was no evidence of Von Recklinghausen's disease. An ultrasonography and computed tomography (CT) scan showed a large heterodense solid mass with areas of calcification and necrosis in the right supra renal region. Pre-operatively, the mass couldn't be easily separated from the kidney; hence the excision of the suprarenal mass with right nephrectomy was done.

Pathological findings

A gross examination showed a large encapsulated grey-brown tumor in the upper pole of the kidney measuring 20 x 15 x 12 cm. The surface was bosselated with nodular areas. A cut section showed white, fleshy, lobular tumour tissue with extensive areas of hemorrhage and necrosis. The tumor was separated from the kidney by a capsule. The right kidney measured 11 x 6 x 5 cm. A cut section showed no gross abnormalities.

Microscopy

The neoplasm was predominantly composed of spindle cells arranged in interlacing fascicles, whorls and a palisiding pattern [Figure 1A]. The tumor showed variable cellularity consisting of densely cellular fascicles alternating with hypocellular and myxoid areas. Spindle cells showed hyperchromatic nuclei with indistinct pale cytoplasm and increased mitotic activity (6 per high power field). A few round plump cells with brightly eosinophilic cytoplasm and hyperchromatic nuclei were seen admixed with neoplastic spindle cells [Figure 1A, inset].

The other predominant tumor cell type was large round to polygonal cells with acidophilic cytoplasm and prominent nucleoli giving an epithelioid-like appearance [Figure 1B]. These cells were arranged in nodules, sheets, or in a nesting pattern-mimicking pheochromocytoma-like areas. Hence, in the early evaluation of this tumor, a possibility of MPNST with pheochromocytoma (composite pheochromocytoma) was considered, but subsequent immunohistochemistry excluded this possibility.

In addition, focal areas of osteogenic differentiation [Figure 1C], lipomatous tissue [Figure 1D] and myxomatous change were also seen. On histology, the kidney showed no significant morphological abnormalities.

Immunohistochemistry stains using S-100, Desmin, Myo D1 (myogenic determination) and chromogranin antibodies were done. S-100 showed focal positivity in spindle cell areas. Epithelioid-like areas showed

diffuse and strong positivity for S-100 [Figure 2A] and negative for chromogranin antibodies suggesting an epithelioid type of MPNST and ruled out the possibility of composite pheochromocytoma (MPNST with pheochromocytoma). Round plump cells showed positivity for Desmin and Myo D1 [Figure 2B] suggesting rhabdomyosarcomatous differentiation.

DISCUSSION

MPNSTs are uncommon spindle cell sarcomas that appear in the setting of neurofibromas or schwannomas and are associated with peripheral nerves. The estimated incidence of MPNST in patients with Nerurofibromatosis Type 1(NF1) is 2–5% as compared with 0.001% in the general population. The most common anatomical sites include proximal portions of upper and lower extremities, the trunk arising from the sciatic, the brachial plexuses and the sacral plexuses, respectively. Most MPNSTs are high-grade sarcomas with a high likelihood of producing local recurrences and distant metastasis. Large tumor size (>5 cm), the presence of neurofibromatosis and a total resection are the most important prognostic indicators of MPNST.[3] Structural abnormalities of chromosome 17 involving the NF1 and p53 loci are common in MPNSTs.

