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Case Report

Malignant melanotic nerve sheath tumour of chest wall: a rare and diagnostically challenging case

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ABSTRACT

Malignant melanotic nerve sheath tumour (MMNST), previously known as melanotic schwannomas (MS) comprise less than 1% of nerve sheath tumors and around 200 cases have been reported in the literature. According to the WHO 5th edition, it is now classified as malignant neoplasm due to its local recurrence rate and metastatic risk. Although it is classified as malignant, the histopathological criteria for malignancy and prognostic factors remain ill-defined due to its rarity. It also poses a diagnostic challenge as it resembles closely other benign as well as malignant melanin producing tumors. We report here a case of 33 year old female who presented with chest wall swelling and was diagnosed as MS (now classified as MMNST) on histopathology and immunohistochemistry. This case highlights the diagnostic difficulties and the importance of careful histological evaluation and long-term follow-up.

Keywords: Melanotic, Nerve sheath tumour, BRAFV600E

INTRODUCTION

Malignant melanotic nerve sheath tumour (MMNST), is a rare variant of nerve sheath tumour composed of variably melanin producing Schwann cells and consisting less than 1% of nerve sheath tumors with around 200 cases been reported.[1,2] For decades, these were considered as benign despite their occasional metastatic potential. However, 5th edition of the WHO classification categorised them as malignant melanotic nerve sheath tumor due to their aggressive behaviour with potential for metastasis and the lack of established histological criteria for malignancy. It is mainly seen in adults usually in the fourth decade and has a slight female predominance. Approximately half of the patients are associated with carney complex.[3] It has been seen that this entity has tendency for late metastases though the data is very limited due to its rarity. Here we report one such case of 33 years old female who presented to us with painful lump over left chest wall.

CASE REPORT

A 33 years old female presented with gradually progressive painful lump over left sided chest and extending to trunk for one year. There was no history of trauma, fever, weight loss or any discharge from swelling. On clinical examination, there was diffuse ill-defined swelling. High resolution USG showed a subcutaneous hypo echoic lesion of heterogeneous echo texture in lower part of chest in mid axillary line of left side measuring approximately 5.3×3.0 cm. On complete work up no other feature of Carney complex was identified. Gross examination of wide local resection specimen was received as brownish black soft tissue piece measuring 6×4×1 cm in size. Cut surface also showed brownish black areas. On microscopy, showed a circumscribed pseudo-encapsulated tumour composed of plump, spindle and epithelioid cells arranged in interlacing fascicles and nests along with accumulation of melanin pigment. Individual cells were moderately

pleomorphic with hyperchromatic to vesicular nuclei, inconspicuous nucleoli and eosinophilic cytoplasm. Many intranuclear cytoplasmic inclusions were noted (Figure 1). There was no evidence of necrosis, atypical mitosis or large macro nucleoli. On immunohistochemistry, HMB-45 and Melan A were diffuse positive in tumour cells. CD 34 and BRAFV600E were negative in tumour cells. Ki67 index was approximately 15% (Figure 2). Margins were free from tumour invasion. Final diagnosis of MS was rendered as at that time it was still considered as benign lesion. Due to increased Ki67 index close follow up was advised. Patient was under follow up and reported recurrence after one year of surgery. As lesion was not resectable, chemotherapy was advised but declined by patient and died of disease after 5 years of onset of lesion.

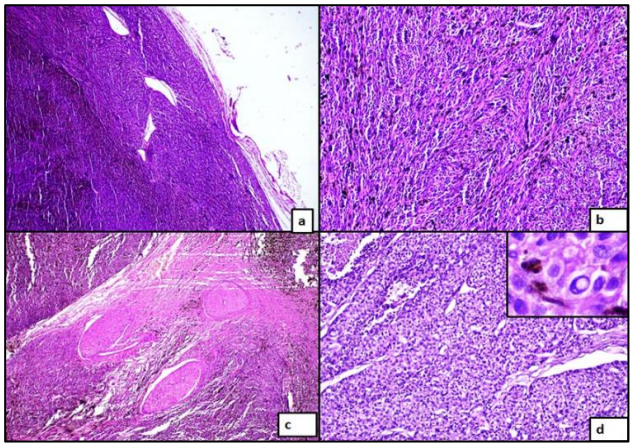

Figure 1 (a-d): H and E section shows well defined pseudoencapsulated lesion (4×) composed of spindle cells disposed in vague fascicles with melanin pigment (10×). Many entrapped large nerve bundles were seen (4×) along with the areas composed of cells with epithelioid morphology and clear cytoplasm. Inset shows intranuclear inclusions (10×).

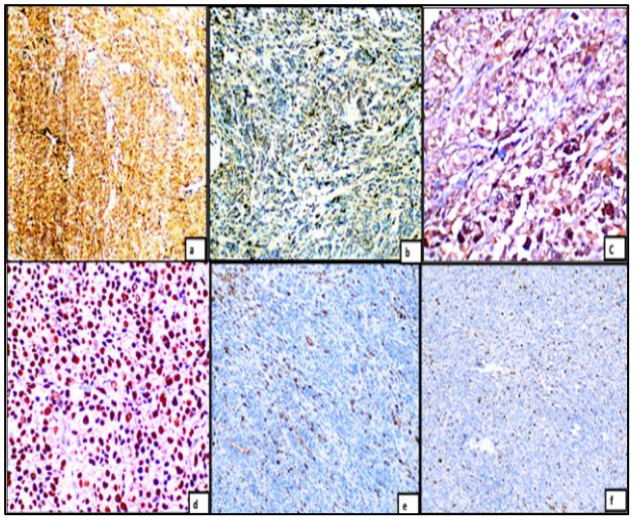

Figure 2 (a-f): 20× shows cells positive for strongly positive for Melan-A, weakly positive for HMB-45, negative for BRAFV600E and ki67 index.

