

Nerve Sheath Myxoma: Report of A Rare Case

AMOOLYA BHAT¹, APARNA NARASIMHA², VIJAYA C³, SUNDEEP VK⁴

ABSTRACT

Nerve sheath myxoma defined by Harkin and Reed is an uncommon benign neoplasm with nerve sheath like features. It has several cytological and histological differential diagnoses. One such lesion is neurothekeoma, which can be differentiated using immunohistochemistry. In most of the previous reports nerve sheath myxoma and neurothekeoma were considered synonymous and were often confused for one another. This case report separates the two using immunohistochemistry. Also, the cytological features of nerve sheath myxoma are not well documented in the past. This case report attempts to display the cyto-morphology of nerve sheath myxoma. We report a rare case of nerve sheath myxoma diagnosed on cytological features confirmed by histopathology and immunohistochemistry in a 32-year-old lady who presented with an asymptomatic nodule over the left cervical area and discuss its cyto-histological mimics.

Keywords: Benign tumour, Muscular tissues, Nerve sheath myxoma, Neurothekeoma

CASE REPORT

A 32-year-old lady presented to the general surgery out-patient department of our institute, with a slow growing painless nodule over the left side of the neck since six months. Examination showed a non tender swelling in the subcutaneous plane measuring about 0.5x0.5cm located in the left upper cervical area. It was firm in consistency and freely mobile, not adherent to underlying muscular tissues. The overlying skin, underlying muscles, the parotid and submandibular salivary glands were unremarkable.

Cervical lymphadenopathy was considered as a clinical diagnosis. A fine needle aspiration cytology of this lesion yielded grey-white jelly like material.

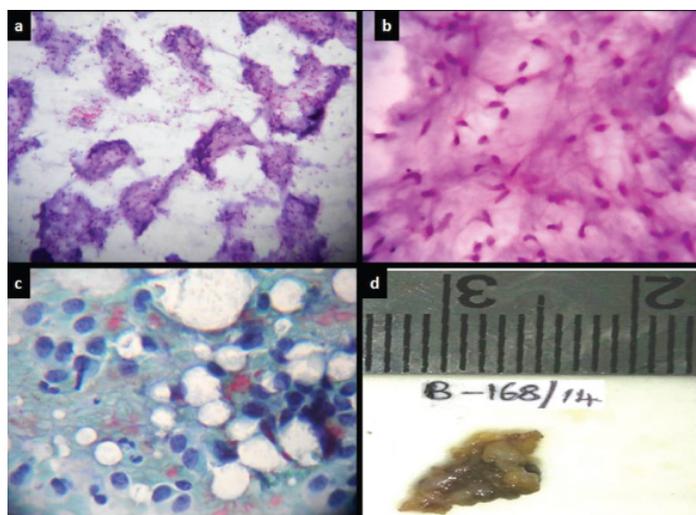
Cytological findings: Smears were cellular, displayed abundant myxoid material with benign spindle and stellate cells having bland nuclei and scant cytoplasm. The stellate cells had multiple elongated cytoplasmic processes. Occasional foci showed rounded to plasmacytoid (epithelioid) cells having round to oval bland nuclei. A cytological diagnosis of spindle cell neoplasm probably a myxoid neurofibroma was made. Differential diagnoses of nerve sheath myxoma and mixed type of neurothekeoma were also

suggested [Table/Fig-1a-c]. The lesion was excised and sent for histopathological examination.

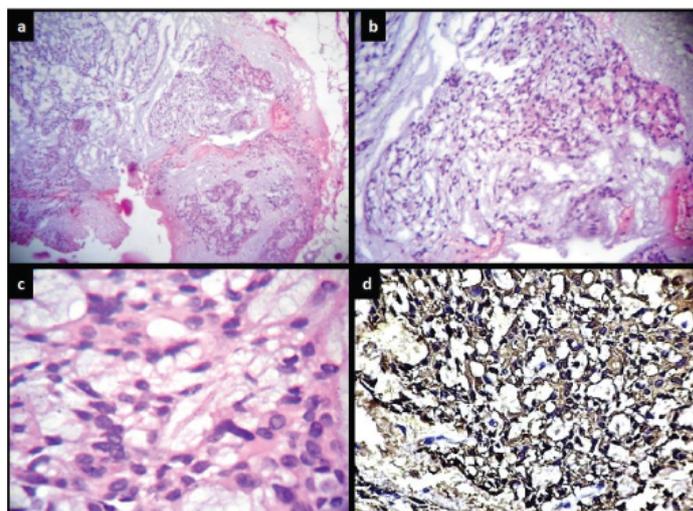
Gross examination: Received a single grey white nodule measuring about 0.4x0.4cm. External surface showed multiple tiny nodules [Table/Fig-1d].

