ORIGINAL ARTICLE

Clinicopathological and Immunohistochemical Study of the Masquerader, Malignant Peripheral Nerve Sheath Tumours (MPNSTs)

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ABSTRACT

Introduction: Malignant peripheral nerve sheath tumours (MPNSTs) are aggressive neoplasms with poor prognosis, necessitating accurate diagnosis and classification for appropriate clinical management. While over 90–95% of Peripheral Nerve Sheath Tumours (PNSTs) are benign, MPNSTs are rare, with an incidence of approximately 0.001% in the general population. This short series highlights the table of clinic pathological spectrum in 25 cases of MPNST.

Methods: The study was conducted over a period of 5 years, comprising a retrospective study of 3 years & prospective study of 2 years in the Department of Pathology at Sher-I-Kashmir Institute of Medical Sciences (SKIMS), Srinagar, Kashmir. Cases which were histopathologically diagnosed as MPNST were reviewed & immunostaining was performed in any case, indicated to rule out the differentials.

Results: A total of 25 cases of MPNST were documented with a wide age range of 18-79 years. Male: female ratio was 4:1. Lower extremities (60%) was found to be the most common site. On Computed Tomography (CT) scan, they mostly showed invasive margins. The histopathological examination revealed conspicuous necrosis in all the cases. Immunostain with S-100 was positive in most of the cases, and all of the cases were positive for SOX-10.

Conclusion: MPNST is a highly aggressive sarcoma with a poor prognosis, characterized by a challenge in its diagnosis, as it has several mimics. These findings underscore the importance of combining clinical, radiological, and histopathological and immunohistochemically techniques for comprehensive PNST evaluation.

Keywords: Malignant peripheral nerve sheath tumour, Ki67, SOX-10

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INTRODUCTION

Malignant peripheral nerve sheath tumours (MPNSTs) are aggressive sarcomas that arise from peripheral nerves or soft tissues exhibiting nerve sheath differentiation[1]. Diagnosing these tumours is particularly challenging due to the lack of definitive morphological criteria and the absence of reliable immunohistochemically or molecular markers, which has historically led to misinterpretation as other non-nerve sheath sarcomas. Most experts agree that a sarcoma intrinsically involving a major nerve—without evidence of an alternative differentiation such as intraneural synovial sarcoma or angiosarcoma—or arising from a pre-existing benign nerve sheath tumour, should be classified as MPNST[2]. Similarly, malignant spindle cell tumours occurring in patients with neurofibromatosis type 1 (NF1) are generally presumed to be MPNST unless proven otherwise.

Although not entirely specific, the commonly observed microscopic features include alternating cellular fascicles, whorled patterns, palisading or rosette-like formations, perineural or intraneural spread (when associated with nerves), subendothelial clustering of tumour cells, and conspicuous areas of geographic necrosis[3]. Heterologous differentiation is sometimes observed with tumours showing elements of cartilage or bone, and less frequently skeletal muscle (malignant Triton tumour), smooth muscle, angiosarcoma, or even glandular structures—especially in

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NF1 patients[4].

MATERIALS & METHODS

The study was conducted in the department of Pathology at Sher-I-Kashmir Institute of Medical Sciences (SKIMS), Srinagar, Kashmir and included a prospective data analysis for two years and garnering retrospective data analysis of three years. The prospective study was carried out from 2023 to 2025, and the study material included cases of malignant nerve sheath tumours in different age groups, received in the department of Pathology, SKIMS Soura. All clinical data, including age, gender, demographic distribution, residence, site of tumour, signs and symptoms, etc, were observed in the patients.

Cases which were histopathologically diagnosed as MPNST were included in our study. The specimens were either incisional biopsies or wide excisions of the tumours. The clinical history and radiological findings were retrieved from the hospital records. Specimens were fixed in 10% formalin, paraffin-embedded embedded and stained by the routine hematoxylin and eosin. In addition to conventional light microscopic studies, immunohistochemistry was performed on paraffin sections using a two-step process; first, the binding of primary antibody to the antigen of interest and second, the detection of bound antigen by a chromogen. Appropriate positive and negative controls were used.

