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CASE REPORT

Neurocutaneous melanosis associated with Dandy–Walker complex and an intracranial cavernous angioma

Kyung Hwan Kim · Sang-Bong Chung · Doo-Sik Kong · Ho-Jun Seol · Hyung Jin Shin

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Introduction

Neurocutaneous melanosis (NCM) is a rare, non-familial phacomatosis that is characterized by large and/or numerous congenital melanocytic nevi and abnormal proliferation of the melanin-containing cells in the central nervous system (CNS) [9–11, 20]. Since Di Rocco et al. reported a 10% incidence of NCM and an association with cystic malformations of the posterior fossae [9], approximately 8% to 10% of patients with NCM have been found to harbor an associated Dandy–Walker malformation [6, 12, 13]. Dandy–Walker malformation is noted for vermian hypoplasia, cerebellar dysgenesis, cystic dilatation of the posterior fossa, and an enlarged fourth ventricle [3, 9, 10]. Intracranial cavernous angioma (CA) represents 1.7% to 18% of all vascular malformations in children, and the most frequent presentations in symptomatic CA are seizures, followed by focal neurologic deficits, hemorrhage, and headache [14].

In this report, we discuss the clinical history, neuroimaging findings, and pathological results related to a unique case in which NCM and Dandy–Walker complex (DWC) coexisted with a CA.

Case report

A previously healthy 8-year-old boy was admitted to the emergency room because of headache and an episode of seizure. His seizure started with vertigo sensations and was followed by eyeball deviation, lip cyanosis, and tonic leg movement lasting 5 s. After that, his condition generalized to complex partial seizure and lasted for 5 min. He began to fall asleep after vomiting in the post-ictal period. On admission, we found multiple hairy melanocytic nevi ranging in size up to 4.2 cm on his back and buttock (Fig. 1). He had no neurologic deficits, and his neurocognitive performance was within normal limits at the time of admission. We obtained an electroencephalogram to evaluate the seizure; there were no specific findings. The patient had been delivered normally after a full-term gestation (38+0 weeks) and was noted at birth to have hyperpigmented skin lesions. No significant familial history was elicited.

The brain magnetic resonance (MR) imaging revealed multifocal, high-signal intensity lesions on T1-weighted images in the ventral portion of the pons, the medial aspect of the bilateral temporal lobes, and the left occipital lobe (Fig. 2). An occipital mass lesion disclosed dark signal intensity on gradient-echo sequence and additional enhancement after gadolinium-contrast infusion (Fig. 3). The MR findings of vermian hypoplasia, cerebellar hemispheric dysgenesis, and a dilated fourth ventricle led us to consider DWC (Figs. 2b, c). The spinal MR imaging studies showed neither leptomeningeal enhancement nor other significant abnormalities. To rule out a systemic disease or malignant melanoma, we performed positron emission tomography with 18-FDG of the whole body. No pathologic deposits were seen in the scan. The patient's skin stigmata and radiological findings suggested concomitant NCM with DWC.

An occipital craniotomy allowed for removal of the left occipital mass, which was located in a relatively safe area to access. The mass was a 1-cm-sized reddish-purple appearance resembling a multi-lobulated mulberry and was well-circumscribed and surrounded by ectatic vessels (Fig. 4). There were several black pigmentations scattered over the

K. H. Kim · S.-B. Chung · D.-S. Kong · H.-J. Seol · H. J. Shin (✉)
Department of Neurosurgery, Samsung Medical Center,
Sungkyunkwan University School of Medicine,
50 Ilwon-dong, Gangnam-gu,
Seoul 135-710, Republic of Korea
e-mail: shinhj@skku.edu

