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Case Report

Pathology Section

Neurocutaneous Melanosis: A Diagnostic Challenge

UMA KUMAR[1], POOJA JAIN[2], UDITA SINGHAL[3], SHALINI TRIVEDI[4]

ABSTRACT

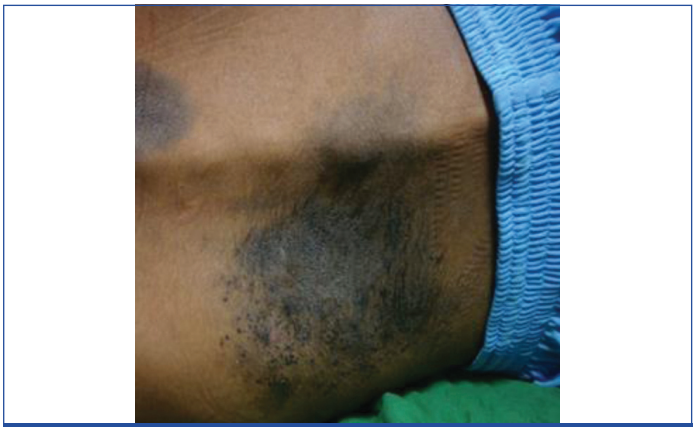
Neurocutaneous Melanosis (NCM) is a rare congenital syndrome presenting as a large or multiple congenital melanocytic nevi and benign or malignant pigment cell tumours of the leptomeninges. The syndrome is defined as an error in the morphogenesis of the embryonal neuroectoderm. It is one of the rare phakomatoses seen in childhood and shows variable presentations. The authors hereby presents a case report of a 15-year-old male patient with NCM, who presented with recurrent episodes of seizures and difficulty in walking. On physical examination, the patient had multiple congenital cutaneous nevi on the trunk, back, and hands. Immunohistochemistry (IHC) with Haematoxylin & Eosin (H&E) staining confirmed the diagnosis of leptomeningeal diffuse melanocytosis was made.

Keywords: Congenital melanocytic nevi, Congenital syndrome, Leptomeninges, Pigment cell tumours

CASE REPORT

A 15-year-old male patient presented with recurrent episodes of seizures for two years. He also complained of difficulty in walking and tremors for five months. He had no medical problems during early childhood and had been performing well in school before these episodes.

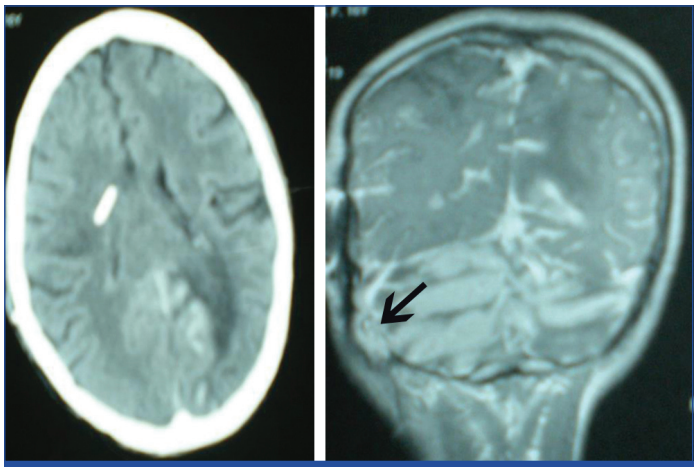
He had been followed in the dermatology clinic since infancy for multiple pigmented lesions all over the body [Table/Fig-1]. He underwent a ventriculo-peritoneal shunt operation one year back. Now the patient presented with complaints of seizures and difficulty in walking. On examination, he was conscious and well-oriented. Central Nervous System (CNS) examination- higher brain functions and cranial nerves were normal. Motor-bulk symmetrical bilaterally, tone-increased, power- 4/5 in all limbs, deep tendon reflexes were present, planters were bilaterally equivocal. Gait could not be assessed because of marked ataxia. The speech was normal and there was no sensory deficit. Cerebellar signs were present-nystagmus, gait ataxia, and dysdiadochokinesia. The finger nose test was positive and tremors became more vigorous in the movement of limbs. Lumbar Cerebrospinal Fluid (CSF) examination was unremarkable.



[Table/Fig-1]: Multiple pigmented nevi over the back of the patient.

Magnetic Resonance Imaging (MRI) showed global leptomeningeal enhancement predominantly involving the posterior fossa along with one solid lesion in the pineal region [Table/Fig-2,3].

