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Case Report

Malignant melanotic nerve sheath tumour: A rare and curious entity

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Abstract

Malignant melanotic nerve sheath tumour (MMNSTs), earlier known as melanotic schwannoma, is an extremely rare variant of peripheral nerve sheath tumour arising from Schwann cells which is characterised by its ability to produce abundant melanin pigment. The melanotic schwannoma is a very rare neoplasm, accounting for less than 1% of all nerve sheath tumours. These tumours are usually seen in young females with average age of 38 years. We report a 45 years old female with a history of headache and vomiting since 2 years which was worsening since 2 months with imbalance in walking since 1 year. She had cerebellar signs such as dysdiadochokinesia and ataxic gait with features of raised intracranial pressure and grade 2 papilledema on fundoscopic examination. A provisional diagnosis of ependymomawas suggested on radiology. She underwent a midline sub occipital craniotomy and posterior fossa tumour excision. A final diagnosis of melanotic Schwanomma was made based on histomorphology, histochemistry, immunohistochemistry along with a history of recurrence. Definitive criteria of malignancy in melanotic Schwanomma are not well established, although a combination of histologic features like large, pleomorphic cells with prominent nucleoliand necrosis, raises concern for aggressive behaviour. The Posterior fossa MS involving floor of fourth ventricle are uncommon and becomes challenging on preoperative diagnosis. Correct diagnosis is extremely important because of its high predilection to recur locally and to metastasize, which emphasizes the importance of diagnostic recognition and close clinical follow-up of patients with melanotic Schwanomma.

Keywords: Malignant melanocytic nerve sheath tumour, Melanotic schwannoma, Nerves, Recurrence, Metastasis.

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1. Introduction

Malignant melanotic nerve sheath tumour (MMNSTs), earlier known as melanotic schwannoma, is an extremely rare variant of peripheral nerve sheath tumour arising from Schwann cells which characterised by its ability to produce abundant melanin pigment.[1]

It was first described by Miller in 1932 and subsequently termed as melanotic schwannoma in 1975. It used to be classified as benign tumour as per WHO 2013 classification, but based on numerous case series and long term follow up data this neoplasm has been reclassified in WHO 2020 into a malignant tumour due to its high incidence of metastasis and recurrences.[2]

It usually arises in spinal or visceral autonomic nerves accounting for < 1% of all peripheral nerve sheath.[3] Tumour with an incidence of 47.2% in lumbosacral, 30.5% in thoracic and 22.2% in cervical region. It can arise from cranial nerve roots also.[1]

These tumours are usually seen in young females with average age of 38 years.[5] These tumours can pose a diagnostic challenge due to its enigmatic presentation on radiology and pathology.[4]

As per the literature, approximately 200 cases of melanotic schwannoma have been reported so far, out which most of case series are from spinal nerve.

We report a case of MMNST in a 45 year old female who presented as a intracranial posterior fossa lesion which posed a challenge on radiology and pathology.

2. Case Report

A 45 years old female presented with history of headache and vomiting since two years which was worsening since two

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months and also she had imbalance in walking since 1 year. She had cerebellar signs such as dysdiadochokinesia and ataxic gait with features of raised intracranial pressure and grade 2 papilledema on fundoscopic examination.

2.1. Radiological findings

MRI of brain showed a lobulated, solid enhancing mass of posterior fossa, in fourth ventricle outflow tract causing mild hydrocephalus (**Figure 1**). The mass lesion was hypo-intense on T2WI and hyper -intense on T1WI. A provisional diagnosis of ependymoma was suggested on radiology. She underwent a midline sub -occipital craniotomy and posterior fossa tumour excision.

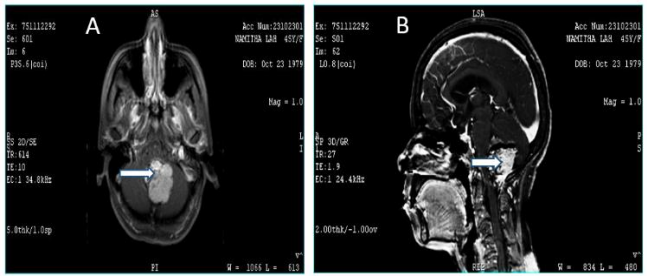

Figure 1: **A):** Axial (left) and **B):** Sagittal (right) T1 postcontrast imaging shows an homogeneous, enhancing, mass located at the floor of fourth ventricle causing mild hydrocephalus.