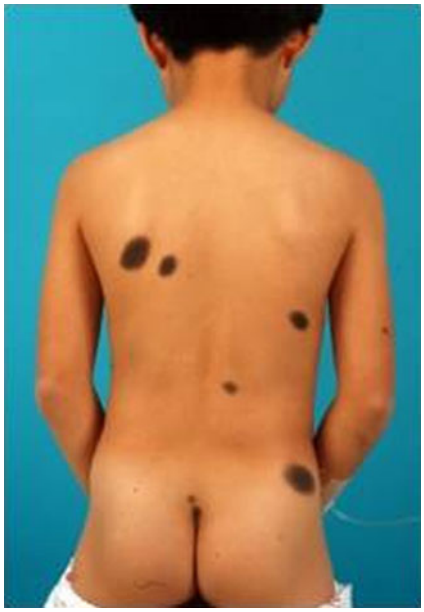

Fig. 1 Multiple congenital melanocytic nevi on the back and buttock

exposed brain cortex. The mass lesion was completely excised for biopsy. The histopathologic analysis of the excised mass revealed many dilated vessels containing blood clots without brain parenchyma, which was compatible with CA. There was also extensive infiltration of melanocytes into the perivascular space (Figs. 5a–c). We performed an excisional biopsy of the skin lesion on the patient's back, which was diagnosed as an intradermal nevus (Fig. 5d).

The patient was discharged 1 week after surgery without any complications. There was no evidence of disease progression or malignant transformation in follow-up MR images. To date (more than 1 year after surgery), the patient has not experienced any neurologic symptoms and has achieved normal developmental milestones.

Discussion

NCM is a rare, non-hereditary congenital syndrome that occurs with equal frequency in both sexes. Over 100 cases have been reported in the literature [1, 4, 7, 9–13, 15–20,

