Malignant Peripheral Nerve Sheath Tumor Arising in a Neurofibroma: A Case Report

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ABSTRACT

Malignant peripheral nerve sheath tumor (MPNST) is a rare variety of soft tissue sarcoma of ectomesenchymal origin. These tumors present diagnostic difficulties in differentiating from other high-grade spindle sarcomas. This is a case of a 45-year-old lady who presented with pain and swelling in the groin for past 4 months, which on excision and histopathology revealed an MPNST in a neurofibroma.

Keywords: Malignant peripheral nerve sheath tumor, soft tissue sarcoma, ectomesenchymal, neurofibroma

Malignant peripheral nerve sheath tumor (MPNST) is a malignant neurogenic tumor that occurs with high frequency (8-13%) in association with neurofibromatosis type 1 (NF-1), arising either *de novo* or in transition from neurofibroma.[1] It either develops from peripheral nerves, pre-existing benign neurofibromas or schwann cells. NF-1 patients are more frequently diagnosed with MPNST in the third or fourth decades of life, whereas the sporadic form of MPNST is most frequently diagnosed in the sixth or seventh decades of life.

CASE REPORT

A 45-year-old female developed pricking type of pain in the right groin extending to right knee for a duration of 4 months. There was also a history of fever on and off for 1 month. She gave a history of neurofibromatosis for 35 years. On local examination, a large neurofibroma was seen in the right inguinal region. Neurofibromas were also seen in the knee and arms (Figs. 1 and 2).

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On ultrasound, there was a well-defined heterogeneous mass involving predominantly deep subcutaneous and muscular planes of proximal right thigh measuring 9.7 × 5.7 × 5.8 cm. Fine needle aspiration cytology (FNAC) of the same lesion showed fibrocytes, mature adipocytes, a few spindle-shaped cells with sharp ends suggestive of wavy nerve fibers. She had history of excision of the swelling in the same region 2 years ago, which was histologically proved to be a neurofibroma.

In the same region, the patient presented with the present swelling. On excision of the mass, histologically it showed an undifferentiated pleomorphic sarcoma (Fig. 3), which was confirmed on immunohistochemistry

Figure 1. Single, small neurofibroma seen on lateral aspect of the left knee.

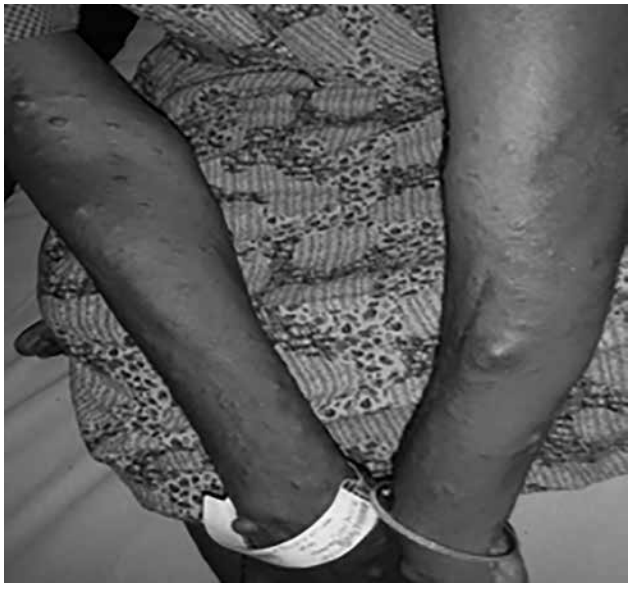

Figure 2. Both arms showing multiple neurofibromas of varying sizes.

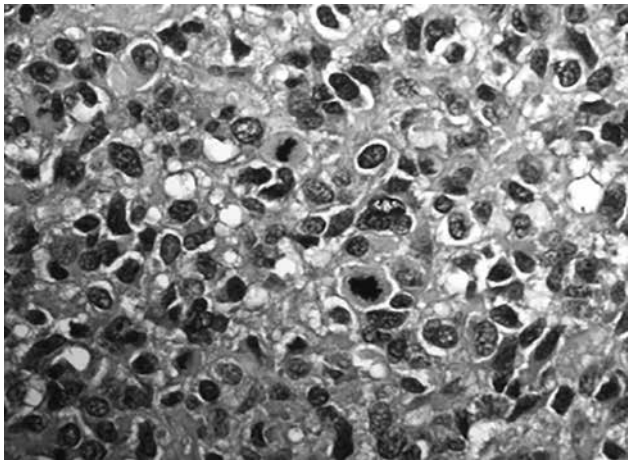

Figure 3. Pleomorphic tumor cells with mitotic figures (H&E x400).

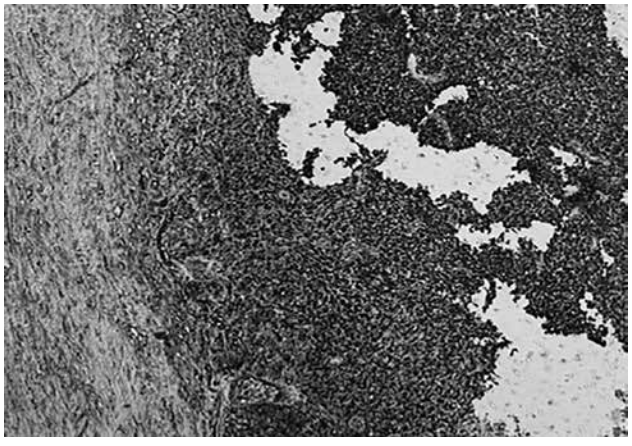

Figure 4. S-100 positivity in the tumor cells (IHC x100).

to be positive for vimentin and S-100 (Fig. 4) suggesting a neural origin. The tumor cells were markedly pleomorphic with increased mitosis, many of them being atypical. Thus, a diagnosis of MPNST in a neurofibroma was given. Patient was referred to a radiation oncologist for further management.

