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Neurocutaneous melanosis with hydrocephalus, intraspinal arachnoid collections and syringomyelia: case report and literature review

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Abstract Neurocutaneous melanosis (NCM) is a rare nonfamilial syndrome, characterised by large or numerous congenital pigmented nevi and excessive proliferation of melanin-containing cells in the leptomeninges. We report the MR findings in the brain and spine of a child with NCM who underwent neurosurgical treatment and was followed up for 8 years. The findings in this child (small hyperintense collections of melanocytes in both temporal lobes, mild meningeal enhancement along the spine and the development of an extensive subarachnoid CSF accumulation with cord compression and syringomyelia) are believed to be exceptionally rare.

Introduction

Neurocutaneous melanosis (NCM) is a rare nonfamilial syndrome named by Van Bongaert in 1948 [1] and characterised by large or numerous congenital pigmented nevi and excessive proliferation of melanin-containing cells in the leptomeninges. Although about 100 cases of NCM have been reported since the first description by Rokitansky in 1861 [2], the radiological analysis of this syndrome is still limited [3–8]. The most commonly described MR findings comprise enhancement of thickened leptomeninges surrounding the brain and spinal cord [4], ventricular dilatation, cerebral parenchyma (especially temporal lobe) involvement and inferior vermian hypoplasia [3, 5, 7–10].

We present rare MR findings in a child with NCM who was followed up for 8 years and compare our results with the literature.

Case report

A boy was born at 3 weeks preterm, birth weight 2.8 kg, and was noted at birth to have multiple, widely distributed pigmented nevi over the entire body. His parents and 15-year-old brother were healthy. At 3 weeks of age the boy developed seizures, which responded to phenobarbital therapy. At the age of 3 months the child developed symptoms of increased intracranial pressure. Sonography of the brain demonstrated marked hydrocephalus, which was treated with a ventriculoperitoneal shunt. One month later, a skin biopsy was interpreted as highly suspicious of neurocutaneous melanoblastosis. Sonographic follow-up and MRI of the brain at the age of 6 months revealed a clear reduction in the size of the ventricles. Small hyperintense lesions were seen in both temporal lobes on T1-weighted (T1-W) unenhanced images (Fig. 1) and interpreted as collections of melanocytes. MRI of the neck showed an extensive, anteriorly situated subarachnoid CSF collection, which reached from C1 to C6, and a second smaller collection from C7 to T4. The cervical CSF accumulation, in particular, produced severe compression of the cord (Fig. 2). MRI of the lumbosacral region revealed meningeal enhancement after gadolinium and was interpreted as a manifestation of melanosis (Fig. 3).

Neurological investigations at this time and at the age of 22 months were unremarkable; the boy could sit and walk without help. Follow-up MRI at 2 and 3 years of age showed no significant change in the brain lesions or the CSF accumulations along the cervical cord. At this age, the boy quite suddenly developed progressive weakness of the shoulders, finally resulting in paraparesis of the upper extremities. Due to the clinical symptoms, the upper of the CSF collections was punctured transdiscally at the level of C3–4 and a small volume of CSF aspirated. There were no tumour cells. After a temporary recovery the patient deteriorated only 4 days later.

