Nerve Sheath Myxoma Presenting as Finger Nodule in 39 year old Female
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Citation

Abstract
Nerve sheath myxoma is a rare benign lesion that has a strong predilection to the extremities. In addition to the extremities, nerve sheath myxoma had been reported in scalp, back, the neck, lateral chest wall, mandible and gingiva. Histologically it has a polylobated appearance and pale staining round nests of spindled and stellate cells separated by thin collagenous septa. The tumor cells show strong positivity with S-100 protein, and GFAP. EMA-positive perineurial cells are also present. We present a case of a typical nerve sheath myxoma in a finger of 39 year old female.

CASE REPORT
Our case is a 39 year old female who presented with a painless nodule in her finger for 6 months duration. The mass was firm, measured 0.5 cm in diameter, and mobile but fixed to the skin surface. The lesion was excised and sent to pathology laboratory for histopathological diagnosis. Macroscopically, the tumor measured 0.5× 0.5 × 0.4 cm and the cut section showed small, well-demarcated, translucent glistening, mucoid nodules. Microscopic examination revealed expansile, myxoid variable sized micro-nodules that are located in the dermis and are loosely clustered in a fibrous matrix. (Fig. 1 and 2). These micro-nodules contain bland looking spindle and stellate cells, and the mitotic figures are rarely seen (fig. 3).
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Figure 2
Figure 2: The micro-nodules are separated by fibrous septae and show myxomatous background, X20.

Alcian blue special stain revealed abundant acid mucopolysaccharides in tumor background (fig. 4).

Figure 3
Figure 3: High power shows bland spindle and stellate cells. X40

Immunohistochemical study showed that the spindle and stellate cells are positive for S100 and glial fibrillary acidic protein (GFAP) indicating Schwannian differentiation (fig 5 and 6). Epithelial membrane antigen (EMA) stain showed scattered perineurial cells seen at the border of the myxoid nodules (fig 7). As expected, vimentin stain showed diffuse and strong positivity (fig 8). Neurofilament, smooth muscle actin and pankeratin were negative.

Figure 4
Figure 4: Alcian blue shows stromal mucin in the background.

Figure 5
Figure 5: S100 immunohistochemistry shows positive result in the spindle and stellate cells. X20
Figure 6
Figure 6: The spindle and stellate cells are positive for glial fibrillary acidic protein (GFAP)

Figure 7
Figure 7: Epithelial membrane antigen (EMA) shows perineural cells around the tumor micro-nodules. X20

Figure 8
Figure 8: Vimentin shows diffuse and strong staining. X20

DISCUSSION
Nerve sheath myxoma (NSM) is a rare benign lesion that was originally defined by Harkin and Reed (1). Gallager and Helwig, under the designation neurothekeoma, described a series of tumors that they interpreted as nerve sheath tumors; the histologic patterns of neurothekeomas shared some general features with those of nerve sheath myxoma (2,3). As a result, there had been confusion regarding a relationship between the two categories. Fetsch et al. have offered a strong support for the neural character of classic NSM (4). The nature of the cellular and mixed neurothekeoma remained a controversy.

Nerve sheath myxoma is most common in middle-aged adults, with a male-to-female ratio ranging from 1:1 to 1:2 (1, 4, and 5). In one study, the age range from 8 to 72 years (4). Our case was 39 year-old female. It usually present as asymptomatic, soft, skin-colored or translucent papule or nodule ranging from 0.5 to 1.0 cm in diameter (6). In Fetsch et al study, the size range from 0.4 to 4.5 cm, and 4 / 57 cases were painful. It is most commonly located on the fingers and knee or pretibial region; other locations affected are hip, thigh, lower leg/calf, ankle, foot, and forearm, palmar surface of the hand, occipital scalp, back, the neck, lateral chest wall, and oral mucosa (4, 7). Our case was a painless 0.5 cm nodule in the finger. Most Nerve sheath myxoma specimens consist of a single piece of tissue that is sometimes covered by skin. It has a rubbery to firm consistency, and on cut section, small, well-demarcated, translucent or whitish glistening, mucoid nodules are often noted (4). Microscopically NSM consists of symmetrically expansile, myxoid variable sized micro-nodules that are
loosely clustered in a fibrous matrix (2). The lesions can involve the dermis only, dermis and subcutis, subcutis only or very rarely the subcutis and adjacent superficial skeletal muscle. Our case was involving the dermis only. These lesions contain spindled, stellate-shaped, ring-shaped, and epithelioid Schwann cells. The epithelioid Schwann cells typically have a corded arrangement or are grouped into syncytial-like aggregates. Rarely, focal moderate pleomorphism of Schwann cell nuclei is noted (4).