DISCUSSION

MPNST is a rare malignant tumor with poor prognosis accounting for 3-10% of all soft tissue sarcomas. It is the second most common variety of soft tissue sarcomas seen. A combination of gross and microscopic findings along with immunohistochemical studies is commonly used to diagnose a case of MPNST.

These tumors occur in equal frequency in males and females and some series have shown a female preponderance. The majority of these tumors are seen involving the extremities; although tumor were also seen in unusual sites, such as the pelvis, retroperitoneum and infratemporal fossa. Imaging is routinely performed to assess the extent of the disease and plan surgical resection. However, it does not reliably determine the malignant transformation from neurofibroma to MPNST. Magnetic resonance imaging (MRI) is the investigation of choice because it can reveal the nerve of origin. Grossly, the tumor size ranges from 4 to 24 cm in greatest dimension.[2]

Histologically, following criteria are used for the diagnosis of MPNST: a) Gross fusiform tumors in relation to nerves; b) microscopic feature of spindle cell with fascicular pattern and varying degrees of mitosis, necrosis and tumor calcification; c) presence of associated benign neurofibroma or schwannanian cells and d) positive immunohistochemical staining for S-100 protein, neuron-specific enolase and others like actin, cytokeratin, smooth muscle actin and vimentin to differentiate from other spindle cell sarcomas. The tumors are classified as low-grade and high-grade on the basis of their cellular differentiation, mitotic count, tumor necrosis and expression of MIB-1 proliferation marker.[3]

However, it is not always possible to demonstrate the origin from a nerve, especially when it arises from a small peripheral branch. This point was exemplified in a series by Nambisan et al, in which nerves could not be identified in 61% of cases of MPNST and in the series Bilge et al, in which nerve origin could be identified only in 45-56% cases.[4] Still, there are several other distinct features, such as proliferation of tumor in the subendothelial zones of vessels with neoplastic cells

herniating into vessel lumen and proliferation of small vessels in the walls of the large vessels, which are very characteristic features of MPNST. Syndromes that are associated with MPNST are NF-1 and NF-2.

Histologically, strict morphologic criteria must be applied to distinguish the spectrums of MPNSTs from cellular schwannoma, atypical and malignant meningioma and from a variety of rarely occurring intracranial sarcomas, such as high-grade pleomorphic sarcoma "malignant fibrous histiocytoma" fibrosarcoma, synovial sarcoma and leiomyosarcoma. On the benign side of the spectrum, cellular schwannoma is another tumor to be distinguished from MPNST. This tumor is particularly prone to be mistaken for malignancy, given the presence of hypercellularity, mitotic activity, and occasional locally aggressive growth. Strong S-100 protein as well as collagen IV/laminin immunoreactivity is the rule in this tumor. With respect to separating MPNST from benign nerve sheath tumors, p53 may be useful, strong immunostaining being seen in the majority of MPNSTs.[5] Ten percent of MPNSTs exhibit focal divergent differentiation, either mesenchymal (rhabdomyosarcoma, chondrosarcoma, osteosarcoma, angiosarcoma) or epithelial (mucin-producing, neuroendocrine or squamous type).

CONCLUSION

MPNSTs are aggressive, high-grade, therapy resistant and associated with poor prognosis. A combination of clinical, pathological and immunohistochemistry helps in diagnosing these tumors. Proliferation marker (MIB-1) can be a good adjunct to grade and tailor the treatment in MPNST. Sex and cellular differentiation are the new adverse prognostic factors for survival of the patients. Postoperative radiotherapy has a definitive role in both disease free and overall survival. Though multimodality therapy, including surgical resection and adjuvant radiotherapy, is available, the prognosis remains dismal. Modern clinical studies and the development of effective targeted chemotherapy are needed to gain control of the disease.

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Stroke

- Every 45 seconds, someone has stroke or paralysis.
- Uncontrolled BP increases paralysis mortality by 45%.

Diagnosis of Acute Kidney Injury

- Increase in serum creatinine by ≥0.3 mg/dL within 48 hours or an increase to ≥1.5 times the presumed baseline value that is known or presumed to have occurred within the last 7 days or a decrease in urine volume to <3 mL/kg over 6 hours or 50% increase (viz., 0.3 mg/dL increase if baseline ≥0.6 mg/dL and 50% increase if baseline is ≤0.6 mg/dL).
- Oliguria (typically defined as <0.3 mL/kg/hour).
- Contrast-induced nephropathy: Either a 25% increase in serum creatinine from baseline or 0.5 mg/dL (44 μmol/L) increase in absolute value, within 48-72 hours of administration of IV contrast.

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- Around 400 national & more than 60 international faculty and experts.
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- Well planned courses & workshops on dermatosurgery, aesthetic dermatology, lasers and other procedural dermatology.

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	SLAB 2 1st May to 31st Aug 2018		SLAB 3 1st Sept to 15th Dec 2018		SLAB 4 / SPOT REG 16th Dec onwards	
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IADVL Members	₹10000	₹12700	₹11500	₹14500	₹15000	₹19000
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Workshops	₹ 2000	N/A	₹ 2500	N/A	₹ 3000	N/A
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