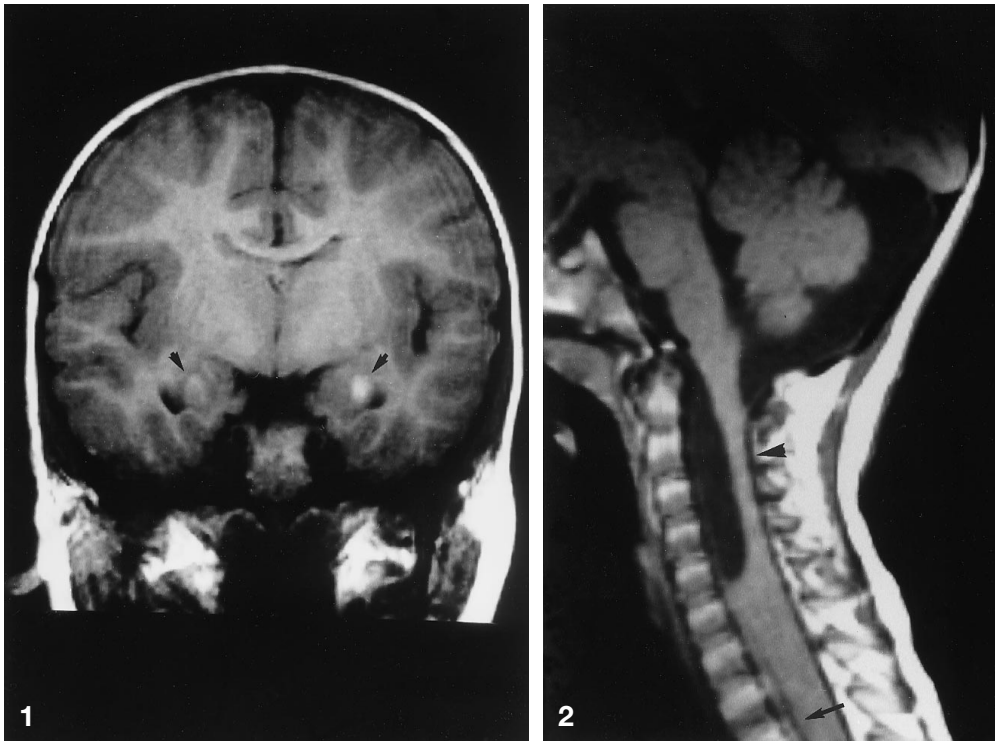

Fig. 1 Coronal T1-W SE image of the brain at 6 months of age. Hyperintense lesions in both temporal lobes are suggestive of melanocytic cell collections (*arrowheads*)

Fig. 2 Sagittal unenhanced T1-W SE image of the brainstem and cervical spine at 6 months of age. An expansile CSF collection extends from C1 to C6 causing severe cord compression (*arrowhead*). A second CSF collection is visible at C7-T4 (*arrow*). The cisterna magna is enlarged

Diagnostic cervical myelography by suboccipital puncture showed communication between a dilated cisterna magna and the subarachnoid CSF collection. Therefore, 10 days later, a shunt from cisterna magna to peritoneum was placed neurosurgically in order to relieve the cervical CSF accumulation indirectly. At the time of surgery the shunt worked perfectly. The first follow-up MRI, 6 weeks after this procedure, showed a clear decrease in size of the CSF collection, resulting in decompression of cord. Shortly after, he relapsed with progressive motor deficits, especially of the upper extremities, and headaches. During the following months the child remained unchanged neurologically, but the hyperpigmented skin lesions showed a rapid increase in number and extent.

At the age of 4 years 6 months, a further MRI of the brain and cervical cord showed no significant change, but he was restless and became anxious at night. At age 7 years the child developed increased headaches and seizures and MRI revealed severe hydrocephalus with dilatation of all four ventricles and syringomyelia of the cervical and upper thoracic cord (Fig. 4). During the consequent neurosurgical intervention the ventriculoperitoneal shunt was found to be disconnected. Follow-up MRI after shunt revision demonstrated decrease in the size of the syrinx (Fig. 5). Nevertheless, motor weakness progressed such that he became dependent on a wheelchair. MRI at the age of nearly 8 years revealed no significant changes.

Discussion

NCM is an uncommon nonfamilial embryonic neuroectodermal dysplasia. It is believed that this disorder may be due to either aberrant migration of the progenitor of melanoblasts from the neural crest to the skin or the action of a lethal gene, surviving by mosaicism [7]. Although NCM commonly develops in patients with malignant melanoma, the two conditions may exist independently. After a definition of NCM by Fox in 1972 [11], Kadonaga and Frieden [7] proposed the following revised criteria for the diagnosis of NCM:

1. Large (is, or is estimated to become equal to, or greater than 20 cm in diameter in an adult/6–9 cm in neonates and infants) or multiple (greater than or equal to three lesions) congenital nevi in association with meningeal melanosis or melanoma.
2. No evidence of cutaneous melanoma, except in patients in whom the examined areas of meningeal lesions are histologically benign.
3. No evidence of meningeal melanoma, except in patients in whom the examined areas of the cutaneous lesions are histologically benign.