The Schwann cells in NSM are immunoreactive for S-100 protein, and glial fibrillary acidic protein (GFAP). These Schwann cells are bordered by collagen type IV. A small number of Schwann cells are immunoreactive with keratin cocktail, possibly because of cross reactivity between keratin and GFAP antibodies. EMA-positive perineurial cells are present in small numbers, usually best seen at the border of the myxoid nodules. Neurofilament protein-positive axons are uncommon (4, 8, and 9). Our case showed S100 and GFAP positive Schwann cells and the tumor nests were bordered by EMA positive perineurial cells. The keratin cocktail and Neurofilament protein were negative.

Electron microscopy findings include features indicated an origin from the peripheral nerve sheath; among the pertinent findings was a single or duplicated external lamina investing the cells, desmosome-like junctions, cytoplasmic microfilaments, myelin figures, and interdigitating cytoplasmic processes (10, 11).

Histological differential diagnosis includes cellular and mixed-type neurothekeomas, Superficial angiomyxoma, Schwannoma, neurofibroma, Perineuroma, soft part (extra skeletal) chondromas, superficial acral fibromyxoma, and some malignant neoplasms with myxoid background as Extra skeletal myxoid chondrosarcoma, myxoid liposarcoma, myxofibrosarcoma, desmoplastic melanoma and metastatic mucinous carcinoma.

Cellular and mixed-type neurothekeomas have much less myxoid matrix, more spindling and sometimes plumper epithelioid cells, more nuclear variability, and greater mitotic activity than true nerve sheath myxoma. They are S-100 protein and GFAP are negative (4).

Superficial angiomyxoma (cutaneous myxoma) can mimic NSM as it forms highly myxoid multinodular masses within the dermis and subcutis. This entity is characterized by a circumscribed collection of spindled and stellate fibroblasts that are admixed with thin-walled blood vessels and embedded in a mucinous stroma. Immunohistologically, the stromal cells are consistently positive for vimentin and focally positive for smooth muscle actin but are negative for S-100, GFAP and desmin (12-17).

Schwannoma and neurofibroma possess a number of features in common with NSM. Both arise from the nerve sheath and may stain for S-100 protein. Fetsch et al. have suggested that nerve sheath myxoma may ultimately proven to be a special type of schwannoma, or less likely, neurofibroma. They suspected a closer relationship to schwannoma because of: 1) sharp demarcation with a peripheral fibrous reaction, 2) generally low numbers of intralesional CD34-positive fibroblasts and EMA-positive perineurial cells, 3) a rarity of intralesional axons, and 4) the infrequent presence of foci suggesting nuclear palisading and/or loose Verocay body formations (4).

Perineurioma have been reported to show focal or abundant myxoid matrix. Histologically, Perineurioma shows distinctive cored, basket weave-like, and whorled growth patterns. Perineurial cells are strongly immunoreactive for EMA and nonreactive for S-100 protein, GFAP, and CD34 (18,19).

Soft part (extra skeletal) chondromas has some features resembling nerve sheath myxoma by its predilection to hands and feets especially fingers and on occasion, and they may have abundant myxoid change. However, areas with typical hyaline cartilage and/or calcific foci are often present that aid in the recognition of this entity. Whereas chondrocytes are S-100 protein-positive, these tumors lack the GFAP expression seen in nerve sheath myxomas (4).

Superficial acral fibromyxoma (SAF) is the recently described soft tissue tumor that tends to present as a solitary, slow-growing mass in the fingers and toes of adults (20). Histologically, SAF shows proliferation of spindle-shaped and/or stellate cells with a storiform and fascicular pattern embedded in a fibromyxoid/collagenous stroma with conspicuous mast cells. Multinucleated cells can be seen. The neoplastic cells are positive for CD34, CD99, epithelial membrane antigen, and negative for S100, desmin, smooth muscle actin.(21).

Since NSM may show focal moderate nuclear atypia, malignant neoplasms have to be excluded especially those with a myxoid stroma as extra skeletal myxoid chondrosarcoma, myxoid liposarcoma, myxofibrosarcoma, desmoplastic melanoma and metastatic mucinous carcinoma.
Clinical, radiological and pathological correlation aid in correct diagnosis.

Fetsch et al. have followed up 34 NSM patients after excision. 16 (47%) patients had one (n = 11) or more (n = 5) local recurrence(s) of their tumor (4). So, complete local excision with attention to margins and follow-up is the best management for this entity.

CONCLUSION

Conclusion: Nerve sheath myxoma has a wide age range, affect males and females almost equally. The diagnosis can be confused with a variety of benign and malignant tumors with myxoid stroma. With Complete Excision which is the treatment of choice, recurrence rates are not high.

References

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