The various antibody markers utilized to substantiate a diagnosis of MPNST and to discern the alternative differential diagnosis included S-100, Ki67, SOX-10 etc. All slides were examined under the light microscope, and analysis was carried out on the following parameters: -

- Age, gender, clinical features and tumor location
- Histological, immunohistochemical and radiological features

STATISTICAL ANALYSIS

Data was entered in a Microsoft excel spreadsheet and presented as mean, standard deviation, frequency and percentages. Significance was defined by p-values less than 0.05 using two-tailed tests. Data analysis was done by IBM-SPSS version 21.0 (IBM-SPSS Science Inc., Chicago, IL)

RESULTS

In our study, we concluded that MPNST constituted 4.34% of all peripheral nerve sheath tumours. Among the 25 cases of MPNST studied, a wide age bracket was observed, with the youngest patient being 18 years of age and the oldest of 79 years. Maximum number of cases (28%) was seen in the age group 30-39 years (Figure 1). Male (80%) patients outnumbered the female group (20%), and the M:F ratio being 4:1

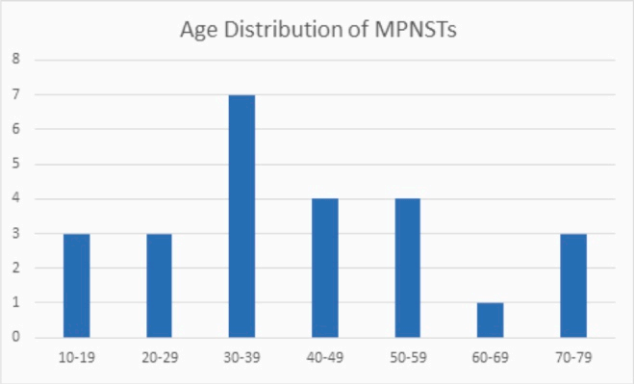


Fig 1: Bar chart depicting distribution of MPNSTs across different age groups.

Location wise 20 cases were deep seated (80%) whereas 5 case (20%) was superficially located (Figure 2).

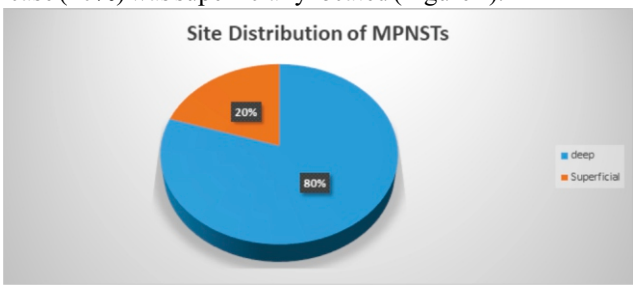


Fig 2: Pie chart depicting location distribution of MPNSTs

The most common site of involvement were the lower extremities (60%) followed by thorax & upper extremities (20%) and head & neck (20%). (Table 1).

Site	No. of cases	Percentage
Thorax	4	16%
Head & Neck	2	8%
Lower Extremities	15	60%
Upper Extremities	4	16%

The size of the tumours varied across a range of 13 to 16 cm (Fig. 3). In almost all cases, a palpable mass on examination was established as a presenting symptom.

Summary of CT findings:

CT features of all twenty-five malignant tumors in our study were reviewed. Twenty-two tumors exhibited invasive

margins, and three showed central enhancement in the lesions radiologically.

Morphological features of MPNSTs on Histopathology

All cases of MPNST demonstrated overt malignant features consistent with their aggressive nature:

All cases showed spindle cells, often arranged in interlacing fascicular architecture with prominent nuclear atypia. Necrosis was identified in 22 cases of the 25, supporting a conspicuous high-grade morphology of the tumour (Fig 7).

A high proliferation index was evident in all cases, with some cases showing median mitotic figures and others exhibiting ≥10 mitoses per 10 high power fields (HPF) (Fig. 5&6), underpinning the poor prognosis of these tumours.