No any intra-operative investigations were performed like squash smear cytology/Frozen section.

2.2. Pathology findings: The tumour was sent for histopathology

On gross examination shows multiple greyish-black friable soft tissue bits, larger bit measuring 3x1x0.5cm and smaller bit measuring 0.5x0.5cm. Cut surface shows grey-brown to grey-white areas.(**Figure 2**)

Figure 2: A): Multiple grey-black friable soft tissue bits, largest measuring 3x1x0.5cm and smallest measuring 0.5x0.5cm.; **B):** Cut surface- grey-black areas seen.

Haematoxylin & eosin stained sections showed a well-encapsulated lesion with extensive areas of blackish pigmentation almost obscuring the morphology of the tumor. The underlying tumor cells were arranged in lobules and clusters separated by thin fibrous septae. The individual tumor cells appeared oval to spindle having an epithelioid appearance containing a round nucleus with small nucleoli and abundant cytoplasm filled with pigment. No mitotic figures were noted. Focal areas of calcification, haemorrhage, necrosis and psammoma bodies were noted. (**Figure 3**)

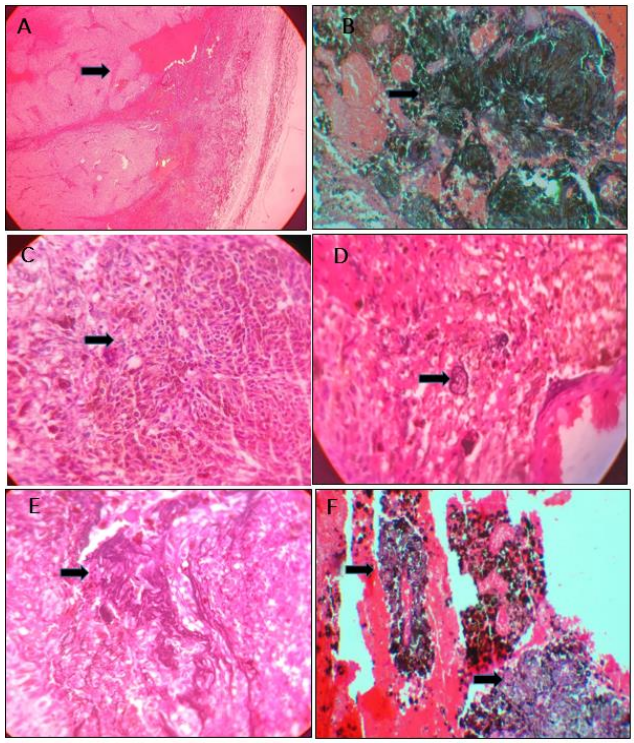

Figure 3: [H &E Sections 40X]. **A):** well encapsulated lesion with underlying tumor cells are arranged in lobules and clusters separated by thin fibrous septae. **B):** Pigments obscuring the morphologic details. **C):** Oval to spindle to epithelioid like cells having round nucleus and small nucleoli with abundant cytoplasm. **D**): Psammoma bodies. **E):** Focal areas of calcification. **F):** Haemorrhage and necrosis are seen

Special stains such as Perl's stain and Periodic acid Schiff were performed to distinguish the type of pigment such as hemosiderin, melanin, lipofuscin. Hemosiderin & lipofuscin pigments were ruled out with negative Perl's stain (**Figure 4**A) and PAS (**Figure 4**B). For melanin pigment as Masson Fontana stain could not be performed, the section were subjected for IHC later on.

The unstained sections showed an intense auto-fluorescence of the pigment under a fluorescent microscope at multiple wave lengths (**Figure 4**C). Reticulin fibers were demonstrated surrounding each tumour cell by the reticulin stain (**Figure 4**D).

Based on radiology, histopathology, special stain, auto-fluorescence a provisional diagnosis of pigmented ependymoma, meningial melanocytoma, calcified meningioma, or metastatic malignant melanoma were considered as differential diagnosis.

Since the patient reported with recurrence of the tumour on CT scan a further workup was done. Immunohistochemistry was performed for 5 markers. Tumour cell showed positivity for HMB 45, vimentin, SOX

10 and negative for Glial fibrillary acidic protein (**Figure 5**). A Ki67 proliferation index was less than 5% of tumour cells showing nuclear immunoreactivity.(**Figure 6**)

A final diagnosis of melanotic Schwanomma was made based on histomorphology, histochemistry, immunohistochemistry along with a history of recurrence.

