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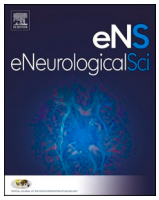

Case report

Spinal melanoma with optic neuropathy –rare manifestation of Neurocutaneous melanosis and PET-MRI findings

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ABSTRACT

Neurocutaneous melanocytosis (NCM) is a rare, sporadic neuroectodermal dysplasia characterized by the presence of large or multiple congenital cutaneous nevi and melanocytic deposits in the central nervous system. Hitherto, unreported we describe a case of NCM with optic neuropathy and spinal cord melanoma from India. A 20 year-old-lady had headache and vomiting for 3 months followed by consecutive profound painless visual impairment. Visual acuity was counting of fingers at 1 m distance in both eyes with normal fundus. There were no symptoms of spinal cord involvement. Clinical examination showed multiple small to large melanocytic nevi over the face and body. Muscle power was normal. Tendon reflexes were exaggerated. Visual evoked potential showed bilateral prolonged P100 latency (Right eye - 144 msec; Left eye - 151 msec). Brain MRI revealed leptomeningeal enhancement of brainstem, cerebellum, oculomotor and facial-abducent nerve complex without optic nerve involvement. MRI spine showed extensive dorsal thoracic cord epidural lesion extending along the entire thoracic cord segment with dorsal cord compression. Positron Emission Tomography (PET) imaging showed Fludeoxyglucose F18 (FDG) avidity along D1-D12 levels of spinal cord. Biopsy from the cord lesion was suggestive of meningeal melanoma. Here we document a rare case of late onset NCM with intracranial meningeal infiltration and asymptomatic large epidural lesion of spinal cord, expanding its phenotypic spectrum. Optic neuropathy in NCM has not been reported earlier. Periodic screening of brain and spine is recommended for early prognostication and lesion identification in NCM.

1. Introduction

Neurocutaneous melanocytosis (NCM) is a rare, sporadic neuroectodermal dysplasia characterized by the presence of large or multiple congenital cutaneous nevi and melanocytic deposits in the central nervous system. NCM most commonly manifests in childhood within the first 2 years of life and less commonly in adults. Diagnosis is often missed and delayed in adults, due to the late onset of neurologic symptoms. Malignant transformation of the meningeal deposits occurs in approximately 2.3% of patients. Here we present a rare case of neurocutaneous melanosis with optic neuropathy and an epidural spinal melanoma manifesting in the second decade of life. This is a retrospective study of a patient with neurocutaneous melanosis and spinal melanoma. Detailed clinical and laboratory findings were recorded. Open surgical biopsy of the spinal lesion and histopathological analysis were performed with hematoxylin/eosin staining and immunohistochemical analysis for S-100 and HMB45 positivity with MIB1 labelling index. Informed consent of the patient was obtained for clinical images and clinical details for publication.

1.1. Case report

A 20-year-old lady born to non-consanguineous parents was evaluated during March 2022. She presented with headache and recurrent episodes of vomiting for three months. There was sequential (right followed by left) progressive painless loss of vision over a period of one