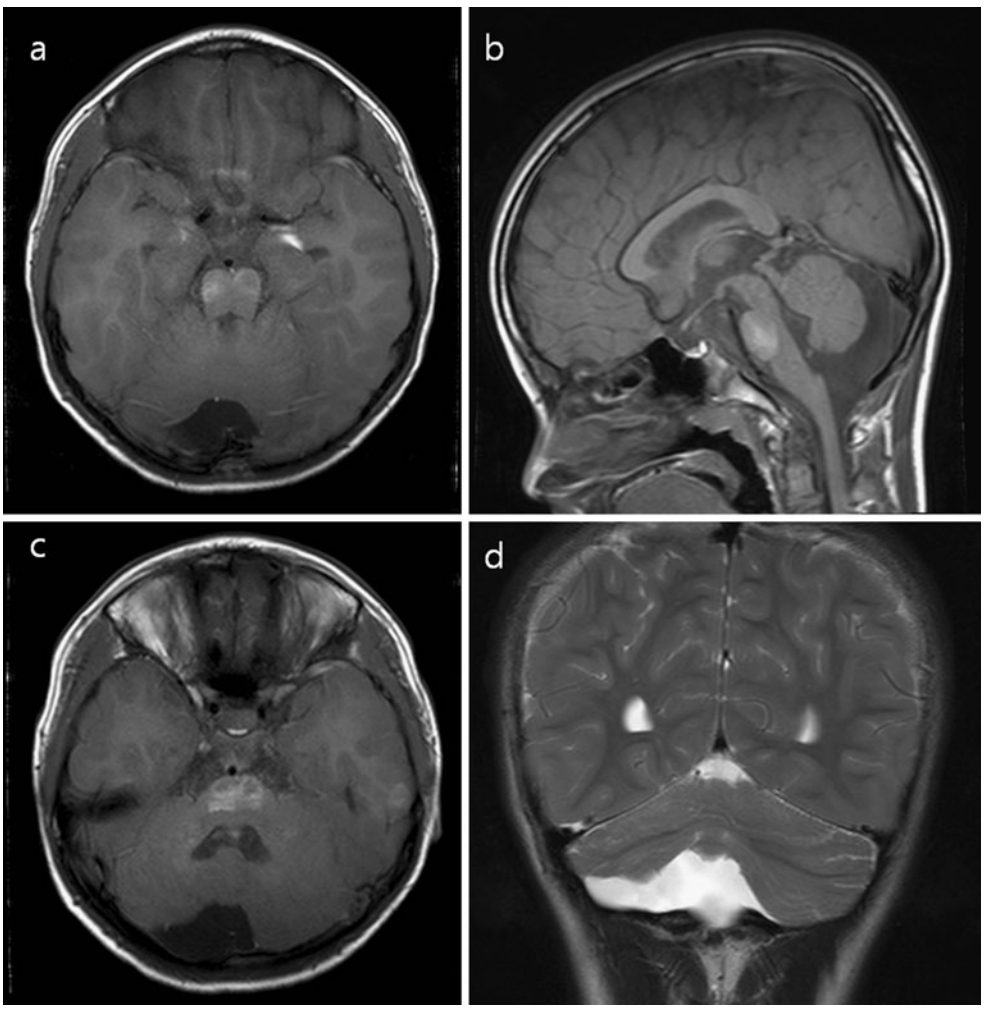

Fig. 2 Preoperative magnetic resonance images demonstrating multifocal, high-signal intensity lesions in the ventral portion of the pons and the medial temporal lobe (**a**) on T1-weighted axial view and (**b**) on T1-weighted sagittal view. Cyst located in the posterior fossae with hypoplasia of the right cerebellar hemisphere and mild dilatation of the inferior fourth ventricle were noted (**c**) on T1-weighted axial view and (**d**) on T2-weighted coronal view