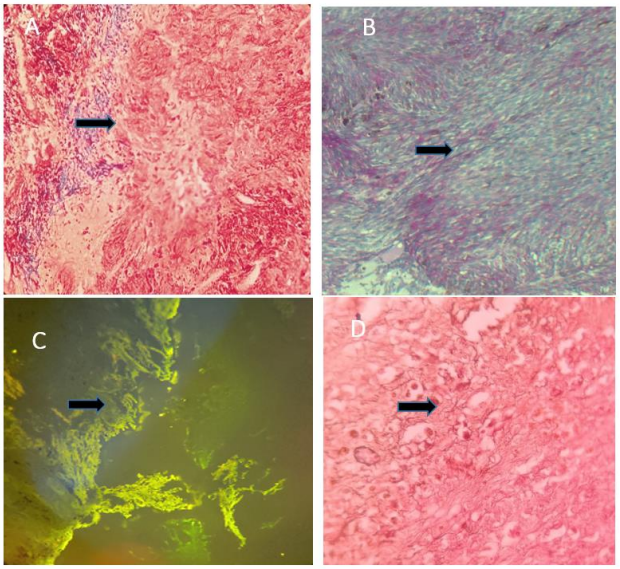

Figure 4: **A):** Perl's stain for hemosiderin was negative. **B):** PAS stain was negative. **C):** Unstained sections examined under a fluorescent microscope at multiple wave lengths, showed an intense auto-fluorescence of the pigment. **D):** Reticulin fibers surrounding each tumour cell. [40X]

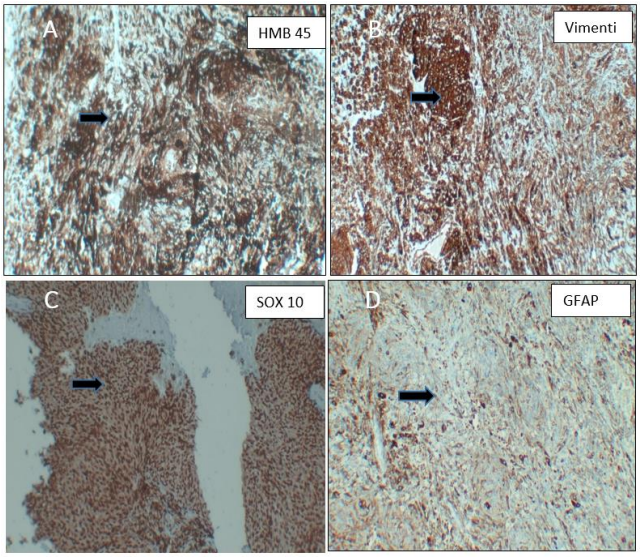

Figure 5: Immunohistochemistry **A):** Tumor cell and stromal positivity for HMB 45. **B):** Tumors cells and stroma positive for vimentin. **C):** SOX 10 shows positive. **D):** GFAP was negative.

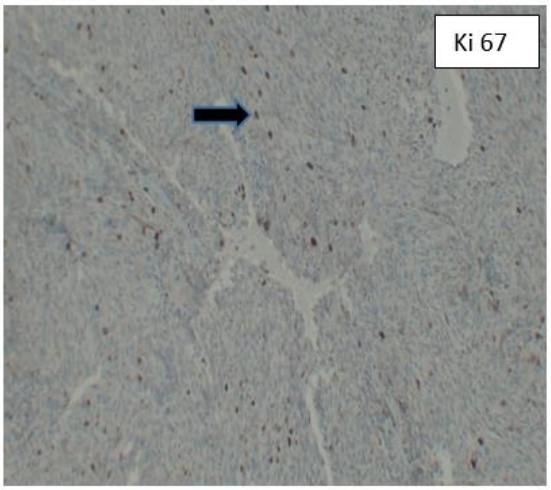

Figure 6: Ki67 proliferative index < 5%.