Histopathology: Sections studied showed tumour cells arranged in lobules separated by delicate fibrovascular septae. The tumour cells within the lobules were arranged in cribriform pattern and in discharges embedded in abundant myxoid stroma. The cells were of three types, stellate with cytoplasmic processes, round to spindle lacking the nuclear atypia and occasional giant cells [Table/Fig-2a-c].

A histological diagnosis of nerve sheath myxoma was conferred. Neurothekeoma was the differential diagnosis considered. Thus based on the clinical and histopathological features, S100 and epithelial membrane antigen (EMA) were chosen as immunohistochemical markers as they help to distinguish the two. Immunohistochemistry revealed S100 positivity [Table/Fig-2d] and epithelial membrane antigen (EMA) negativity in the tumour cells confirming the diagnosis of nerve sheath myxoma, ruling out neurothekeoma.



[Table/Fig-1]: Cytology smears showing (a) Cells embedded in abundant myxoid material H&E, 40X. (b) Benign stellate and spindle cells H&E, 100X. (c) Benign round to oval cells with moderate cytoplasm Pap, 400X. (d) Gross specimen showing multinodular external surface



[Table/Fig-2]: Photomicrograph showing (a) Tumour cells arranged in nodule separated by fibrous septae, H&E, 40X. (b) Benign spindle-stellate cells in myxoid background H&E, 100X. (c) Round to oval cells along with spindle cells against a myxoid background H&E, 400X. (d) Tumour cells showing S100 expression in nucleus and cytoplasm S100, 400X

DISCUSSION

Nerve sheath myxoma was initially defined by Harkin and Reed as a micronodular, myxoid and loosely cellular benign tumour of neural origin [1] arising from Schwann cells [2]. It is rare and commonly presents as an asymptomatic soft nodule in dermis and subcutaneous tissue of face and upper extremities of females of 21-36 y, ranging in sizes between 0.5-1 cm [3,4].

The cytological features of nerve sheath myxomas are less frequently documented in the past. The smears from nerve sheath myxomas show spindle-stellate cells and epithelioid cells with bland nuclei arranged in loose clusters, groups or whorls within a metachromatic myxoid background. Binucleated and multinucleated cells may be found [5,6]. The histopathological sections reveal a well-defined multinodular tumour composed of myxoid nodules separated by fibrous septae, with nodules having loose clusters of benign spindled-stellate and epithelioid cells embedded in myxoid stroma. The markers that can be used for diagnosing nerve sheath myxoma are S100, glial fibrillary acidic protein, vimentin, and collagen type IV. They are EMA negative [4].

The cytological differentials include nerve sheath myxoma, mixed neurothekeoma, myxoid neurofibroma, plexiform neurofibroma, myxoid schwannoma, extraneural perineuriomas, cutaneous myxoma, intramuscular and juxta-articular myxomas, cutaneous mucinosis, and hamartomas. All these lesions show myxoid material along with benign spindled to stellate cells on cytology. Histopathology and immunohistochemical examinations are extremely important in arriving at the right diagnosis. Because of rarity of other entities, spindle cell neoplasm probably myxoid neurofibroma was offered as the first cytological diagnosis.

In mixed type of neurothekeomas the myxoid areas are localized to the periphery of the broad fascicles and nodules made of spindled-stellate cells and are S100 and EMA negative [4]. Myxoid neurofibromas are well circumscribed, unencapsulated and also lack lobulated appearance. Histologically they lack multinodularity and contain interlacing bundles of Schwann cells with wavy bland nuclei, shredded carrot collagen, scattered lymphocytes, histiocytes and intralesional nerve fibres in a fibrillary background. They show patchy S100 expression unlike our case [7]. Plexiform neurofibromas arise from proliferation of neurofibroblastic cells [6]. They show multinodularity, myxoid change and express S100; however they involve larger nerve trunks and are often associated with neurofibromatosis. The skin over the swelling shows hyperpigmentation and folding [7]. In our case, the lesion was single and did not involve large nerve trunks. Myxoid schwannomas show occasional foci of Antoni A areas with Verocay bodies. They lack multinodularity but express S100 [7]. Extraneural perineuriomas are multinodular and are composed of slender fibroblast like cells in storiform, whorled and fascicular pattern in a myxoid or collagenised stroma. They are EMA positive, S100 negative [7,8].

