CASE REPORT

Neurocutaneous melanosis: Follow-up and literature review

Mélanose neurocutanée : suivi et revue de la littérature

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Summary Neurocutaneous melanosis is a rare, congenital, non-inherited syndrome characterized by numerous and/or large congenital nevi with intracranial leptomeningeal melanocytosis. This report describes two patients, presenting with a giant congenital nevus involving a major portion of the posterior trunk with satellite congenital nevi scattered all over the body, who developed seizures at 4 and 6 months of age, respectively. Changes in follow-up magnetic resonance (MR) examinations over an 8-year period were seen in case 1, while parenchymal melanocytic accumulation was reported in the region of the amygdala in case 2. These cases emphasize that neurocutaneous melanosis should be suspected in patients with giant congenital nevus with or without neurological symptoms. Also, neuroaxial MR screening should be performed in all cases and, ideally, before myelination of the brain to provide the highest sensitivity for detecting melanin deposits in the leptomeninges.

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Introduction

First described by Rokitanki in 1861, neurocutaneous melanosis (NCM) is a neuroectodermal dysplasia wherein melanocytic deposits, whether benign or malignant, are found within the central nervous system (CNS) \cite{1}. NCM is believed to arise from an embryological defect in the migration of melanoblasts from the neural crest to the leptomeninges and skin \cite{2}.

In 1991, Kadanoga and Frieden proposed the currently accepted criteria summarized in Fig. 1. By this classification, large congenital melanocytic nevi (LCMN) are defined as those \( \geq 20 \) cm in adults, or \( \geq 9 \) cm on the head or \( > 6 \) cm on the trunk in neonates. "Multiple" is defined as more than three. These specific diagnostic criteria allowed their distinction from CNS metastases of a primary skin melanoma \cite{1}. 

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Case report

Case 1

This 5-month-old female infant referred for neurological evaluation was the first child of non-consanguineous parents and had an uneventful gestational history; she had been born by normal delivery and at term.

At birth, a massive hairy nevus was noted on her posterior trunk along with the presence of multiple smaller (>20 cm) nevi scattered all over her body. There were no other such cases in the family. At the age of 4 months, she developed seizures described as loss of consciousness, global hypotonia and cyanosis, afebrile, and only a few seconds in duration. The neurological examination and electroencephalogram (EEG) were normal. Skin biopsy showed benign intradermal nevi.

Cranial magnetic resonance imaging (MRI) at age 7 months showed rounded high-signal areas in the medial portion of the temporal lobes, thalami and mammillary bodies on T1-weighted images that were not visualized on either T2- or FLAIR (fluid-attenuated inversion recovery) weighted images. Follow-up MRI examinations over an 8-year period showed that the abnormal sign in the temporal lobes had decreased, whereas the signal changes in the right thalamus and mammillary body had disappeared completely (Fig. 2).

Valproic acid at a 30-mg/kg dose was started and achieved good seizure control. During subsequent assessments, the patient continued to experience sporadic episodes of seizures associated with mild cognitive delay. The skin lesions remained stable over the 8 years of follow-up with no evidence of malignant transformation (Fig. 3).

Case 2

This female infant was born with multiple pigmented nevi on the neck, face and extremities, and a giant hairy skin nevus on the lower back. Her prenatal and perinatal history was normal. Physical examination revealed hemihypotrophy of the left leg, but no bone-length differences (Fig. 4).

At the age of 6 months, she presented with a single episode of a complex seizure. Neurological examination and developmental evaluation revealed no abnormalities. MRI examination showed a hyperintense area in the amygdala of the right temporal lobe. Post-contrast images showed no abnormal enhancement within either the lesion or leptomeninges (Fig. 5). MRI of the cervical and thoracic spine was also normal. She is now 1 year old and taking an antiepileptic drug with good seizure control.

Discussion

NCM is rare, characterized by a proliferation of melanocytes in the CNS in patients who have LCMN or multiple nevi, although it probably still represents one of the most common intracranial malignant melanomas in children.

The prevalence of LCMN is estimated to occur in less than one in 20,000 newborns. The risk of NCM in patients with LCMN is reported to vary from 1 to 12%, depending on the study and whether asymptomatic patients were investigated [3]. Patients with LCMN along the posterior axis, especially when associated with satellite melanocytic nevi, are at greater risk of the development of manifest NCM [4]. Those usually affected are children under 10 years of age. The majority are asymptomatic until the time of presentation with, most usually, an acute cerebral event such as seizures, headache and vomiting. As the disease progresses, patients may also present with ataxia, aphasia, hemiparesis or paraparesis involving multiple cranial nerves, particularly nerves VI and VII [5].