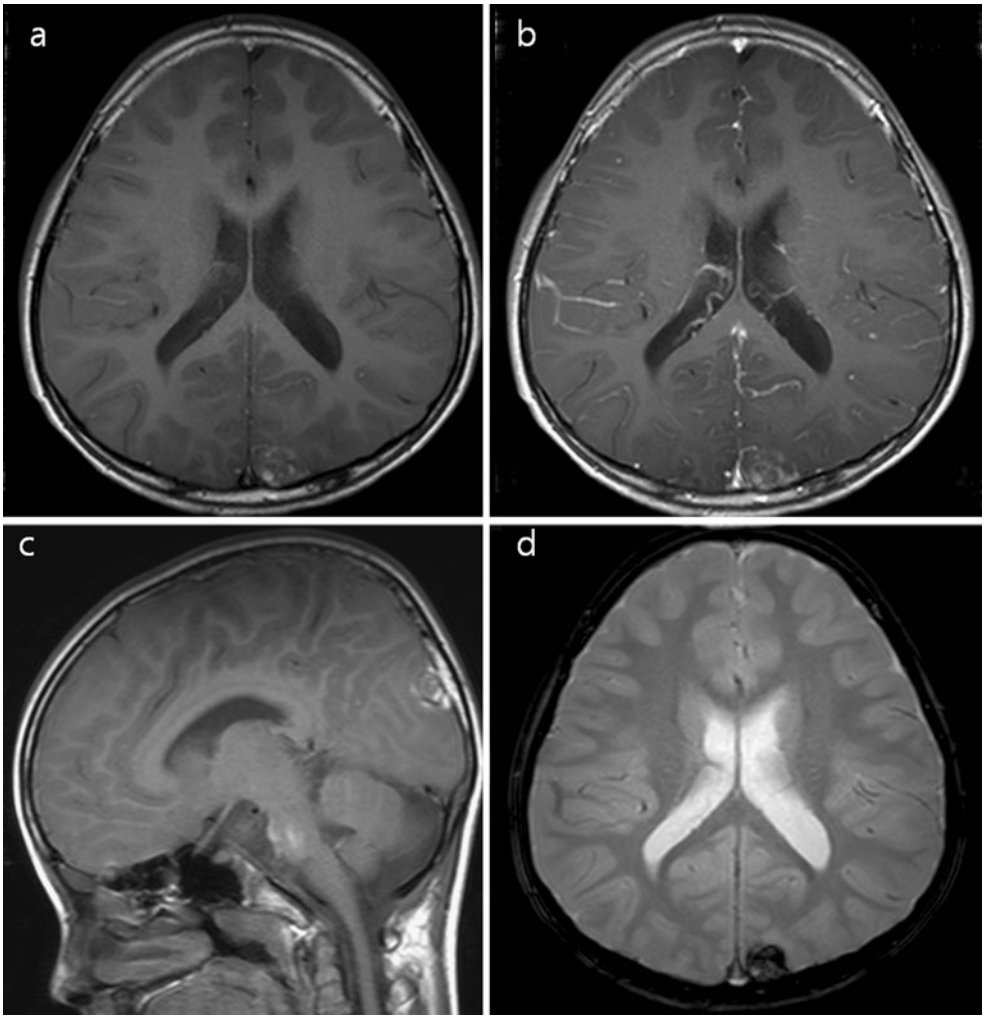

Fig. 3 Preoperative magnetic resonance images demonstrating an occipital mass lesion. (**a**) T1-weighted axial image showing a mass lesion with heterogeneous signal intensity. (**b**) T1-weighted axial image with contrast enhancement. (**c**) T1-weighted sagittal image indicating a hypo-intense rim surrounding the mass lesion. (**d**) Dark signal in gradient-echo protocol suggesting bleeding in the mass

22–24]. NCM is characterized by giant or multiple congenital nonmalignant melanocytic nevi associated with benign or malignant melanocytic proliferation in the leptomeninges or brain parenchyma [9, 11, 16]. The current diagnostic criterion of NCM was established by Kadonaga and Frieden [11]: large or multiple congenital melanocytic nevi associated with meningeal melanosis or melanoma. To distinguish this syndrome from a possible occurrence of primary melanoma with synchronous brain metastasis, they emphasized that there should be no evidence of cutaneous melanoma except in patients in whom the examined portions of the meningeal lesions are benign, and vice versa. The diagnosis of NCM in cases that lack histologic confirmation of the lesions in the CNS is considered provisional. The pathogenesis of NCM is not clearly understood; however, it may be related to an error in migration of neural crest-derived pleuripotent precursor cells. In NCM, melanocytes proliferate in the skin and leptomeninges to form a marked perivascular infiltrate that characteristically fills the Virchow–Robin spaces [11]. MR imaging with contrast enhancement is the current diagnostic modality of choice in patients in whom NCM is suspected [10, 21]. The most frequent finding is increased signal intensity on a T1-weighted image, which represents an accumulation of melanocytes and enhancement of tumor-infiltrated meninges with the typical aspect of leptomeningeal melanosis. These findings are most frequently seen in the anterior temporal region close to the amygdala and over the cerebellum. Some authors have also

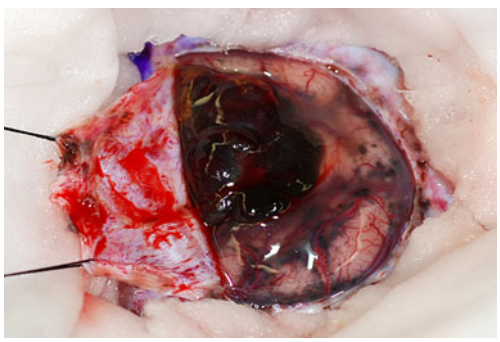

Fig. 4 Intraoperative photograph after opening the dura mater: reddish-purple-colored multi-lobulated mass and black pepper-like pigmentation scattered on the brain cortex