Cutaneous myxomas lack S100 protein [7]. Intramuscular myxomas and juxta-articular myxomas were ruled out as clinically, the lesion was tiny, non adherent to underlying muscular tissues, freely mobile and located in the subcutaneous tissue plane. They are S100 negative [7]. Cutaneous mucinosis present as a single nodule and are associated with deposition of large amounts of mucopolysaccharides in dermis [9]. Histologically dermal collagen is separated by aggregates of basophilic material and stellate fibroblasts are present, they lack multinodularity and S100 expression [9].

The adipose tissue around the lesion may prompt the possibility of hamartoma. However, hamartomas display disorganized bundles of nerves, mesenchymal derivatives and these nerve bundles would have stained positive for EMA [4]. The lesion was in subcutaneous tissue plane, which would have been a possible source of these adipocytes. Here is a tabulation of all reported cases of nerve sheath myxoma with the diagnostic immunohistochemical findings [Table/Fig-3]:

Authors	Clinical features	Immunohistochemistry
Kim BW et al., [3]	25-year-old lady with subcutaneous tender nodule over left thumb	Immunoreactive for S100 protein, neuron specific enolase (NSE), vimentin, NK1/C3, and nonreactive for glial fibrillary acidic protein (GFAP), smooth muscle actin (SMA), CD10, CD68
Akhtar K et al., [10]	3-year-old boy, lesion in left thumb	Strong positivity for S-100 and focal positivity for neuron specific enolase (NSE).
Mukul Vij et al., [11]	45-year-old lady, lesion in cerebellopontine angle	Diffusely immunoreactivity for S100 and negative for glial GFAP, EMA and neurofilament (NF)
Alexandru D et al., [12]	40-year-old man, lesion in posterior fossa	The tumour cells were positive for S100 antibody, and negative for GFAP.
Safadi RA et al., [1]	32-year-old lady with gingival swelling	S100 protein positive; NSE - variable positivity; EMA, GFAP, CD68, SMA and HMB45 negative.
Al-Buainain H et al 2009 [13]	5-month-old child, lesion over the left thumb.	S100 positivity
G Mehdi et al., [14]	35-year-old lady with growth in right ring finger	S100 positivity
Present case	32-year-old lady with a tiny nodule in the left side of the neck.	S100 positive; EMA negative

[Table/Fig-3]: Clinical and immunohistochemical findings of various reported cases of nerve sheath myxoma

Wide local excision with tumour free surgical margin is the treatment of choice for nerve sheath myxoma [4]. Local recurrences have been reported in about 50% cases; however malignant transformation has not been documented [4].

CONCLUSION

We have described a rare case of nerve sheath myxoma whose definition and histological classification was controversial. The nerve sheath myxomas and myxoid neurothekeomas which were considered synonymous in the past could be distinguished by use of immunohistochemical marker S100, which was positive for nerve sheath myxoma and negative for neurothekeoma as seen in our case. Thus application of immunohistochemistry is pivotal in arriving at the right diagnosis, and histopathological features alone are not sufficient for making the diagnosis. This differentiation may be important clinically as nerve sheath myxomas have higher propensity to cause local recurrences.

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PARTICULARS OF CONTRIBUTORS:

1. Assistant Professor, Department of Pathology, Sapthagiri Institute of Medical Sciences and Research Centre, #15,Chikkasandra, Hesarghatta Main Road, Bangalore, India.
2. Professor, Department of Pathology, Sapthagiri Institute of Medical Sciences and Research Centre, #15,Chikkasandra, Hesarghatta Main Road, Bangalore, India.
3. Professor and HOD, Department of Pathology, Sapthagiri Institute of Medical Sciences and Research Centre, #15,Chikkasandra, Hesarghatta Main Road, Bangalore, India.
4. Assistant Professor, Department of Surgery, Sapthagiri Institute of Medical Sciences and Research Centre, #15,Chikkasandra, Hesarghatta Main Road, Bangalore, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:

Dr. Aparna Narasimha,
No.22, Moyenvilla, Moyenville Road, Langford Town, Bangalore-25, India.
E-mail : Sonrichie14@gmail.com

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