Cases with histological confirmation are considered definite; all others are considered provisional diagnoses. By this definition our patient receives a provisional diagnosis of NCM. In a review of 52 reported cases, of which 13 cases were excluded because they did not meet the revised criteria, Kadonaga and Frieden [7] found that leptomeningeal melanoma was present in 62 % of the 39 cases. All cases were confirmed at autopsy except for seven, of which five were confirmed through surgical

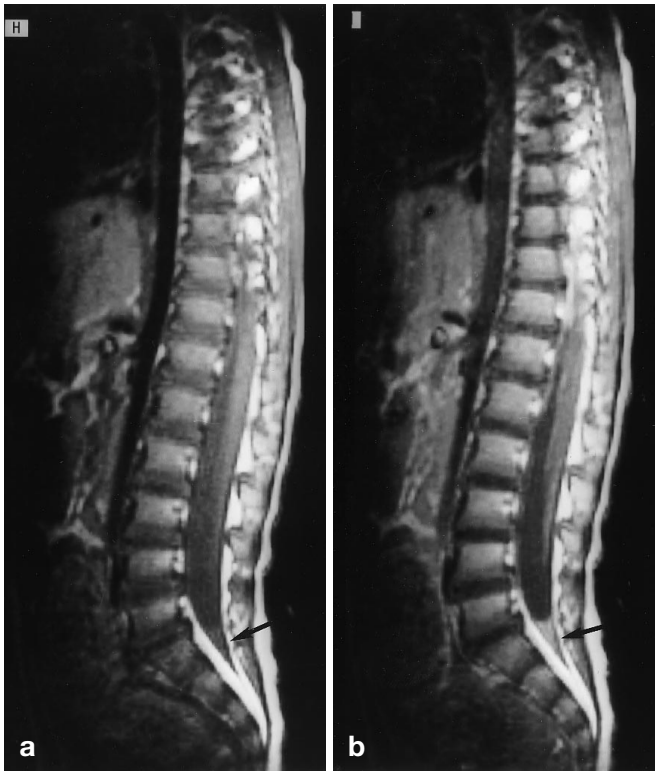

Fig. 3 a, b Sagittal T1-W SE image of the lumbar spine. **a** Leptomeningeal melanosis is barely visible on the unenhanced study. There is accumulation of melanocytes in the caudal spinal canal (*arrow*). **b** Following Gd-DTPA there is mild leptomeningeal enhancement (*arrow*)

procedures or biopsy, or both [6, 10, 12]. Most patients with NCM present in the first 2 years of life with neurological manifestations of increased intracranial pressure, mass lesions or spinal cord compression.

There might be extension of melanotic cell infiltration along the Virchow-Robin spaces, cells having been described lying within the ventricular ependyma and within the choroid plexus [11, 12]. The leptomeningeal, perivascular and ependymal infiltration by melanotic cells is frequently accompanied by melanin-laden macrophages, the so-called 'melanophores'. They are responsible for the parenchymal pigmentation described in the basal ganglia, dentate nucleus, cerebellar hemisphere, pons, thalamus and amygdaloid body (the region in the anterior temporal lobe particularly affected in our patient) [3, 11–13].

It is suggested that the melanocytes spread to these locations because they are close to the basilar meninges, which are known to contain an excessive number of melanocytes in NCM [3]. Until recently, diagnosis of leptomeningeal involvement was impossible in vivo. Earlier reports used cranial CT, and in some cases myelography or angiography, for diagnosis [6, 10, 14]. MRI is now the best method to diagnose leptomeningeal melanosis because intraparenchymal melanin deposits usually lead to severe shortening of T1 relaxation time due to paramagnetic effect. The cause of this effect is still controversial; it might be the result of the presence of stable free radicals in melanin in which the unpaired electrons interact with water protons via an electron-proton dipole-dipole interaction, with subsequent short-