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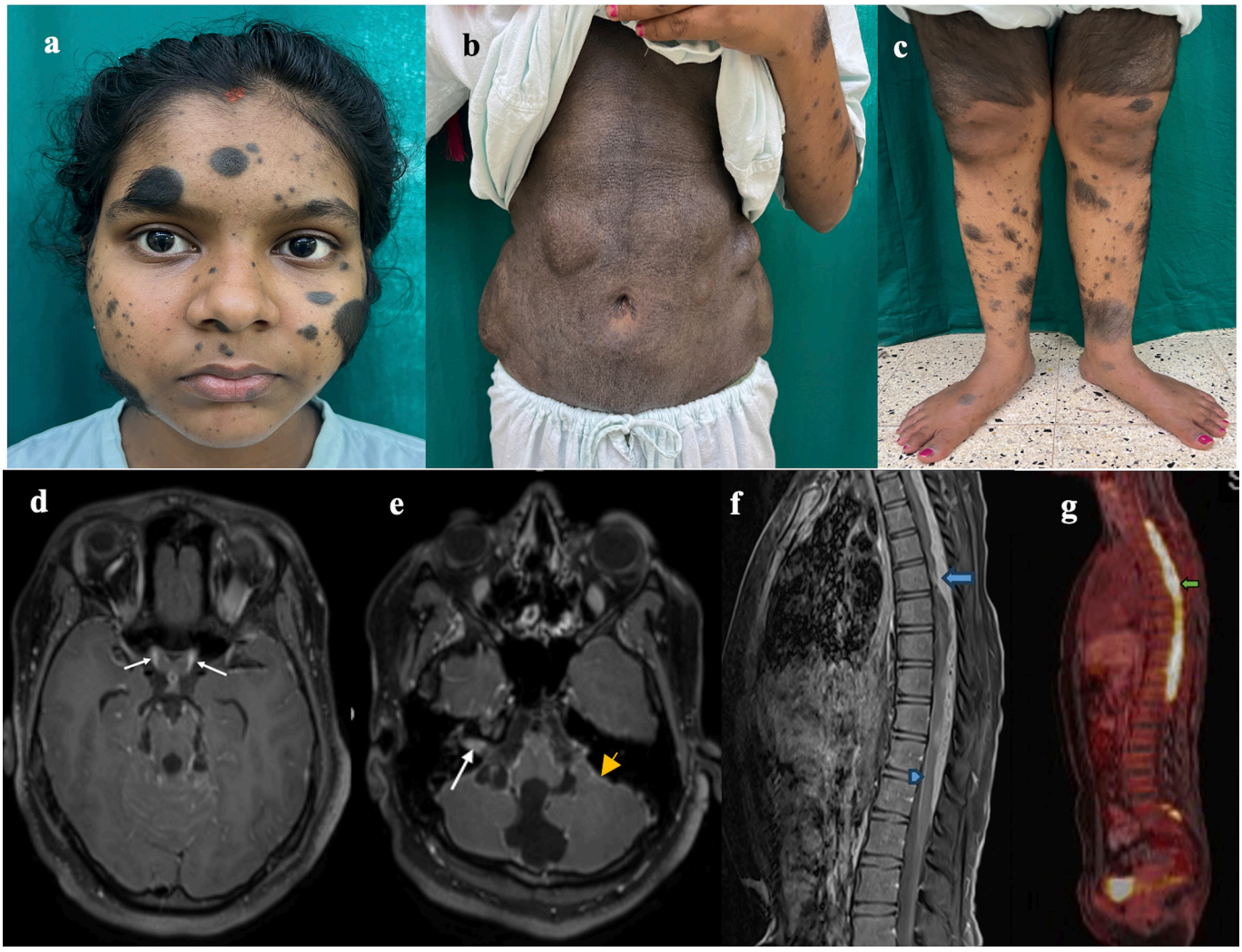

Fig. 1. a-c: Clinical images of the patient:
Multiple giant hairy melanocytic nevi with satellite nevi over the face (**a**), anterior trunk, upper limbs (**b**) and lower limbs (**c**).
d-g: MRI of brain and spine and PET imaging of the patient:
d and e - post contrast T1W images of MRI brain showing leptomeningeal enhancement along brainstem and cerebellar surface (orange arrow), cerebellar folia, bilateral oculomotor nerves (white arrow in **d**), right facial – vestibulocochlear nerve complex (white arrow in **e**).
f- post-contrast gadolinium enhanced T1W sagittal image showing patchy enhancement on dorsal cord [blue arrows]. Enhancement along anterior surface of cord near the conus [blue arrowhead] can also be noted.
g – Positron Emission Tomography (PET) imaging showing Fludeoxyglucose F18 (FDG) avidity noted along level D1-D12 level of spinal cord (green arrow), corresponding to the enhancement noted along the spinal cord suggestive of a dural based mass.

month. She had low backache for 2 months on prolonged sitting or lying down without any radiating pain, weakness of lower limbs, bowel or bladder symptoms. There was no fever, seizures or altered sensorium. Birth and development were normal. There was no family history of any cutaneous lesions or neurological illness.

On clinical examination, she had multiple large, hairy nevi over the face, trunk, back and thigh with satellite nevi, which were present since birth (Fig. 1**:a-c)**. No clinical signs of malignant transformation of skin lesions were observed. Neurological examination revealed signs of meningeal irritation. Visual acuity was severely impaired with just counting of fingers at one metre distance in both eyes. The dilated optic fundus examination was normal. Other cranial nerves were normal. Muscle strength was normal. She had mild intentional tremors of hands, exaggerated tendon reflexes and flexor plantar response.