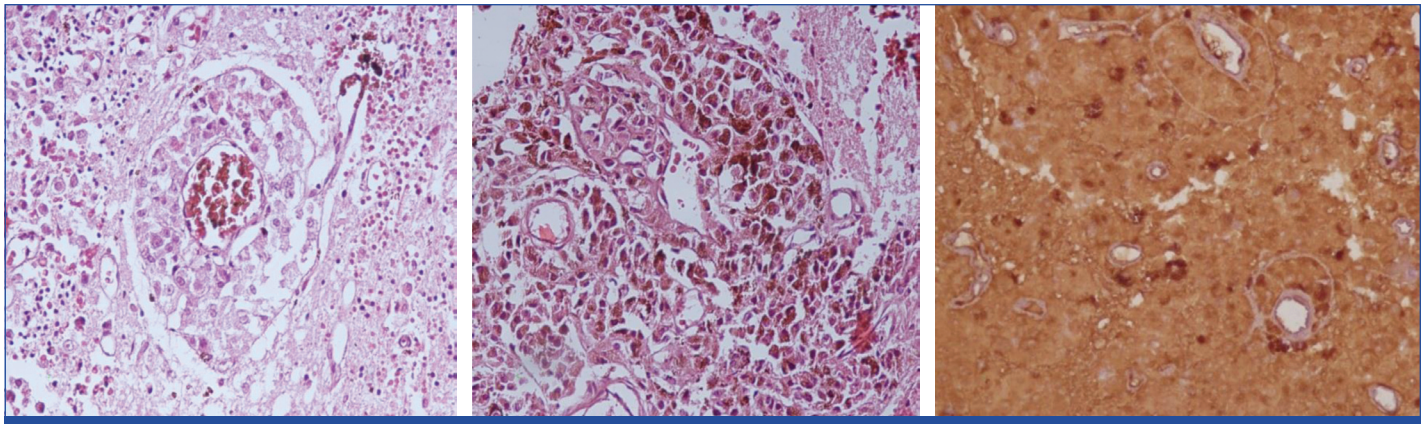
A provisional diagnosis of a mass lesion probably a brain tumour was made. After two days of admission, the patient's general condition worsened, and had to be intubated. The patient was taken-up for emergency surgery after resuscitation. Posterior fossa midline craniotomy with tumour decompression was done. Peroperatively the dura was tense and pulsations were absent. Bluish black spots could be seen underneath the dura. The cerebellar surface was studded with black spots bilaterally. The deep pial surface also showed black spots on the left-side and tumour nodules were seen on the right-side. Good pulsations could be seen after decompression. Biopsies from the dura, cerebellum, and skin lesions were taken-up for histopathological examination.



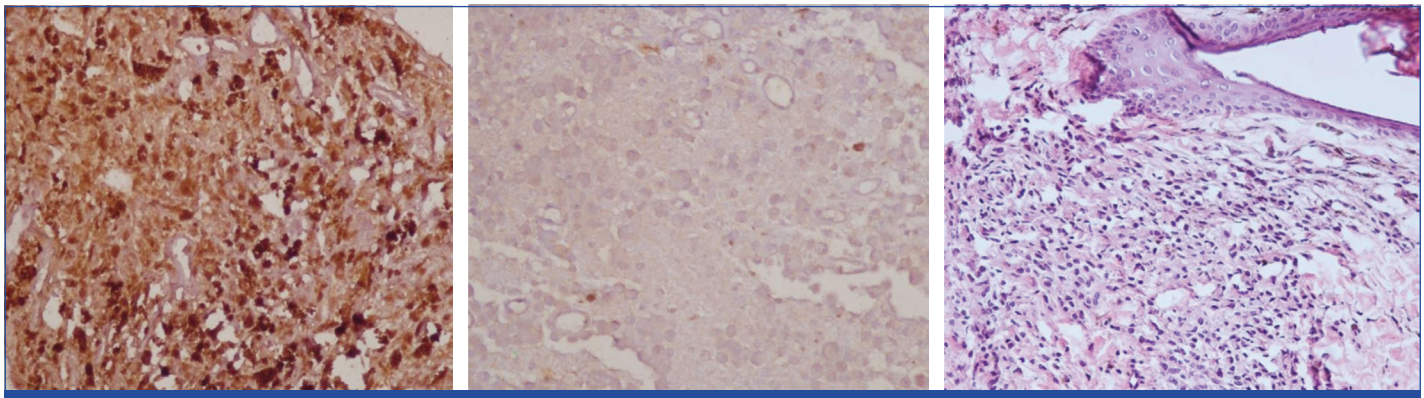
[Table/Fig-2,3]: Magnetic Resonance Imaging (MRI) of the brain demonstrates global leptomeningeal enhancement. (Black arrow). (Images from left to right)

Multiple sections taken from tumour nodules showed cells arranged in solid sheets, cords and nests. Cells displayed abundant eosinophilic cytoplasm and round nuclei with minimal pleomorphism and a single eosinophilic macronucleus. Abundant intracellular melanin pigment was seen, at places obscuring the cell morphology. These cells were seen within Virchow-Robin space, involving the cerebellar cortex and also the arachnoid tissue [Table/Fig-4,5]. No mitosis or necrosis was noted. Histological features were diffuse melanocytosis. IHC showed reactivity for S-100B and Human melanoma [Table/Fig-6,7]. The proliferation index (Ki-67) was very low [Table/Fig-8].

