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Case Report

Malignant Transformation of Neurofibroma with Emphasis on S100 - A Rare Case

Varshini Sindhiya Chanda[1]* and Neethu GV[2]

1Postgraduate, JJM Medical College, RGUHS, Karnataka, India

2Associate Professor, JJM Medical College, RGUHS, Karnataka, India

***Corresponding Author:** Varshini Sindhiya Chanda, Postgraduate, JJM Medical College, RGUHS, Karnataka, India.

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Abstract

Malignant peripheral nerve sheath tumor (MPNST) is a rare neoplasm arising from peripheral nerve and may arise from a pre-existing nerve sheath tumor in neurofibromatosis type 1 (NF 1). This is a rare case of 26 year old female presented with swelling on posterior aspect of left thigh since 1 month. Fine needle aspiration cytology (FNAC) suggestive of Malignant spindle cell tumour. Surgery was done and specimen sent for biopsy showed transformation from Neurofibroma to Malignant peripheral nerve sheath tumour (MPNST). Immunohistochemistry with S-100 protein was diffusely positive. Complete surgical resection with wide negative margins is the optimum management of high-grade MPNST and that early diagnosis and potential prevention of MPNST should be prioritized. The 5-year overall survival (OS) rate of all patients with MPNST was 69.5%. Whereas the precursors for MPNST like neurofibroma should be surgically resected and wide margins is not necessary, and preservation of neurological function is of paramount importance. Thus the management of neurofibroma differs from MPNST as the survival rate of the former is better than the latter.

Keywords: Biopsy; Fine- Needle; Immunohistochemistry; Adult; Female

Introduction

Malignant peripheral nerve sheath tumor (MPNST) is a rare neoplasm arising from peripheral nerve and May arise from a preexisting nerve sheath tumor in neurofibromatosis type 1 (NF 1) [1].

Clinical Summary

A 26 year female presented with swelling on posterior aspect of left thigh since 1 month to cytology department. Has a positive family history for neurofibromatosis type 2(NF 2). On examination, the swelling measured 2x1cm, tender, firm in consistency and restricted mobility.

Pathological findings

Aspiration cytology done yielded hemorrhagic aspirate. Microscopy showed groups and scattered spindle shaped cells densely stained with irregularly condensed chromatin. These nuclei are elongated, blunt ends with scant cytoplasm suggestive of Malignant spindle cell tumour (Figure 1A). Patient underwent surgery and specimen sent for histopathology. Grossly received grey yellow to grey white soft tissue mass measuring 4x3x2cm (Figure 1 B, C). Cut surface- Light tan, glistening and showed few yellow patches. Microscopy showed a neoplastic spindle cell tumour. The cells are arranged in long fascicles with hyperchromatic, thin nuclei with few focal buckled nuclei (Figure 2A). Hypo and hypercellular areas with atypical mitoses 1-3/10 hpf seen (Figure 2 B, C). One section showed transformation from Neurofibroma to hypercellular

area suggesting MPNST arising from Neurofibroma. The specimen sent for immunohistochemistry showed diffuse positivity for S-100 protein (Figure 2D).

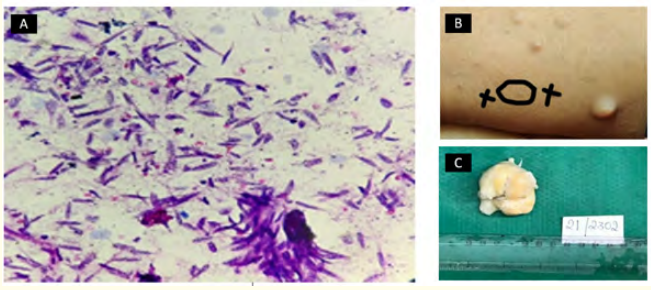

Figure 1: (A) Cytology showing groups and scattered spindle shaped cells densely stained with irregularly condensed chromatin. These nuclei are elongated, blunt ends with scant cytoplasm suggesting Malignant spindle cell tumour. (B) Site of the lesion and (C) Gross image of specimen.