Epilepsy is one of the most common symptoms, and often manifests as generalized seizures, sometimes with infantile spasms, within the first months of life. In addition, patients can manifest psychiatric symptoms, and signs of spinal cord and root involvement [6,7].

Of the 39 cases reviewed by Kadonaga and Frieden, there was no familial occurrence, and gender was equally represented (ratio: 1.05). However, it is possible that NCM is associated with more frequent complications in boys, a phenomenon that was recently recognized for congenital melanocytic nevi [8].

Melanocytes are normally found in the CNS, most commonly in the pia mater covering the cerebral and cerebellar hemispheres, anterior surface of the brain stem, basal surface of the brain and anterior surface of the spinal cord. Also, normal deposits of melanin can occasionally be seen on MRI along the ventral aspect of the medulla oblongata [9].

MRI findings for NCM are variable, including hyperintense areas in the temporal lobe on T1-weighted images without leptomeningeal enhancement. The characteristic MRI finding is T1 shortening of the involved structures (hyperintensity on T1-weighted images) due to the presence of melanin pigment. Calcium, blood and fat are other causes of T1 shortening on MRI [10].

The anterior temporal lobe, particularly in the region of the amygdala, is the most frequent location for parenchymal melanocytic accumulation, as exemplified in case 2.

Case 1 demonstrated the variability of MRI findings in NCM according to age and brain development, and strongly suggests that MRI should ideally be done before myelination of the brain to provide the highest sensitivity for detecting melanin deposits in the leptomeninges, or as soon as possible.
Figure 2  Skin examination of case 1 shows multiple small nevi scattered all over the body and a giant “bathing nevus”, affecting predominantly the posterior trunk, at 7 months (A, B) and 8 years of age (C, D).

as possible in the presence of neurological symptoms or signs.

We speculate that the mechanism leading to the indistinct lesions seen on MRI may be due to factors such as a limited ability to detect this abnormality using conventional techniques of structural MRI, an increase in brain volume and progressive brain myelination, rather than the possibility of a progressive reduction of abnormal deposits of melanin.

Leptomeningeal involvement is difficult to appreciate unless malignant degeneration has occurred, in which case, contrast-enhanced images may show leptomeningeal enhancement. Such enhancement is often ascribed to the paramagnetic metal scavenging of melanoma cells resulting in spontaneous melanin high signals on T1-weighted images, or attributed to paramagnetic free radicals known to occur in melanin [10].

Recognition of malignant transformation of NCM on MRI may be difficult, although other suggestive findings include focal nodular or thick plaque-like enhancement and any growth of pre-existing or new lesions, particularly if associated with edema or necrosis [10].
Figure 3  T1-weighted MR images of the case 1 patient shows the locations of melanin deposition in the brain at (A) 7 months, seen as rounded areas of high signal in the mammillary bodies, thalami and medial portions of the temporal lobes (arrows), at (B) 4 years and (C) 8 years, at which time, the signal changes in the right thalamus and mammillary body had completely disappeared.

Distinguishing between benign proliferative melanosis and invasive malignant melanoma on histological examination may also be difficult. The melanotic cells may be pleomorphic or predominate in multiple histological forms. However, confirmation of benign non-invasive disease can be histologically supported by a lack of necrosis and cellular atypia or excess mitotic activity. Furthermore, melanoma can be differentiated from melanocytosis by immunohistochemical labeling of proliferation-associated antigens such as Ki-67 [7]. A marked perivascular infiltrate of melanocytes extending into the Virchow–Robin spaces in brain tissue is another characteristic histological finding in NCM,
especially in cases where a parenchymal mass is present [5].

In general, the prognosis for patients with symptomatic NCM is poor, even in the absence of malignancy, whereas the prognosis for patients with asymptomatic NCM detected via screening is more variable and more difficult to predict [7].

Nevertheless, more effective therapies are needed for patients with NCM. In addition, the care of such patients presents significant challenges to both physicians and par-
Figure 5  Axial (A, B) and coronal (C, D) T1-weighted images of case 2 show hyperintensities in the amygdala of the right temporal lobe (arrows), suggestive of melanocytic parenchymal cell deposits.

ents, and the medical as well as psychosocial consequences of the disease need to be addressed by an interdisciplinary team that provides support and a better understanding of the disease for patients and their families.

Disclosure of interest

The authors declare that they have no conflicts of interest concerning this article.

References