Immunohistochemical Findings

S-100 protein expression was observed as 18 cases, demonstrating positive, and 7 cases as negative, reflecting the variability and stipulating the reduced expression in malignant counterparts. All 25 cases exhibited a Ki-67 index ≥10%, consistent with high proliferative activity and aggressive tumour behavior. SOX-10, a stem cell and neural crest marker, was positive in all 25 cases, signifying the neural crest origin and thereby aiding in the diagnosis of MPNST (Fig 8).



Fig. 3: Gross image showing globular lesion (MPNST)

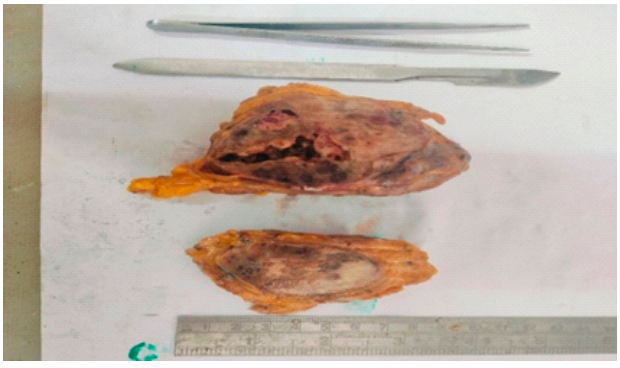


Fig. 4: Cut section grey brown with areas of necrosis and cavitation (MPNST)

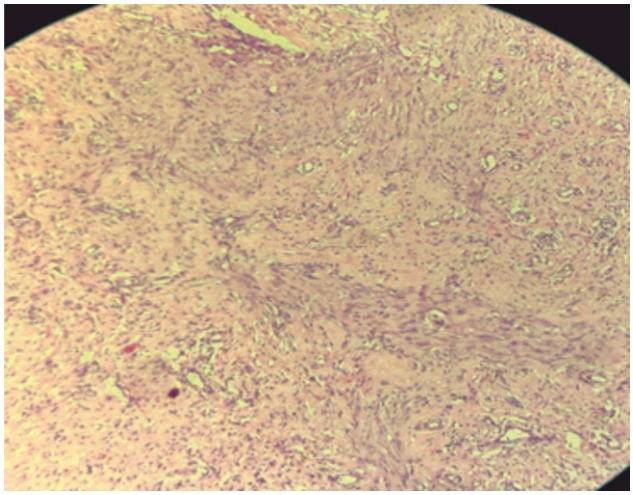


Fig. 5: Photomicrograph showing MPNST (H&E; 10X)

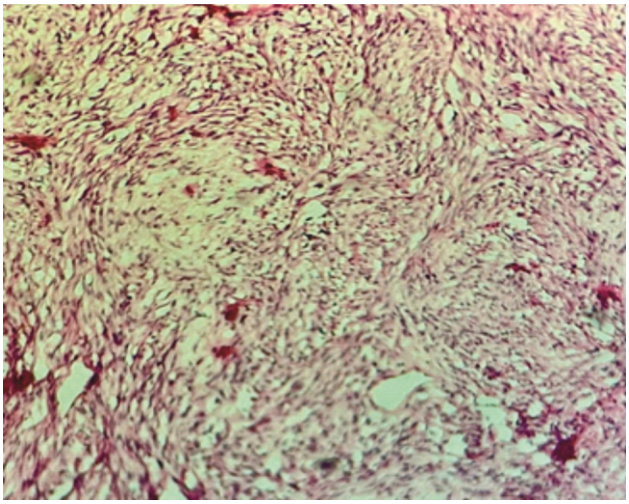


Fig. 6: Photomicrograph showing hypo & hypercellular areas (MPNST H& E: 20x)

