

# A Case of Neurocutaneous Melanosis in a 46-year Old Man

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Neurocutaneous melanosis is a very rare congenital syndrome characterized by the presence of large or multiple congenital melanocytic nevi and benign or malignant melanotic tumors of the central nervous system.

We report herein a case of neurocutaneous melanosis with leptomeningeal melanosis and a malignant melanoma of the right temporal lobe in a 46-year old man. The case is exceptional as regards the late onset of symptoms and death.

Even without a malignant melanoma, the symptomatic neurocutaneous melanosis has a fatal course. The syndrome is rare but lethal, so the dermatologist should be aware of this syndrome when evaluating the patients with large or numerous congenital melanocytic nevi so as to watch for the usual signs of increased intracranial pressure and to take prompt palliative measures. (*Ann Dermatol* 9:(4):293~297, 1997).

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**Key Words :** Neurocutaneous melanosis , Adult onset

Neurocutaneous melanosis (NCM) is a rare congenital syndrome first described by Rokitsanski in 1861. This syndrome is characterized by the association of giant or multiple congenital melanocytic nevi with benign or malignant melanotic tumors of the central nervous system. The total number of neurocutaneous melanosis is less than 100 cases. Patients with neurocutaneous melanosis most frequently display signs of neurological disorders resulting from increased intracranial pressure and spinal compression during the first two years of their life.<sup>1-5</sup> We report herein a case of neurocutaneous melanosis with leptomeningeal melanosis and a malignant melanoma of the right

temporal lobe in a 46-year old man which has not been reported in Korean dermatological literature.

He had eight congenital pigmented nevi which were smaller than six centimeters. The case is exceptional as regards the late onset of symptoms

and death.

## REPORT OF A CASE

A 46-year-old Korean man had been referred to our dermatological department by the neurosurgical department in our hospital because of his large, multiple congenital pigmented nevi. He had suffered from a 5-month history of headache and gradually increasing eyeball pain. He was a previously healthy man and had no personal or family history of medical or skin diseases. Physical examination showed no abnormality including oral mucosa but ophthalmological examination revealed mild papilledema of fundus. Skin examination showed eight congenital, some hairy, black to brown pigmented nevi varying in size from several millimeters to a few centimeters across (largest diameter: 5.7 centimeters) on the back, buttocks (Fig. 1), right sole, and limbs. There was no evidence of the rapid growth, asymmetry, and satellite lesions indicating the malignant changes of the pigmented nevi. Other physical examinations revealed no abnormality including lymph nodes, head and neck, oral mucosa, chest and abdomen. But the funduscopic examination revealed the slight

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**Fig. 1.** Multiple and small congenital pigmented nevi on the buttocks, right thigh and back.

**Fig. 2.** Skin biopsy at the lesion of the right buttock shows that nevus cells are present near and around appendages and the deep dermis (H&E stain,  $\times 200$ ).

**Fig. 3.** The involved area of brain parenchyma is characterized by large pigmented cells with much pleomorphic or atypical features (H&E stain,  $\times 400$ ).

**Fig. 5.** The atypical melanocytic cells form a marked perivascular infiltrate and characteristically fill into Virchow-Robin spaces with positivity in S-100 (S-100,  $\times 400$ ).

**Fig. 4.** Diffuse melanosis of leptomeninges adjacent to the right temporal lobe. Note sparing of dura mater which is from a different embryologic origin (H&E stain,  $\times 100$ ).

papilledema. Neck stiffness was not demonstrated. The following laboratory investigations were negative or within normal limits : complete blood cell count, urinalysis, liver function test, and roentgenogram of the chest. Magnetic resonance imaging (MRI) revealed the mass lesion of high signal intensity with the cystic portion of low signal intensity of right temporal lobe in T1 images as the mass of the size of  $5 \times 4$  cm compressed the ipsilateral lateral ventricle and the