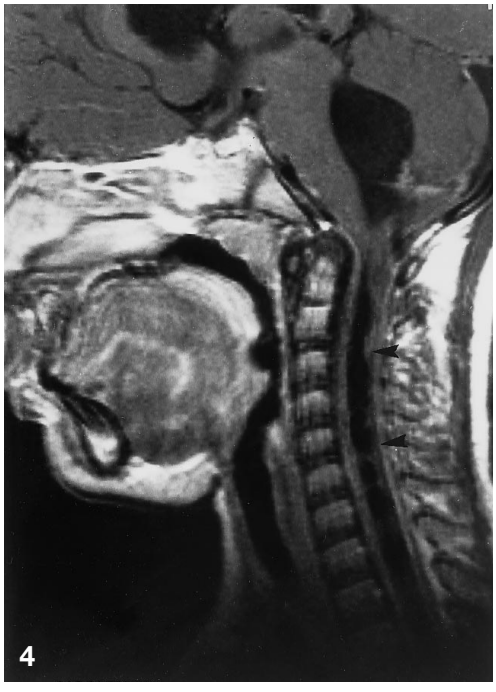

Fig. 4 Sagittal T1-W SE image of the cervical spine at the age of 7 years (after Gd-DTPA). An extensive cervico-thoracic syringomyelia has developed (*arrowheads*). There is dilatation of the third and fourth ventricles. Contrast enhancement is not well seen because of the signal intensity of epidural fat

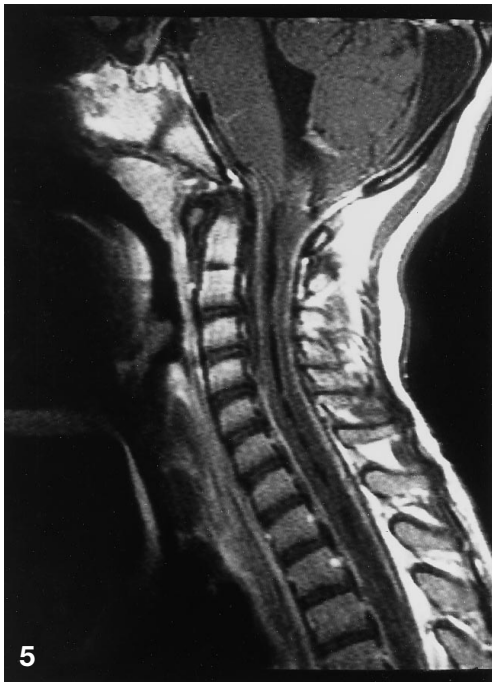

Fig. 5 Sagittal T1-W contrast-enhanced MRI after revision of the ventriculoperitoneal shunt. There is normalisation of ventricular size and incomplete regression of the syringomyelia. Leptomeningeal enhancement can now be better distinguished from epidural fat

ening of both T1 and T2 relaxation times [15]. Nevertheless, there are also reports of melanin deposits without signal abnormality on unenhanced MRI [6, 8]. However, because MRI shows a high incidence of melanin in the brains of patients with giant cutaneous nevi, the incidence of NCM might be much higher than was previously suspected.

Differential diagnosis of NCM includes melanotic neuroectodermal tumour of the cranium of infancy, melanotic nerve sheath tumour (the so-called 'nevus of Ota') and congenital nevi without CNS involvement. The first is a benign pigmented tumour arising from neural crest cells, which often involves the region of the anterior fontanelle. It has an excellent prognosis following early complete excision of the tumour or effective radiotherapy in incompletely resected lesions. The melanotic nerve sheath tumour is an unusual, solitary, melanin-bearing plexiform neurofibroma. It is slowly growing, benign, does not metastasise, is usually located subcutaneously and is a tumour of young adults [9]. A more localised form of probable congenital dysplasia involving the neural crest stem-cell pool is the 'nevus of Ota', also called oculodermal melanocytosis, which often occurs among Mongolian races. It is located unilaterally in the distribution of the trigeminal nerve and is sometimes associated with the development of an intracranial malignant melanoma [16].