DISCUSSION

MS was first described by Muller in 1932 as malignant melanotic tumor of sympathetic ganglion cells and Later in 1961, Hodson described it as form of schwannoma.[4,5] For decades, this was considered as a benign tumor but with the publication of clinico-pathological immunohistochemical and gene profiling of study of 40 cases, the local recurrence and distant metastasis in 35% and 42% patients, WHO 5th edition reclassified it as Malignant and is now called MMNST.[6] This tumour can occur sporadically or as part of Carney complex. When found in association with Carney complex, these are usually psammomatous type while the sporadic cases are non psammomatous type.[3] The presence of melanin in schwannoma can be correlated with the fact the during embryologic development neural crest cells migrate and differentiate into divergent tissue such as melanocytes, Schwann cells, neurons of peripheral nervous system and adrenal medulla.[7,8] This is seen occurring mainly in adults with peak incidence in forth decade with slight female predominance.[9] The most common site of origin is spinal nerves and paraspinal ganglia. Other uncommon sites are gastrointestinal tract, cerebellum, orbit, soft tissues, heart, oral cavity, uterine cervix, retroperitoneum and the parotid.[10]

Clinical symptoms are usually pain, sensory symptoms and mass effects. The other features are related to the site of occurrence. Spotty pigmentation of skin, endocrinopathies, myxomas of skin, heart and other sites may be seen when found as part of carney complex. Approximately 29% of patients can be asymptomatic.[11] Radiology also plays an important role in diagnosis. Usually, schwannoma shows hypointense lesion on T1 and hyperintense lesion on T2 weighted image on MRI. While MS show hyperintense lesion on T1 and iso to hypointense lesion on T2 image.[12]

Grossly these tumors are usually well circumscribed limited by thin fibrous pseudo capsule.[13,14] Cut surface can be solid grey to pitch black in colour as seen in our case.[11] Microscopically, this is different from classic schwannoma with absence of true capsule and Antoni A and Antoni B areas. MS show variable melanin pigment deposition. This cellular tumour is disposed in short fascicles comprising of plump spindle and Epithelioid cells having nucleo cytoplasmic ratio, enlarged vesicular nuclei, prominent nucleoli and moderate eosinophilic cytoplasm. Psammoma bodies are also seen in psammomatous type. There are no definite histological criteria for establishing its malignancy. Presence of macro nucleoli, large areas of necrosis, capsular invasion and distant metastasis are seen in malignant schwannoma.[15,16]

The entity has to been differentiated from other pigmented lesions like Melanotic melanoma pigmented neurofibroma, meningeal melanocytoma and pigmented dermatofibrosarcoma protuberance. It is important to

differentiate it from malignant melanoma as both these entities share similar IHC profile. Both MMNST and malignant melanoma are positive for S100, SOX10, HMB-45 and Melan A but MMNST lack BRAFV600E mutation as was seen in our case while BRAF V600E mutation is seen in more than 90% of melanomas.[2,17,18] Presence of psammoma bodies, adipose like cells, abundant cytoplasm with indistinct cell borders, low proliferation index favours MMNST. Also, reticulin stain envelopes each individual cell while in melanoma, larger groups of tumour cells are surrounded by reticulin.[19] Pigmented neurofibromas have cells with small and elongated nuclei while cells of MMNST are usually round to oval with conspicuous nucleoli. Pigmented neurofibromas are positive for CD34 while MMNST are CD34 negative (Table 1).[20]

Table 1: Differential diagnosis of MMNST.

Differential diagnosis	Histopathological findings	Immunohistochemistry
MMNST	Spindle or epithelioid cells with melanin deposition, psammomatous bodies in some cases	Positive for S100, HMB-45, Melan-A; negative for BRAFV600E
Malignant melanoma	Atypical melanocytes with pagetoid spread; often marked nuclear atypia and prominent nucleoli	Positive for S100, HMB-45, Melan-A; often positive for BRAFV600E mutation
Meningeal melanocytoma	Uniform melanocytes with minimal pleomorphism, no psammoma bodies	Positive for S100, HMB-45, Melan-A; negative for Ki-67 (low proliferative index)
Pigmented neurofibroma	Spindle cells with smaller elongated nuclei; no psammoma bodies	Positive for CD34; negative for HMB-45 and Melan-A
Pigmented dermatofibrosarcoma	Fibroblastic spindle cells arranged in storiform pattern with pigmented dendritic cells. Adipocytes seen as ‘pearl beads “entrapped within the tumor	Strongly positive for CD34; Negative for S-100, Melan-A, HMB-45 and BRAFV600E

The primary management includes complete resection of the tumour as MMNST. Chemotherapy and radiotherapy may be given in cases with locally infiltrative lesions or with evidence of distant metastases however, they have limited roles due to the tumour’s resistance to these modalities. Due to limited data, there is insufficient information regarding prognosis. As per reviewed literature, it shows late metastases.[9,15] Zhang et al in their study concluded the recurrence rate of 18.2% and metastasis in 9.1% of the cases following complete excision.[21] However, Torres-Mora et al reported recurrence rate and distant metastatic rate of 35% and 42% respectively with a follow up ranging from 1-300 months.[6] Common sites for metastasis are lung and pleura.[13,16]

CONCLUSION

As Malignant melanotic nerve sheath tumor is a rare tumor which is diagnostically challenging both radiologically and pathologically with undetermined prognosis and management, it needs to be correlated well with its clinico-radiological details. This helps to understand the anatomical relationship and making correct diagnosis. It is also important to keep the patient in regular follow up to monitor local recurrence or distant metastasis.

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