Skin biopsy showed a thinned-out epidermis, hyperkeratosis, follicular plugging, and increased basal pigment. The upper dermis showed nests of round to oval cells with bland nuclei and a moderate amount of cytoplasm. These nests were seen in the close vicinity of follicular plugs [Table/Fig-9]. Histological features and IHC confirms the diagnosis of NCM. Patients of NCM may develop malignant melanoma in 40%-60% of cases. Malignant transformation is



[Table/Fig-4]: Section showing pigmented cells within Virchow-Robin space. (H&E 40X) section. **[Table/Fig-5]:** Section showing pigmented cells arranged in solid sheets, cords and nests. (H&E, 40X). **[Table/Fig-6]:** Section shows (IHC) HMB-45 positivity. (40x). (Images from left to right)



[Table/Fig-7]: Section shows (IHC) S-100 Positive. (40x). **[Table/Fig-8]:** Section shows a very low proliferation index. (Ki-67, 40x). **[Table/Fig-9]:** Sections from skin lesion show nests of round to oval cells with bland nuclei and a moderate amount of cytoplasm. (H&E 10X). (Images from left to right)

heralded by the development of intraparenchymal invasion or intracranial or intraspinal masses taken-up regularly followed the patient for both the neurological as well as for cutaneous lesions at intervals of 3-6 months.

DISCUSSION

Diverse entities of pigmented lesions of CNS have been seen that range from benign to malignant disorders [1]. NCM is a rare neuroectodermal disorder with variable presentations and is associated with other neurocutaneous syndromes like Sturge Weber syndrome, NF type 1, and Dandy-Walker syndrome [2]. It is proposed to be due to abnormality in neural-crest-derived melanoblast of skin and piamater. It is defined by the association of giant or multiple, non malignant, pigmented cutaneous nevi with leptomeningeal melanosis or melanoma [3]. Noronha C and Rocha L reported a similar case of meningeal melanocytosis in a 22-year woman [4].

The indicators of malignant change are infiltration into the brain parenchyma, destruction, haemorrhage, and microscopic indicators of numerous atypical mitoses, necrosis, pleomorphic nuclei, hyperchromasia, prominent large nucleoli, clear cytoplasm, and granular brown pigments [5,6]. In 1972, Fox H defined diagnostic criteria for NCM [7]:

Kadonaga JN and Frieden IJ revised the criteria, which are as follows [8].

- Large (greater than 20 cm in diameter in adults and 6-9 cm in infants) or multiple (≥ three) congenital nevi associated with meningeal melanosis or CNS melanoma.
- No evidence of cutaneous melanoma.
- No evidence of meningeal melanoma except in patients whose skin examination reveals no malignant lesions.

Association of NCM with other neurocutaneous syndromes such as Sturge-Weber syndrome is seen frequently. Dandy-Walker syndrome is seen in 8%-10% of children with NCM [9]. It has been seen that frequent association with these syndromes is a marker of profound infiltration of melanocytes in the CNS and is also found to be a marker of increased risk for malignant transformation [9]. Contrast-Enhanced MRI (CE-MRI) is the most useful diagnostic tool for detecting leptomeningeal involvement in patients with NCM [9].

Histopathological examination reveals leptomeningeal melanosis with dural sparing. This melanosis is mostly seen in areas of physiological melanocytic distribution-the inferior surface of the cerebellum, the frontal, temporal, and occipital lobes, and the ventral surface of the pons, medulla, cerebral peduncles, and upper cervical cord. The anterior temporal lobes and cerebellum are the most common locations for melanocyte accumulation, whereas the temporal lobe is most often affected in parenchymal NCM. Melanocytic infiltration of ependymal cells and perivascular spaces can also occur [10].

The histopathologic presentation of congenital giant nevus is the presence of nevus cells around skin appendages and between fibres of the reticular dermis [11]. The most common age of presentation is below 2 years; less commonly, symptomatic NCM presents between 10 to 20 years of age. Two-thirds of patients presented with neurological signs and symptoms due to hydrocephalus as in our case [9].