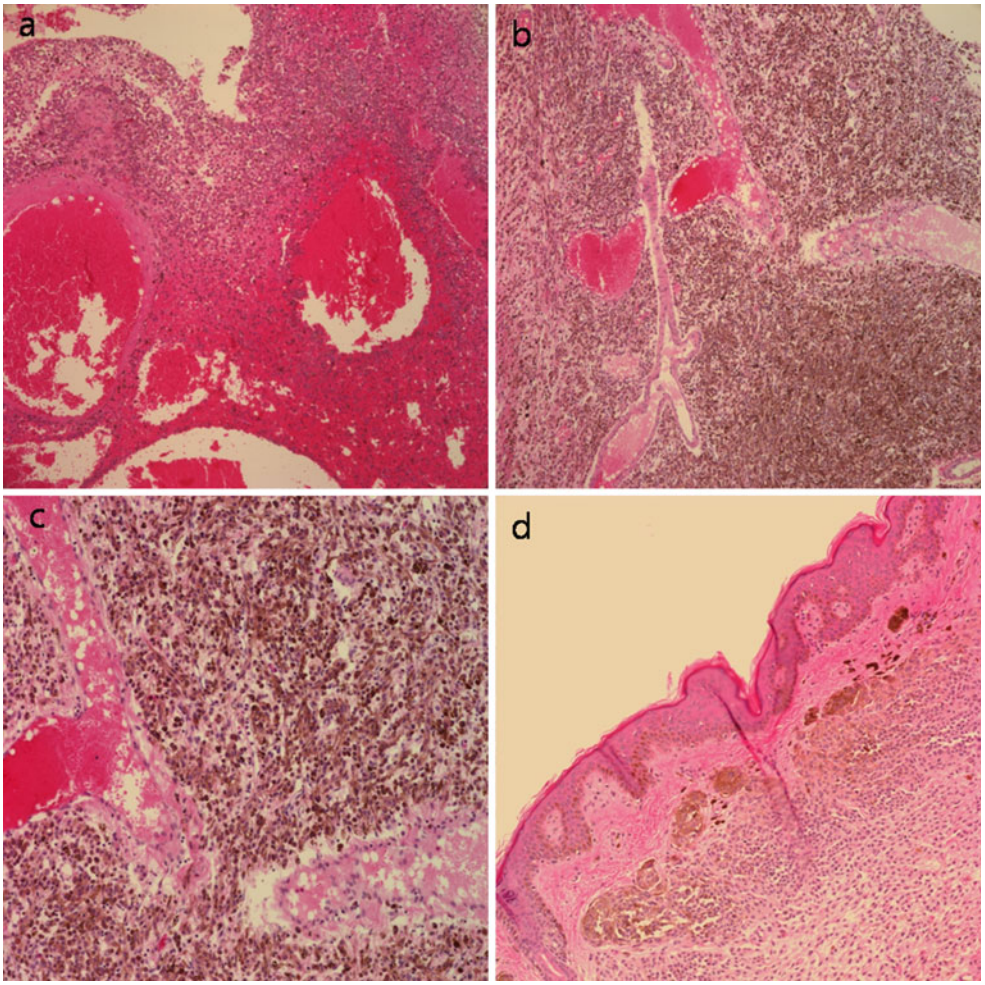

Fig. 5 Histopathologic findings of the occipital mass and skin lesion. (**a**) The specimen disclosed many enlarged vessels containing blood clots, which is consistent with cavernous angioma (hematoxylin and eosin; original magnification ×100). (**b**) and (**c**) Numerous melanocytes and their perivascular distribution along the Virchow–Robin space, which are other histological features of neurocutaneous melanosis (hematoxylin and eosin; (**b**) original magnification ×100, (**c**) original magnification ×200). (**d**) The specimen from the skin lesion was compatible with intradermal nevus (hematoxylin and eosin; original magnification ×200)

reported marked and diffuse enhancement of the infiltrated leptomeninges of the spinal cord [10].

Neurologic manifestations of NCM occur generally in the first 2 years of life, and neurologic symptoms are broad and nonspecific as they depend on the extent of leptomeningeal or parenchymal involvement. Two thirds of patients reportedly develop hydrocephalus and other neurologic manifestations including developmental delays, partial or generalized seizures, movement disorders, and myelopathy [4, 10, 11, 16]. Most of these manifestations are related to increased intracranial pressure due to diffuse leptomeningeal melanosis or melanoma.

