Malignant peripheral nerve sheath tumour with perineurial differentiation and hyaline eosinophilic globules (thanatosomes): A rare tumour

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Abstract

Malignant peripheral nerve sheath tumour (MPNST) with perineurial differentiation is a rare variant of MPNST. The pathological features and clinical significance of this variant remain to be characterised. We reported the clinicoradiological and pathological features of a case of recurrent right arm mass related to the ulnar nerve in a 42-year-old female patient. On pathological examination, the tumour showed dual features of conventional and perineurial MPNST which was proven by positive immunostaining for S-100 and EMA. The pathological diagnosis was MPNST with perineurial differentiation. In addition, a peculiar and rare finding of intracytoplasmic eosinophilic hyaline globules (thanatosomes) within tumour cells is reported. We document a rare tumour with hybrid features between conventional and perineurial MPNSTs. Further studies are needed to establish its biological behaviour.

Keywords: Malignant peripheral nerve sheath tumor, perineurial differentiation, malignant perineurioma, hyaline globules

INTRODUCTION

Malignant peripheral nerve sheath tumours (MPNST) are uncommon malignant tumours accounting for less than 5% of all malignant soft tissue tumours.¹ They commonly arise from a peripheral nerve or in extraneural soft tissue and show nerve sheath differentiation. Cases associated with neurofibromatosis type 1 (NF1) occasionally exhibit heterologous differentiation in the form of cartilage, bone, or less commonly skeletal muscle (so-called malignant triton tumor).²

A rare variant of MPNST demonstrates histological and ultrastructural features of perineurial differentiation. These tumours are positive for epithelial membrane antigen (EMA) and negative for S100.¹,²

CASE REPORT

A 42-year-old female patient presented with a history of recurrent right arm and forearm mass related to the medial epicondyle and right ulnar nerve with positive Tinel’s sign. The mass was surgically excised five times over a period of 5 years and was diagnosed at an outside medical facility as benign peripheral nerve sheath tumour. No histopathology slides were available for review. There was no clinical evidence or family history of associated NF1.

Two years after the fifth recurrence, the patient presented with a rapidly expanding mass, over a period of two months, in the mid-arm, reaching down to the right elbow. The overlying skin was stretched and thinned out, with engorged superficial veins. The lesion was firm in consistency, very painful and restricting elbow extension. Ultrasonography revealed a sizable subcutaneous highly vascular aggressive soft tissue tumour. Magnetic resonance imaging (MRI) confirmed the presence of a sizable expanding soft tissue tumour (8.5 x 6.5 x 9 cm) with well-defined lobulated outlines and marked post-contrast enhancement. The mass was involving the medial aspect of the distal arm, crossing the elbow joint and extending into
the proximal forearm along the course of distal ulnar nerve without gross muscle infiltration (Fig. 1A).

Operatively, the tumour was greyish in colour showing areas of degeneration. It was surgically removed with a safety margin from the proximal end of the ulnar nerve (Fig. 1B). Histopathological examination revealed a cellular pleomorphic and spindle cell tumour featuring fibrosarcoma-like areas merging with pleomorphic so-called malignant fibrous histiocytoma-like areas. The spindle cells were arranged in fascicles with focal herringbone arrangement and focal marble-like effect created by alternating hypocellular and hypercellular areas (Fig. 2A). Focal subtle storiform and whorled patterns, and focal myxoid matrix were seen (Fig 2B). Nuclear palisading was not detected. Variable nuclear pleomorphism with low grade areas exhibiting thin buckled nuclei was appreciated. The pleomorphic areas were composed of large pleomorphic cells with multinucleated giant forms and frequent intracytoplasmic eosinophilic hyaline globules (Fig 2C). Focally, rhabdoid-like eosinophilic cells were noted. Brisk mitotic activity (>30 mitoses/10 high power fields) including atypical forms and focal apoptosis were observed. Infiltration of fat was focally noted. Focal aggregates of xanthoma cells and focal haemorrhage were seen. The tumour was intimately associated with nerve fascicles with focal entrapment of nerve fibres. A neuroma-like proliferation composed of disorganised nerve fascicles was seen. The resection margin from the ulnar nerve was devoid of tumour involvement.