Even in the absence of malignant melanoma, symptomatic NCM has an extremely poor prognosis. Kadonaga and Frieden [7] found that in the vast majority of patients the clinical course showed progressive deterioration and early death. The interval between the patient's age at initial presentation with NCM and death ranged from a few days to 21 years. Patients who were treated with palliative surgery, such as shunt placement to reduce intracranial pressure as in our patient, improved at least transiently, whereas antineoplastic therapy did not significantly ameliorate symptoms.

Because there are also cases with good medium-term prognosis, as our case shows, Diaz-Insa et al. [17] stated that MRI should be done periodically. To recognise malignant transformation in NCM is difficult with MRI. An important criterion is the degree of contrast enhancement because enhancement of leptomeningeal or intraparenchymal lesions may correlate with malignancy [8]. Another specific pattern representing malignant transformation might be focal nodular or thick, plaque-like meningeal enhancement [18]. Additionally, any growth of pre-existing lesions is suspicious of malignant transformation, as well as oedema or necrosis of the deposits [3]. The overall incidence of malignancy within the involved meninges is estimated in the order of 50 % [11]. In our child, apart from the development of hydrocephalus and syringomyelia, intracerebral deposits and the subdural cervicothoracic melanotic arachnoid collections showed no significant changes suspicious of malignant transformation.

Fox [11], reported pigmentation of the leptomeninges of the brainstem and cerebral base in 85 %, of the spine in 20 % and of the cerebellum in 25 %. Kadonaga and Frieden [7] described marked melanosis of the meninges in 97 % of 39 cases, cranial involvement in 88 % and spinal involvement in 88 %, but 34 of these 39 patients proved not to have melanocytic cells in the liquor, as in our patient. Knowledge of these locations can aid in the differentiation of metastases secondary to malignant degeneration of cutaneous nevi, found in 2–13 % by Leaney et al. [12], from melanotic deposits that are a part of the disease. Melanotic pigmentation of the leptomeninges leads to disturbance of CSF circulation, a factor in the wide range of complications in NCM. As in our patient, hydrocephalus is reported to be the most common complication [4, 9, 10]. It is due to obstruction of CSF circulation, either at the fourth ventricle outlets or within the basal subarachnoid cisterns. Communicating hydrocephalus is attributed to accumulation of melanotic cells in the basal subarachnoid cisterns, while aqueduct stenosis leads to the noncommunicating type [7].

Myelopathy in children, described by Byrd et al. [4], was due to spinal cord invasion with proliferating malignant cells of the leptomeninges. On MRI, all these children demonstrated marked leptomeningeal enhancement, attributed to the malignant form of NCM. Leptomeningeal enhancement in our child was only mild and the exceptionally long duration of the disease is unlikely to represent malignant melanosis. The cause of the cervical myelopathy in our child was the development of an expansile CSF collection with cord compression. The most probable reason for the CSF accumulation with mass effect is a nonbacterial arachnoiditis due to leptomeningeal melanosis. To the best of our knowledge this complication has not previously been described in patients with NCM.

Another striking MR feature in our child was the development of syringomyelia, which has previously been described only once in a child with NCM [12]. Displacement of the ventriculoperitoneal shunt in combination with chronic arachnoiditis was the most probable reason for syringomyelia accompanied by dilatation of all ventricles. This was emphasised by the fact that shunt revision led to regression of the syringomyelia and normalisation of ventricular size.

Chemotherapy has been shown to have little effect on the rapid course of NCM with malignant leptomeningeal involvement. The most important palliative treatment in children with NCM and hydrocephalus is insertion of a shunt, as occurred in our patient. Shunting itself, however, may lead to dissemination of melanoma throughout the peritoneal cavity with melanotic metastatic lesions not only in peritoneum, omentum, abdom-

inal lymph nodes, but also in liver and pleura [9, 10]. A filter must be placed in the shunt to prevent this complication.

Conclusion

Neurocutaneous melanosis is a phakomatosis with potential for serious neurological complications that can best be diagnosed by Gd-enhanced MRI. Besides the malignant form of NCM in which myelopathy typically is caused by cord invasion with malignant leptomeningeal cells, myelopathy can develop in the more benign form due to an expansive subarachnoid CSF collection with mass effect and cord compression. The MRI findings in our child add an exceptional case to the spectrum of imaging abnormalities seen in children with NCM.

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