3. Discussion

Melanotic Schwannoma are rare peripheral nerve sheath tumours. As per the current literature only two hundred cases have been reported so far. Earlier it was called as Melanotic Schwanomma (MS).[2]

MMNSTs are tumours with characteristic feature of melanin pigmentation and biologic behaviour which is distinct from conventional schwanomma.[1]

The conventional schwannomas involve other nerves, including cranial nerves. MMNSTs tend to occur in posterior spinal nerves and ganglia but can also occur at other sites.[3] In this case tumour was arising from the floor of fourth ventricle in posterior fossa possibly from cranial nerve.

MMNST are slightly more common in females (1.4:1 female to male).[4] Their average age of presentation is 38 years for sporadic tumours. In this casetoo the tumour was seen in a young female.

These tumours are many a times diagnosed as ependymoma or meningioma based on the location and findings on imaging. Similarly in this case too a diagnosis of ependymoma was made on CT scan based on its hyper intensity on T1 and hypo intensity on T2. Contrast-enhanced images demonstrated homogenous enhancement, which was evident on the MRI images for this case.

Grossly MMNSTs are typically solitary partially encapsulated and heavily pigmented.[5] They range from 0.5 cm to 25 cm in diameter but most exceed 5 cm.[6] In this case also grossly it was brown black pigmented and encapsulated mass measuring 3x1x0.5cm.

MMNSTs are differentiated from schwannomas by generally lacking Antoni A and B regions and hyalinised blood vessels histologically.[7] This case showed well encapsulated lesion with underlying tumor cells arranged in lobules and clusters separated by thin fibrous septae. The individual tumor cells having an epithelioid appearance

containing a round nucleus with small nucleoli and abundant cytoplasm filled with pigment.

MMNSTs can be differentiated from calcified meningioma by lacking meningothelial whorls and intranuclear pseudo inclusions. MMNSTs can also be differentiated from melanoma by tumour location and morphological appearance because MMNSTs have a more spindled cell shape, greater nuclear pleomorphism and lower mitotic rate than melanomas.[8] In this case it shows spindled to epithelioid cells with prominent nucleoli. Metastatic melanoma was ruled out as there was no cutaneous melanoma. Even though the MMNST is known for recurrence and metastasis, its Ki67 labelling index is low, which was evident in this case as less than 5% as well as it shows positive for SOX10.

MMNSTs are although derived from nerve sheath cells, differentiated from conventional schwannomas in part by their melanin expression and lack of glial fibrillary acidic protein staining.[10] MMNST often stain positive for SOX10 and vimentin. In addition, they tend to stain positive for melanocytic markers such as HMB45 and negative for GFAP which differentiates them from conventional Schwannoma.[10] In this case also the tumour cells showed positive for HMB 45, vimentin, SOX 10 and negative for GFAP.

Based on immunohistochemistry the initial diagnosis of ependymoma was ruled out as the tumour was GFAP negative. The other differential like melanoma was not considered even though the tumour was HMB 45 positive, as the marker like vimentin was negative. Similarly meningeal melanocytoma was ruled out as even though vimentin and HMB 45 was positive but the marker for Schwann cells SOX 10 was negative in it. The SOX 10 positivity along with vimentin and HMB 45 favoured towards melanotic schwanomma.

Immunohistochemical studies are extremely helpful in the diagnosis in concurrence with the histological appearance.

Based on radiology, histopathology, special stains, auto fluorescence, immunohistochemistry, a final diagnosis Melanotic schwannoma (MMNST) was given.

The genetics of MMNST are not completely defined, but can be associated with Carney complex.[11] Carney's complex is a multiple endocrine neoplasia syndrome characterized by skin pigmentations called lentigines, cardiac myxomas, adrenocortical hyperplasia with Cushing's syndrome, pituitary adenomas with acromegaly, gonadal, thyroid tumours, and MMNST.[12]

Achieving long-term survival in MMNST is hampered by its tendency to metastasize and recur and its propensity to involve the spine or other structures which prevent complete surgical resection.[13-15] One study reports a 20-year remission rate of 67% with total resection. However Torres-Mora et al reported MMNST local recurrence and metastatic rates of 35% and 44% respectively.[4] In this case too there was a recurrence just after month of surgery.

4. Conclusion

Posterior fossa MS involving floor of fourth ventricle are uncommon and challenging in diagnosing preoperatively. Its rarity and the biological behaviour makes it a curious entity and therefore arriving at a final diagnosis needs complete workup such as histomorphology, histochemistry, autofluorescence, immunohistochemistry.

5. Source of Funding

None.

6. Conflict of Interest

None.

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