

An Unusual Case of Nerve Sheath Myxoma with Schwannomatous and Perineural Differentiation

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ABSTRACT

Nerve sheath myxoma (NSM) is a rare benign tumour of peripheral nerves. It is seen in middle aged adults with slight female predilection and presents as a slow growing painless mass. The commonest sites are extremities, scalp, back and neck. Microscopically it has a typical morphological appearance. It is multilobulated and is composed of spindle and stellate shaped cells set in an abundant myxoid stroma. The cells show strong positivity for S-100 protein and are EMA negative or it stains only few perineural cells, indicating its close relationship with schwannoma or neurofibroma. But we report a rare case of nerve sheath myxoma in a 40 year old woman which showed typical microscopic features of NSM. However it showed an unusual co-expression of S100 and EMA indicating a bidirectional schwannomatous-perineural differentiation. The clinicopathological features, various differential diagnosis, its histogenesis and brief review of literature are discussed below.

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Introduction

Nerve sheath myxoma is a rare benign tumour which arises from the peripheral nerves. Harkin and Reed were the first to define the nerve sheath myxoma in the year 1969. Subsequently Gallager and Helwig named this lesion as Neurothekeoma in 1980.^[1] Other synonyms for this tumour are cutaneous lobular neuromyxoma, myxomatous perineuroma, bizarre cutaneous neurofibroma, myxoma of nerve sheath and dermal nerve sheath myxoma.^[2] Here we present an unusual case of nerve sheath myxoma in a 40 year old female which showed bidirectional schwannomatous and perineural differentiation.

Case Report

A 40 year old female presented with a slow growing mass over the right lower leg since 1 year. It was gradually increasing in size, not associated with pain, soft to firm in consistency. There was no history of antecedent trauma. Patients past medical history was unremarkable and all clinical investigations were within normal limits. No history of similar swelling elsewhere in the body. Systemic examination was within normal limits. A clinical diagnosis of lipoma was given. It was completely excised and sent for histopathological examination.

Gross examination: Received skin covered mass which measured 3.5x2x1.5cms. The cut surface showed multiple small well demarcated, translucent, glistening, mucoid nodules of varying sizes. (Figure 1).

Microscopic examination: Sections studied showed a skin covered multilobulated mass having a fibrous

pseudocapsule, located in the dermis (Figure 2a). It was seen reaching upto the subcutaneous tissue. The lobules were of varying sizes, separated by thin fibrous septae and are composed of many scattered spindle shaped cells and stellate cells embedded in abundant myxoid matrix (Figure 2b). Mild atypia was noted (Figure 2c). Many multinucleated giant cells were noted, few showed presence of intranuclear inclusions (Figure 2d). Immunohistochemical study (IHC) showed that the spindle cells and stellate cells were diffusely positive for S100 (Figure 3). Epithelial membrane antigen (EMA) staining showed diffuse positivity for the perineural cells scattered at the periphery of the tumour nodules (Figure 4).



Fig. 1: Gross photography showing cut surface of the mass with multiple small well demarcated, translucent, mucoid nodules of varying sizes.