NCM is sometimes associated with other neurocutaneous syndromes and is present in up to 10% of cases with Dandy–Walker malformation [9, 10]. The Dandy–Walker malformation is a rare congenital disease of neuroaxis characterized by vermian hypoplasia, cystic dilatation of the posterior fossa, and an enlarged fourth ventricle [3]. When enlargement of the posterior fossa is not present and the volume of the posterior fossa is normal, then the malformation is called Dandy–Walker variant [19]. Barkovich et al. suggested a new term, Dandy–Walker complex, for these lesions instead of the current terms existing for this condition (Dandy–Walker malformation, the Dandy–Walker variant, and the mega cisterna magna) since these are not discrete entities but instead are consecutive events of the same embryological process [2]. They also hypothesized that excessive meningeal melanosis may result in defective ectodermal–mesodermal interaction, slowing development of the cerebellum and fourth ventricle [2, 10]. A few cases of NCM associated with DWC have been reported, which raises the probability of these two entities having the same origin [1, 4, 7, 10, 12, 13, 17, 18, 23, 24]. Signs and symptoms of NCM in DWC patients are mostly related with hydrocephalus, which includes clinical manifestations of irritability, lethargy, hemiparesis, developmental delays, psychomotor symptoms, hypotonia, and spastic paraparesis. A quarter of this group suffered from seizure, as was seen in the present case.

Generally, the prognosis of NCM associated with DWM is dismal; once the neurologic symptoms manifest, the course is progressive and fatal [4, 7, 10]. In Kadonaga and Frieden's review of 39 patients, the median survival time was 6.5 months after onset of symptoms, with more than

50% of deaths occurring within the first 2 years of life [11]. The proper palliative therapies (such as ventriculoperitoneal shunt and removal of the intracranial mass) were effective in controlling the progression of the neurologic manifestation [1, 13, 24]. Chemotherapy and radiation therapy did not show any efficacy and did not alter the fatal course of symptomatic NCM when malignant involvement of CNS was diagnosed [16].

A minority of patients with symptomatic NCM has been reported to have an intracranial mass. These patients became symptomatic at a somewhat later age (median 8.5 years) and are more likely to develop focal seizures, localized sensorimotor deficits, or psychiatric symptoms [22]. Patients with symptomatic NCM have a significant risk of CNS melanoma with a prevalence of 50–64% and a median age at death of 3 years [5, 8, 11]. However, histologically confirmed intracranial mass (except malignant melanoma) is rare. Kang et al. only reported one patient who had intracranial meningeal melanocytoma and dermoid tumor synchronous with NCM and DWC [13]. They suggested the possibility that the leptomeningeal melanosis interferes not only with the normal inductive effects of primitive meningeal development, but also with ectodermal development.

The patient in this report was unique in that the unusual entities of NCM, DWC, and benign intracranial mass (CA other than malignant melanoma) occurred together. To the best of our knowledge, we are not aware of any previous description of the concurrence of intracranial CA in a patient with NCM. Furthermore, the patient presented with a single event of complex partial seizure as his first neurologic symptom at a relatively late age of 8 years. There were no other associated symptoms or abnormalities, such as mental retardation, developmental delay or hydrocephalus, which are commonly found in patients with NCM and/or DWC. Although the patient had multifocal, high-signal intensity lesions in the medial aspect of the bilateral temporal lobe, the semiology was different from that of temporal lobe epilepsy, and no abnormal epileptic discharges were observed from temporal electrodes on waking and sleep electroencephalograms. Because there were no further seizure events during the year after resection of the occipital lesion, we presumed that CA was the cause of seizure. We are, however, also conscious of the possibility that he may experience another type of seizure event caused by melanocytic infiltration in the medial temporal lobe and occipital cortex.

It is unclear what underlying relationship exists between NCM and CA development; however, this type of unusual presentation should be added to the spectrum of NCM. Our case illustrated that NCM associated with DWC can present as a seizure episode that might be caused by another intracranial benign mass lesion. Contrary to the reported prognosis of a fatal disease course and a short life expectancy, the prognosis is not uniformly rapid or fatal, as was seen in our patient.

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