The provisional diagnosis was high grade pleomorphic spindle cell sarcoma in favour of high grade malignant peripheral nerve sheath tumour (MPNST). Immunostaining for S100 protein showed largely negative tumour cells with only faintly positive few scattered tumour cells (Fig. 2D). EMA immunostaining showed patchy positive membranous staining of spindled and giant tumour cells (Fig. 2E), which implied perineurial differentiation. Tumour cells were negative for cytokeratin (AE1/AE3), glial fibrillar acidic protein (GFAP), desmin, myogenin, and CD34. Proliferative index, assessed by Ki67 immunostaining, was moderately high at 40% (Fig. 2F). Based on the clinicoradiological, histological and immunohistochemical findings, we concluded that this tumour represents a malignant peripheral nerve sheath tumour (MPNST), with perineural differentiation.

**DISCUSSION**

Malignant peripheral nerve sheath tumours (MPNST) are malignant tumours exhibiting nerve sheath differentiation. About half of the cases are sporadic, the rest show association with NF1. The diagnosis of MPNST in our patient was based on the association of the tumour with ulnar nerve together with histopathological findings of spindled and pleomorphic tumour cells. Focal S100 reactivity indicated Schwannian differentiation which is characteristic of
MPNST WITH PERINEURAL DIFFERENTIATION

FIG. 2: MPNST with perineurial differentiation. (A) Marble-like effect created by alternating hypocellular and hypercellular areas of spindled cells (H&E, x100). (B) Vague whorled pattern (H&E, x200). (C) Pleomorphic giant cells with intracytoplasmic eosinophilic hyaline globules (H&E, x400). (D) Focal faint nuclear positivity for S100 (S100, x400). (E) Membranous EMA positivity in tumour cells (EMA, x200). (F) Ki67 highlighting an abnormal mitotic figure (Ki67, x400).

conventional MPNST. The latter, however, lacks EMA expression except in cases featuring perineurial differentiation.

Our current case exhibited features of both conventional MPNST and perineural MPNST (also known as malignant perineurioma). Features favouring conventional MPNST were the intrinsic involvement of the ulnar nerve and the focal weak S100 immunoreactivity. Earlier reports of malignant perineurioma have shown negative staining for S100 and no association with major nerves except in one case (phrenic nerve). Perineural MPNST was suggested by the focal whorled pattern and EMA positivity. We suggest that our case represent a malignant hybrid tumour featuring both Schwannian and perineurial differentiation.

Dual S100 and EMA positivity in MPNST
is a rare finding that was previously reported by Hirose et al.\textsuperscript{3} in 5/12 cases and Sasidharan et al.\textsuperscript{5} in 3/11 cases. Ultrastructurally, cells intermediate between perineurial and Schwann cells were also reported in 1/7 cases of perineurial MPNST.\textsuperscript{3} Previous reports of MPNST with perineurial differentiation demonstrated the presence of EMA-positive multinucleated giant cells\textsuperscript{6,7} which was seen in our case.

EMA-positivity in our case raised the possibility of intraneural synovial sarcoma. However, the lack of pancytokeratin reactivity together with the presence of pleomorphic tumour giant cells and atypical mitoses excluded this possibility. Some tumour cells demonstrated rhabdoid appearance that morphologically suggested rhabdomyoblasts. However, the lack of immunoreactivity for desmin and myogenin excluded MPNST with rhabdomyoblastic differentiation, known as triton tumour. The peculiar neuroma-like proliferation adjacent to the tumour might represent a reactive lesion or intraneural perineurioma. However, EMA staining highlighted the perineurial layer around the nerve fascicles without significant proliferation of EMA-positive perineurial cells.

Hyaline globules, also known as thanatosomes\textsuperscript{8}, were rarely reported in MPNST. Kim et al.\textsuperscript{9} reported a case of recurrent intracranial MPNST with hyaline globules and elaborated that this could represent a degenerative process occurring in association with recurrence. Papadimitriou et al.\textsuperscript{9} studied hyaline globules in various tumours and concluded that they are not specific to any tumour but represent a degenerative phenomenon related to apoptosis, common to all cell types, benign or malignant. Previous reports have advised distinction of perineural MPNSTs from conventional MPNSTs because of its presumed less aggressive biological course.\textsuperscript{3} We report a rare tumour with hybrid features between conventional and perineural MPNSTs. Further studies are needed to establish its biological behaviour.

REFERENCES