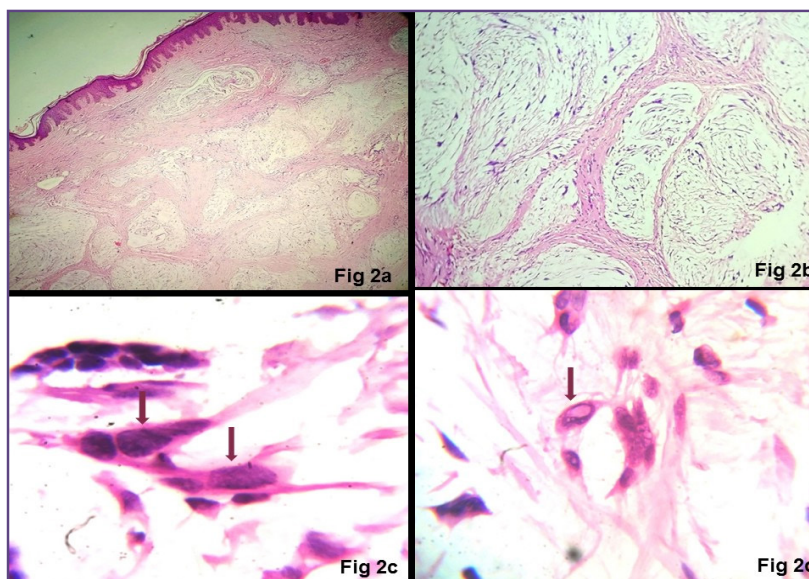


Fig. 2: Microphotography showing a) skin covered multilobulated mass with apseudocapsule. (H&E,X40) b) lobules composed of spindle and stellate shaped cells lying within the mucinous stroma. (H&E,X100) c) Cells with mild nuclear atypia. (H&E, X1000) (Red arrows) d) multinucleated giant cells with intranuclear inclusions. (H&E, X1000) (Red arrows).

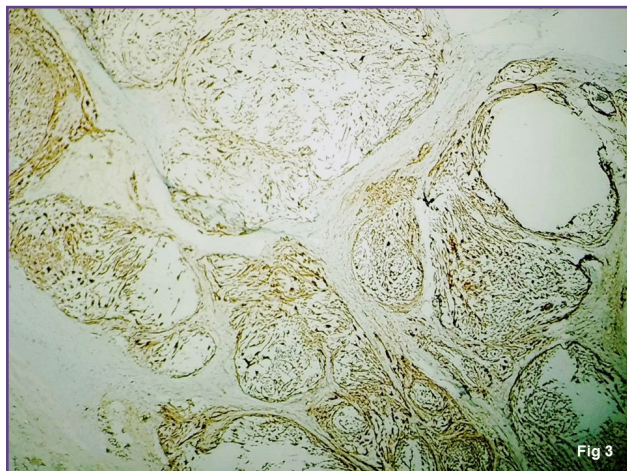


Fig. 3: Microphotography showing S100 positive spindle and stellate cells. (S100,X100).

Discussion

Nerve sheath myxoma was originally described by Harkin and Reed in 1969. Later on in 1980 Gallager and Helwig described a series of tumour under the name “Neurothekeoma”. Many authors suggested neurothekeoma as a variant of nerve sheath myxoma.^[3] The clinical and histological pattern of neurothekeoma and nerve sheath myxoma have many overlapping features, which have been discussed in the differential diagnosis and these lesions should be differentiated from each other as they are entirely different entities.

NSM is commonly seen in middle aged adults with a male to female ratio are approximately 1:2. It commonly arises from fingers, knee, pretibial region, hips, thigh, lower leg, ankle, foot, trunk, head and neck region.^[4] Other rare sites are oral mucosa, gingival, hallux and CNS.^[5,6] In our case, a 40 year old female patient presented with a mass the over anterior aspect of right lower leg.

It typically presents as a firm, slow growing, painless nodule or mass with size ranging from 0.4 to 4.5 cms. On cut section, the lesion shows multiple tiny well demarcated, translucent whitish mucoid nodules. Microscopically the lesion is located in the dermis or sometimes in dermis and subcutaneous tissue. It is characterised by multilobular structure and each lobule is composed of spindle and stellate shaped cells arranged in swirling, lamellar and concentric patterns, embedded in abundant myxoid stroma. Mild nuclear pleomorphism and rare mitosis may be seen.^[4] In our case all these typical features were seen, however mitosis was not seen.

Immunohistochemically, the tumour cells are strongly positive for S100 protein, GFAP and Vimentin. EMA