Investigations showed normal complete blood count, renal and liver function tests. Visual evoked potential in both eyes showed prolonged P100 latency (Right eye - 144 msec, Left eye - 151 msec). Cerebrospinal fluid (CSF) analysis showed xanthochromic fluid with 9 cells (all lymphocytes), high protein (1558 mg/dl) and low glucose (5 mg/dl) level. CSF cytopathology showed lymphocytes with no evidence of melanocytes or atypical cells. Serum NMO-MOG, vasculitis profile, paraneoplastic profile, viral markers such as HIV, HbsAg and anti-HCV were negative. Magnetic Resonance Imaging (MRI) of brain showed leptomeningeal enhancement along the brainstem surface and cranial nerves (Fig. 1**: d,e**). MRI spine showed heterogenous epidural lesion extending along the entire thoracic cord segment with dorsal cord compression suggestive of meningeal disease and focal spinal lesion. Fludeoxyglucose F18 - Positron Emission Tomography (FDG – PET) of the whole body was done showing increased FDG avidity along meninges and dorsal cord corresponding to MRI lesions (Fig. 1**: f,g**).

The patient underwent T5 laminectomy and biopsy of intradural extramedullary lesion. Histopathological examination showed a melanotic lesion composed of spindled cells with S-100 and HMB45 positivity suggestive of malignant melanocytes. MIB1 labelling index of 6% was noted (Fig. 2). The features were suggestive of dorsal epidural melanoma. However, patient expired following an episode of status

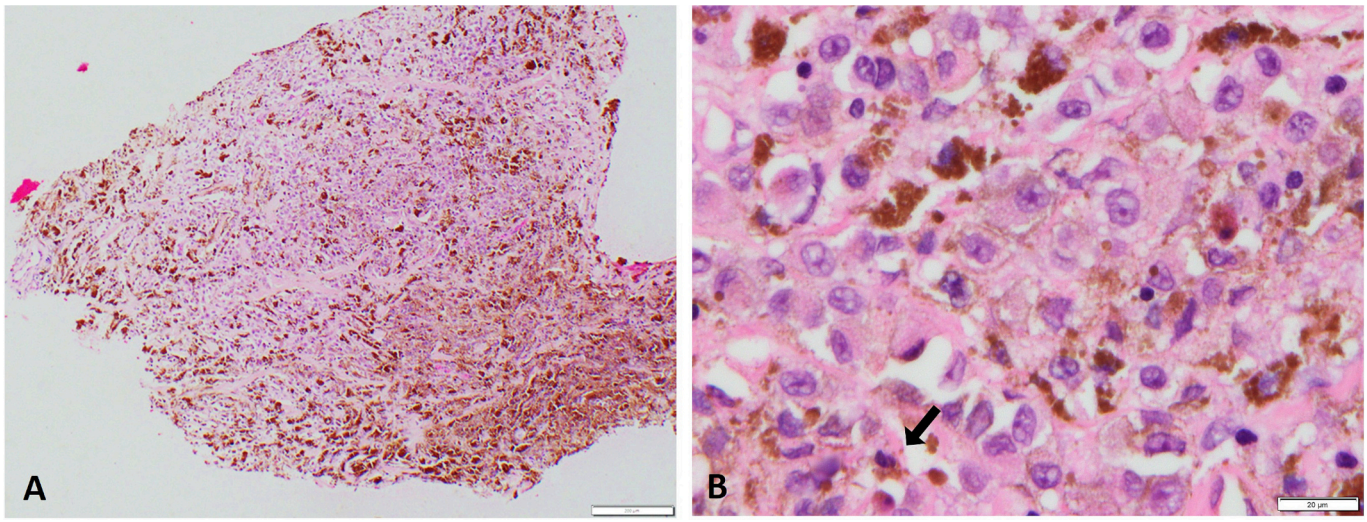

Fig. 2. Histopathological images of the spinal lesion.
A: A lesional fragment of the meninges showing a cellular tumor with lobules and sheets of pigmented polygonal/spindle cells. Lower right area shows sheets of pigmented melanophages (HE stain).
B: The neoplastic cellular component is composed of closely packed polygonal cells with enlarged pleomorphic nuclei, single large macronucleoli, cytoplasmic melanin pigment and mitotic activity (black arrow) (HE stain). The tumor cells are immunopositive for HMB-45 and S-100. Immunolabelling for Ki-67, a proliferative marker, showed increased labelling index. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

epilepticus during assessment at an oncology centre.