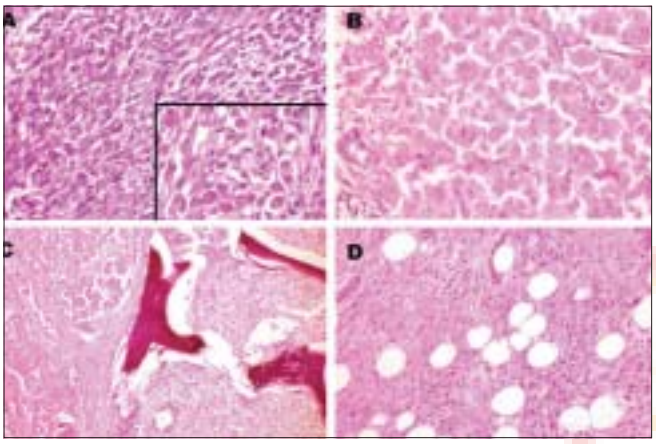

Figure 1: Tumour is composed of spindle cells (Fig 1A); round plump cells with brightly eosinophilic cytoplasm (Fig 1A inset); Epithelioid like cells (Fig 1B); osteogenic areas (Fig 1C) and lipomatous components (Fig 1D) (H&E, x400)

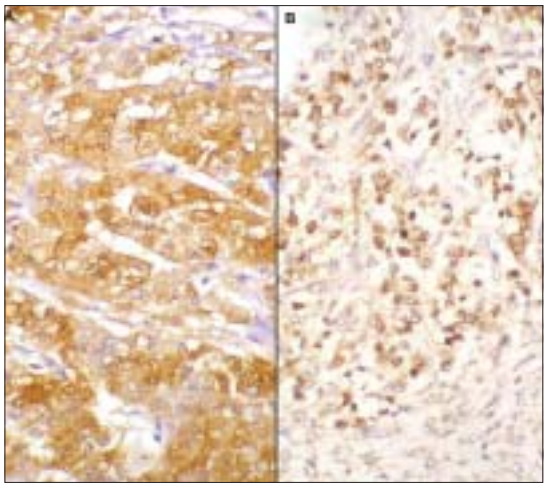

Figure 2: Epithelioid component showing Diffuse and strong positivity for S 100 (Fig 2A); Rhabdomyoblastic component showing strong positivity for MyoD1 (Fig 2B) (x400)

MPNSTs occasionally show histological evidence of focal divergent differentiation to rhabdomyosarcoma, osteosarcoma, chondrosarcoma, angiosarcoma, epithelial elements or in combination. Ducatman, *et al.* noted divergent differentiation in 19 out of 120 MPNST cases (19%) and the presence of divergent differentiation did not significantly affect the prognosis.[3] Mature islands of bone and cartilage are the most common heterologous elements in MPNSTs.

Malignant triton tumor (MTT) refers to MPNSTs with rhabdomyosarcomatous differentiation. Rhabdomyosarcoma is the most frequently encountered example of divergent differentiation in MPNSTs.[4] Nearly 70% of patients with MTT have NF 1 and the prognosis is poor as compared with classical MPNSTs with 2 and 5-year survival rates of approximately 33% and 12% respectively.[5]

Less than 5% of MPNSTs show epithelioid differentiation. Epithelioid-like components show strong positivity for S-100 as compared with focal positivity seen in classical MPNSTs. They show less association with NF1.[6] Interestingly, most of the MPNSTs that have arisen from the malignant transformation of benign Schwannoma have been of the epithelioid type.

A few cases of MPNST with foci of glandular differentiation are reported in the literature.[7] A total of 75% of patients have NF 1 with a high mortality rate. A single case of MPNST with liposarcomatous component is noted in the literature.[8]

The finding of these heterotrophic elements in nerve sheath sarcomas is believed to illustrate the differentiating capacity of neuroectodermal tissue. The occurrence of mesenchymal differentiation in primary tumors of the central nervous system, such as intracerebral and meningeal rhabdomyosarcomas, gliomas with muscle, bone and cartilage provide additional supportive evidence.[9,10]

Although the capacity of MPNSTs to undergo epithelioid, rhabdomyoblastic, osteogenic and very rarely lipogenic differentiation is reported in literature, the occurrence of all these differentiation in the same case has not been not described in literature before. To the best of our knowledge, this is only the second MPNST case with lipomatous differentiation. Diagnostically, it is crucial to recognize the "primary" sarcoma in such tumors correctly and distinguish it from the "secondary" divergent elements, so as to avoid diagnostic errors.

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