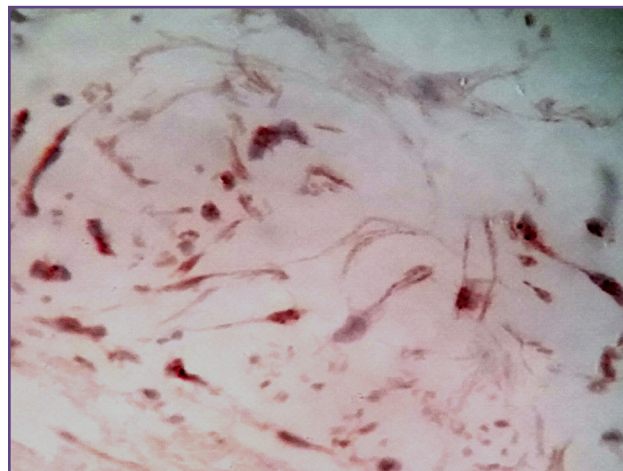


Fig. 4: Microphotography showing Epithelial membrane antigen (EMA) positivity in the perineural cells around the tumour micronodules. (EMA,X1000).

will be absent or positive in small number of perineural cells.^[7] In our case, S100 was diffusely positive in spindle cells as well as EMA showed diffuse positivity among the perineural cells, which were present more in number at the periphery of the lesion, indicating bidirectional schwannomatous differentiation. Similar case with bidirectional differentiation was reported previously by Zamecniket al in his case report.^[2] Electron microscopic findings include single or duplicated external lamina investing the cells, desmosome like junctions, cytoplasmic microfilaments, myelin figures and interdigitating cytoplasmic processes.^[8] Recent study was done on gene expression profiles of NSM and neurothekeoma. The neurothekeoma expressed gene that primarily encoded glycoprotein and metalloproteinase from macrophages and fibroblasts. The S100 B gene was differentially expressed gene between NSM and NTK. Hence this gene expression study strongly supports that NSM are of peripheral nerve sheath origin and are distinct neoplasm from NTK.^[9]

NSM can be confused with many myxoid soft tissue tumours and spindle cell tumours. The myxomatous nature of NSM can be confused with other myxoid tumours such as myxoid neurothekeoma, superficial angiomyxoma, myxoid MFH, myxoid liposarcoma, myxoid neurofibroma, focal mucinosis, soft part chondromas, metastatic mucinous carcinoma etc. Other differential diagnosis for spindle cell lesion includes schwannoma, perineuroma, desmoplastic melanoma, cellular and mixed neurothekeoma. The clinical appearance, gross and microscopic picture of NSM is indistinguishable from that of myxoid variant of NTK. However NSM are S100, GFAP, and Vimentin positive while EMA is negative of focally positive. NTK are

S100 negative and EMA positive. Recent ultrastructural studies have differentiated these two entities which are already discussed.

All malignant myxoid tumours are characterised by increased cellularity, vascular pattern and specific cellular elements such as lipoblast etc.^[10] Superficial angiomyxoma consists of spindle and stellate shaped fibroblasts admixed with thin walled capillaries. The tumour cells are vimentin positive. Schwannoma shows presence of verocay bodies. Myxoid neurofibroma lacks the lobular pattern, is unencapsulated and may have fibrillary background. Tumour cells may be admixed with collagen bundles. Cellular and mixed neurothekeoma have less myxoid stroma, more spindly plumper epithelioid cells and greater mitotic activity. They are S100 and GFAP negative. Focal mucinosis have no sharp circumscription, paucity of cells and complete absence of vascular structures. Perineuroma has distinct corded basket weave like whorled pattern. Cells are EMA positive, S100 negative. Soft part chondromas have areas of typical hyaline cartilage/ calcification. They are S100 positive but lack GFAP. Superficial acral fibromyxoma is composed of spindle or stellate cells with a storiform & fascicular pattern embedded in a collagenous or fibromyxoid stroma. It is CD 34, CD 99, EMA positive, but S100 negative.^[2, 5]

Treatment: Complete surgical excision with margins is the mainstay of treatment as NSM has got high chances of recurrence.

Conclusion

To conclude, we report a very rare case of nerve sheath myxoma exhibiting bidirectional differentiation. Pathologist should be aware of the possible EMA expression in NSM. Since NSM may show focal moderate nuclear atypia and mitosis, it should be differentiated from benign and malignant myxoid neoplasms. The use of terms nerve sheath myxoma and neurothekeoma as synonyms or as variants of the same tumour should be avoided because they represent two distinct lesions.

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Competing Interests

None Declared

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