Hydrocephalus is the most common presentation and may be due to meningeal thickening, CSF outflow obstruction, or decreased CSF reabsorption. Other complications which are reported in the literature include subdural or parenchymal haemorrhage, syringomyelia, and spinal arachnoiditis. Around 20% of cases show spinal involvement and develop symptoms and signs of myelopathy, radiculopathy, or bowel and bladder dysfunction [12].

Satisfactory treatment of this disorder has not been available till now although surgical resection is performed to prevent the development of malignant melanoma or for cosmetic effects. ventriculo-peritoneal shunt, chemotherapy, radiation, and curettage have been tried. Multiple surgeries are usually done in cases of giant nevi [13].

CONCLUSION(S)

The most common age of presentation is below 2 years while our patient was 15-year-old. Although the congenital nevus was presented since birth, the neurological presentation was late. Dermatologists should keep in mind this rare presentation while treating cutaneous nevi, and regular follow-up is advised. Unfortunately, no therapy is available for this disorder and the prognosis is poor.

REFERENCES

[1] Brat DJ, Perry A. Melanocytic lesions. In: Louis DN, Ohgaki H, Wiestler OD, Cavenee WK, editors. WHO classification of tumours of the central nervous system. 4. Lyon: IARC; 2007. pp. 181-183.

[2] Sarwar M, Tripathy L, Jain H, Basu S, Sengupta A. Neurocutaneous melanosis with hydrocephalus and Dandy-walker variant. Asian J Neurosurg. 2021;16(4):876-80.

[3] Fox H, Emery J, Goodbody R, Yates PO. Neuro-cutaneous melanosis. Arch Dis Child. 1964;39(207):508-16. Doi: 10.1136/adc.39.207.508.

[4] Noronha C, Rocha L. Meningeal melanocytosis: A challenging diagnosis. Lancet Oncol. 2019;20(6):e343.

[5] David EE, Roslalie E, George FM, Xu X. Benign pigmented lesions and melanoma. Levers Histopathology of Skin. 2011,726-29. https://www.researchgate.net/publication/305165614_Benign_pigmented_lesions_and_malignant_melanoma.

[6] Cruz MA, Cho ES, Schwartz RA, Janniger CK. Congenital neurocutaneous melanosis. Ped Dermatol. 1997;60:178-81.

[7] Fox H. Neurocutaneous melanosis. In: Vinken PJ, Bruyn GW, eds. Handbook of clinical neurology. Vol 14. Amsterdam: Elsevier, 1972;414-28.

[8] Kadonaga JN, Frieden IJ. Neurocutaneous melanosis: Definition and review of the literature. J Am Acad Dermatol. 1991;24(5 pt 1):747-55.

[9] Kadonaga JN, Barkovich AJ, Edwards MS, Frieden IJ. Neurocutaneous melanosis in association with Dandy-Walker complex. Pediatric Dermatol. 1992;9:37-43.

[10] Chaloupka JC, Wolf RJ, Varma PK. Neurocutaneous melanosis with the Dandy-Walker malformation: A possible rare path-etiologic association. Neuroradiology. 1996;38:486-89. Available at: https://doi.org/10.1007/BF00607285.

[11] Peretti-Viton P, Gorincour G, Feuillet L, Lambot K, Brunel H, Raybaud C, et al. Neurocutaneous melanosis: Radiological pathological correlation. Eur Radiol. 2002;12:1349-53.

[12] Acosta FL, Binder DK, Barkovich J. Neurocutaneous melanosis presenting with hydrocephalous. J Neurosurg Pediatrics. 2005;102:96-100. Doi: 10.3171/ped.2005.102.1.0096.

[13] Chu WCW, Lee V, Chan YL, Shing MMK, Chik KW, Li CK, et al. Neurocutaneous melanosis with a rapidly deteriorating course. AJNR Am J Neuroradiol. 2003;24(2):287-90.

PARTICULARS OF CONTRIBUTORS:

1. Assistant Professor, Department of Pathology, Janakpuri Superspeciality Hospital, New Delhi, India.
2. Chief Medical Officer, Department of Pathology, ESIC Hospital and Dental College, Rohini, New Delhi, India.
3. Associate Professor, Department of Pathology, ESIC Hospital and Dental College, Rohini, New Delhi, India.
4. Specialist and Head, Department of Pathology, ESIC Hospital and Dental College, Rohini, New Delhi, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:
Pooja Jain,
463, GH2, Baghban Apartment, Sector 28, Rohini, New Delhi, India.
E-mail: drpoojajain83@gmail.com

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