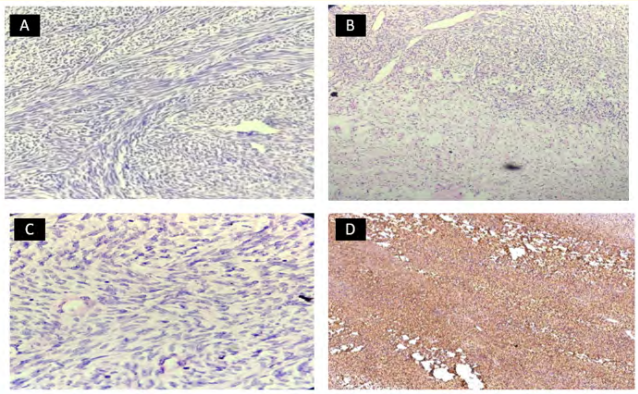

Figure 2: Histological features- (A) Long fascicles (B) Hypo and Hypercellular areas, (C) 1-3 mitotic figures per High Per Field (HPF) and (D) Diffuse S-100 protein positivity.

Discussion

Malignant Peripheral Nerve Sheath Tumour is a rare neoplasm that occur sporadic in 50%, 40 - 50% in neurofibromatosis type 1 and 10% in the setting of prior radiation therapy [1,2].

Evans DG *et al* study on NF1 patients with MPNST were ascertained from two sources from north west England population of 4.1 million in the 13 year period 1984-1996: the North West Regional NF1 Register and review of notes of patients with MPNST in the North West Regional Cancer Registry. Twenty-one NF1 patients developed MPNST, equivalent to an annual incidence of 1.6 per 1000 and a lifetime risk of 8-13%. There were 37 patients with sporadic MPNST.

The median age at diagnosis of MPNST in NF1 patients was 26 years, compared to 62 years in patients with sporadic MPNST ($p < 0.001$). In Kaplan-Meier analyses, the five year survival from diagnosis was 21% for NF1 patients with MPNST, compared to 42% for sporadic cases of MPNST ($p = 0.09$). Patients with NF1 are younger than those associated with sporadic. This study findings were consistent with present case affecting younger age group [3].

Miettinen MM *et al* study further differentiated atypical neurofibromatous neoplasm of uncertain biologic potential (ANNUBP) from MPNST because both features are quiet similar. ANNUBP has atleast 2 of the following features: cytologic atypia, loss of neurofibroma architecture, hypercellularity, mitotic index of > 1/50 HPF and < 3/10 HPF. Whereas MPNST, low grade: features of ANNUBP but with mitotic index of 3 - 9/10 HPF and no necrosis. So this case features are consistent with low grade MPNST rather than ANNUBP. ANNUBP which is a recently added entity in WHO 2017 and MPNST have overlapping histological features and differ prognostically. Hence it is necessary to differentiate between ANNUBP and MPNST [1].

Rosenbaum T *et al* study also indicated that neurofibromas affect few NF1 patients and are thought to be present already at birth. They are associated with major nerve trunks or plexi, may appear as a large, disfiguring mass, and can progress to malignancy with an estimated lifetime risk of 8-13% [4].

Krol EM *et al* study did pathologic evaluation of the lesion after excisional biopsy revealed transformation of neurofibroma into MPNST with high mitotic activity and increased cellularity within the lesion as well as positive S-100 stain which was consistent with findings of our study [5].

Conclusion

Complete surgical resection with wide negative margins is the optimum management of high-grade MPNST and that early diagnosis and potential prevention of MPNST should be prioritized.

The 5-year overall survival (OS) rate of all patients with MPNST was 69.5%. Whereas the precursors for MPNST like neurofibroma should be surgically resected and wide margins is not necessary, and preservation of neurological function is of paramount importance. The management of neurofibroma differs from MPNST as the survival rate of the former is better than the latter [6,7].

Acknowledgment

None.

Disclosure

The authors declare no conflicts of interest.

Institutional Ethical Committee clearance has been obtained for this study.

Approval of the Research Protocol

Yes.

Informed Consent

Yes.

Registry and the Registration No. of the study/trial: ECR/731/Inst/KA/2015/RR-18 issued under Rule 122DD of the Drugs and cosmetics Rules 1945, Ref no:- JJMMC/IEC-42-2022.

Animal Studies

No.

Research Involving Recombinant DNA

No.

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