2. Discussion

Neurocutaneous melanosis (NCM) is a rare sporadic phakomatosis characterized by large or multiple congenital melanocytic lesions over the trunk and neck associated with meningeal melanosis or melanoma. According to the diagnostic criteria given by Fox et al., [1], single large or multiple congenital nevi without malignant transformation and histologically diagnosed neurological lesion defines the syndrome of NCM. Since its first description by Rokitansky in 1861, more than 200 cases has been reported till date. The proposed pathogenesis is abnormality and growth deregulation of neural crest cells differentiation which is the common origin of melanocytes in the nervous system. The various phenotypic manifestations of NCM include congenital melanocytic nevi (CMN) of the skin as large (LCMN) or giant and/or multiple (MCMN) melanocytic lesions, proliferative melanocytic nodules and melanocytic infiltration of the brain parenchyma and leptomeninges [2]. Symptomatic NCM occurs in 1–10% of children with CMN with very poor prognosis. Most of these patients present within first two years of life. Rarely patients can present in the 2nd decade or later [3]. Our patient had multiple congenital melanocytic nevi with onset of symptoms in late second decade. Presence of large CMN in posterior axial region with multiple satellite nevi has more risk of developing symptomatic NCM than those with extremity lesions without satellite nevi. The most common symptoms reported were headache and vomiting due to raised intracranial pressure with hydrocephalus, seizures, cranial nerve palsies especially sixth cranial nerve and meningeal signs.The involvement of spinal leptomeninges is noted in 20% of NCM cases [4]. Our patient presented with signs of meningeal irritation and optic nerve involvement which has not been described in NCM previously. Though radiologically extensive epidural cord lesion was noted, patient was not symptomatic for the same.

MRI remains the modality of choice in the diagnosis and characterization of CNS melanosis in NCM. The typical lesions of NCM appear hyperintense in T1 weighted images and involve amygdala, brainstem, thalami, cerebellum, basal frontal lobe and spine [5]. Due to the normal presence of melanotic cells, NCM preferentially occurs in the above areas but the extent of melanotic infiltration is indicative of disease, rather than its distribution. Our patient showed patchy leptomeningeal enhancement along brainstem, oculomotor nerves and facial-vestibulocochlear nerve complex. Since MRI of orbits and optic nerves were normal, the etiology of optic neuropathy with clinical and electrophysiological evidence, remains unclear. In addition, paraneoplastic optic neuropathy was less likely in the current patient as normal optic fundus examination and negative paraneoplatic profile were observed. Thus, the proposed hypothesis of occult melanocytic deposits in optic nerve or its sheath is put forth as these can be missed on MRI. Comparison with previously reported late onset NCM are given in **Supplementary Table.** Thus, periodic MRI of asymptomatic patients with giant congenital nevi is recommended to detect early progress of intracranial or spinal melanosis. Treatment of NCM is mainly palliative with chemotherapy and radiotherapy. Experimental studies with MEK inhibitors are underway while surgery may be options for mass lesions and hydrocephalus.

3. Conclusion

Thus we report a late onset NCM with intracranial meningeal infiltration and spinal cord epidural melanoma. The novel finding noted in our patient is optic neuropathy possibly due to occult infiltration. This expands the phenotypic spectrum of NCM and stresses the importance of periodic screening of brain and spine in CMN for early prognostication in these patients.

CRediT authorship contribution statement

Dipti Baskar: Writing – review & editing, Writing – original draft, Methodology, Investigation, Formal analysis, Data curation. **Seena Vengalil:** Writing – review & editing, Supervision, Resources, Project administration, Conceptualization. **Priyanka Chakkera:** Writing – original draft, Data curation. **Sai Bhargava Sanka:** Data curation. **Pritam Raja:** Data curation. **Karthik Kulanthaivelu:** Investigation, Data curation. **Preetham Patavardhan:** Investigation. **Keerti Sitani:** Investigation. **Yasha T. Chickabasaviah:** Methodology, Investigation. **Nupur Pruthi:** Methodology, Investigation. **Atchayaram Nalini:** Writing – review & editing, Supervision, Conceptualization.

Declaration of competing interest

none

Data availability

Data will be available on request from the corresponding author.

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Thank individuals who contributed to the study or manuscript preparation but who do not fulfill all the criteria of authorship.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ensci.2024.100504.

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