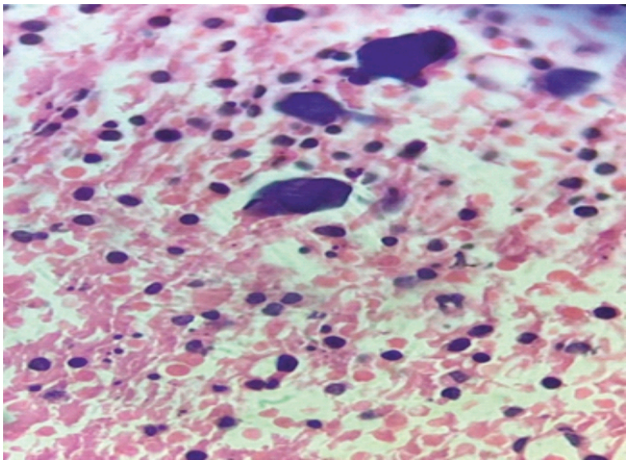


Fig. 7: Photopictograph of MPNST showing areas of necrosis

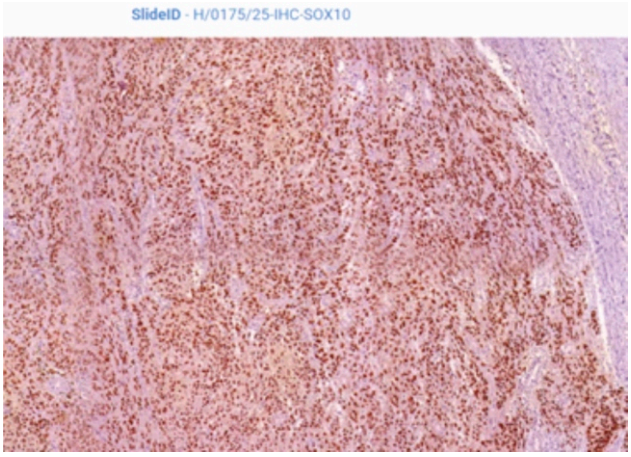


Fig. 8: IHC for SOX-10 showing positivity in tumour cells (MPNST)

DISCUSSION

In the present study, a total of 25 cases of MPNST were studied. A wide range of age groups were noted, ranging from 18 to 79 years. The majority of cases were seen in the 4th decade. This corresponds to the age range from the study of Sasidharan S et al[5] and Shams et al[6]. In our study, males (20/5) outnumbered female patients (5/25), which is contrary to the studies of Pekmezci M et al[7], Lucas CHG et al[8] and Chikkannaiah et al[9]. In the studies of Lucas CHG et al (8) and Chikkanaiah et al[9], most of the tumours were deep-seated (~70%) and around (~30%) were superficially located. Further, they found that the most common site of involvement is the thorax, followed by the head and neck region, extremities, etc, which is in concordance with our study. On the other hand, our radiological findings differed as their study did not exhibit central enhancement on either CT or MRI. Instead, enhancement was primarily seen in peripheral regions, which was attributed to central necrosis and haemorrhage. An invasive margin pattern was noted in twenty-two out of twenty-five malignant tumours, while none of the benign tumours showed such a pattern. Similar findings were reported by Ogose A et al., 1999(10) and Yu YH et al., 2016[11].

Grossly, a capsule was observed in 40% of these MPNSTs, with most tumours appearing firm and fleshy on cut section (Fig. 4). Degenerative changes such as necrosis were present in 80% of the MPNSTs. These findings are consistent with previous reports by Chikkannaiah et al.[9] and Pekmezci M et al.[7]. The MPNSTs in our study demonstrated a median Ki-67 (≥20%) proliferation index. In contrast, the studies by Pekmezci M et al[7] reported higher Ki-67 proliferation. Although diffuse S-100 expression may occasionally be observed in rare MPNSTs, this marker should be interpreted cautiously and in conjunction with the other morphological and immunohistochemical findings. Previous studies also suggest that using a combination of immunohistochemical markers could enhance the diagnostic sensitivity for MPNST. Furthermore, studies have shown that SOX10 is expressed in the majority of MPNSTs, like Pekmezci M et al[7]. Therefore, as supported by our study, additional investigations into SOX10 expression in other benign nerve sheath tumours could provide deeper insight into its significance in MPNST diagnosis.

CONCLUSION

MPNSTs mostly affected middle-aged males and typically presented as painless mass lesions. Radiological investigations like CT scans played a critical role in tumour characterisation, while immunohistochemistry and histopathological examination were essential for accurate diagnosis and distinguishing benign from malignant tumours. The findings underscore the importance of combining clinical, imaging, and pathological tools for comprehensive PNST evaluation.

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