midbrain accompanying peritumoral edema, and the diffuse melanosis of leptomeninges. The lesion was highly enhanced. The neurosurgeons, at first, thought the brain lesion was a metastatic lesion from the other organs, so all systemic organs were examined including gastroscopy, small bowel series, ophthalmologic examination and chest-abdomen-pelvic computed tomography(CT). But there was no evidence of primary lesion of malignant melanoma. Skin biopsy was performed in all the congenital pigmented lesions. And they showed compound nevi or intradermal nevi, in which the nest of nevus cells were located adjacent to hair follicles(Fig. 2), nerves, sweat glands and the cells in one specimen showed a neuroid differentiation. There was neither dysplastic nevus nor malignant melanoma of the skin. So the metastasis of cutaneous malignant melanoma was ruled out. In a few days, severe headaches, blurred vision and subsequent mental change developed. A prompt frontotemporal craniotomy as a palliative neurosurgical procedure was done. Soon he appeared to improve. Operative biopsy revealed the malignant melanoma of a right temporal lobe (Fig. 3) and diffuse melanosis of leptomeninges (Fig. 4) which were also confirmed malignant by the pathologists, in that the infiltrating cells had pleomorphic cell pattern, hyperchromatic nuclei, and many mitotic figures including atypical mitosis in the brain parenchymal cells. Besides, the cells of leptomeningeal cells had the pattern of invasion to brain parenchyma, as they characteristically filled the Virchow-Robin space (Fig. 5). Special staining as S-100 and HMB-45 had been proved to be positive in the malignant cells. However, in spite of temporal lobectomy and post-operative radiotherapy, unfortunately he expired one month thereafter presenting with the deterioration of respiration, anisocoric pupilar response and the comatose status. The spinal MRI and follow-up CT demonstrated the hemorrhagic lesions in the temporal lobe regions and the diffuse spinal seeding

## DISCUSSION

The association of giant congenital melanocytic nevi with primary malignant melanoma of meninges is very rare. Since the original description by Rokitsanski in 1861, fewer than 100 cases of NCM have been reported. In 1991, Kadonaga et al<sup>1</sup> reviewed 52 patients with NCM and found

that 66% exhibited giant nevi (i.e., at least, 20 cm in their largest diameter); the others had multiple congenital nevi without a prominent large lesion. In patients with giant nevi, two thirds had lesions in a bathing trunk or lumbosacral distribution, and the other one third had lesions in the occipital area or on the upper back. Posterior midline lesion and head or neck lesions are common lesions of nevi in NCM.

In one study<sup>2</sup>, all the patients with manifest NCM had a large congenital pigmented nevus (LCMN) in a posterior axial location. Our patient did not have a large congenital pigmented nevus but multiple small congenital pigmented nevi in posterior midline areas.

One possible explanation for the association of posterior axial LCMN and NCM is that if the melanocytic malformation occurs during the development and migration of the neural crest, from which both cutaneous and leptomeningeal melanocytes originate,<sup>1-5</sup> the risk that the malformation will involve both the central nervous system and the skin of the nearby posterior axis is increased.<sup>2</sup>

This concept can be applied to the cases of multiple small congenital nevi. In the previous articles written in English, small or medium-sized congenital pigmented nevi in NCM included the scalp and neck in most cases<sup>1-10</sup>.

Neurocutaneous melanosis (NCM) is postulated to represent a congenital error in the morphogenesis of the embryonal neuroectoderm. The neural crest, where precursor cells of both cutaneous and leptomeningeal melanocytosis are formed, gives rise to the melanotic cells of both skin and leptomeninges.<sup>6</sup> When the normal migration or differentiation of the cells is disturbed, congenital pigmented nevi and/or leptomeningeal melanosis can develop<sup>1-6</sup>.

There are three diagnostic criteria(Fox et al., 1972): 1) unduly large or unusually numerous congenital pigmented nevi in association with leptomeningeal melanosis or melanoma

2) no evidence of malignant changes in any of the cutaneous lesions except in patients in whom the examined areas of the meningeal lesions are histologically benign,

and 3) no evidence of malignant melanoma in any organ apart from the skin lesion, except in patients whose cutaneous lesions are histologically benign<sup>1-2,6</sup>.

The background of the criteria is that when both cutaneous and meningeal melanoma are present the possibilities of malignant metastasis cannot be excluded either from the skin to the meninges or vice versa considering that CNS metastasis of cutaneous melanoma is about 40%.

The revised Fox's criteria included 'large melanocytic nevus' correspond to more than 20cm in diameter and 'numerous melanocytic nevi' to more than three. In cases of neonates or infants, large is more than 9cm in diameter on the head and 6cm in diameter on the body<sup>1,2</sup>. The disease affects both sexes equally and seems to occur more frequently in whites<sup>1,3</sup>. The cases with NCM are stillbirth, neonate, and occasionally second decade or later and usually have no family history with sporadic occurrence<sup>1,3</sup>.

The patients with NCM most frequently present neurologic manifestations within the first two years of life such as irritability, vomiting, seizures which result from increased intracranial pressure and hydrocephalus. The patients with manifest NCM in the second decade or later in life tend to have a intracranial mass lesion, spinal cord compression of intracranial lesions, or psychiatric symptoms<sup>1,2,5</sup>.

There have been very few reported cases of later onset than in the fifth decade.

Even symptomatic NCM without melanoma has extremely poor prognosis, because there is no effective treatment except palliative measures such as shunt placement<sup>1,7</sup>. Symptomatic NCM is almost fatal due to repeated increased intracranial pressure (IICP) although functioning shunt.<sup>8-12</sup>

Increased intracranial pressure is caused by the presence of an abnormal mass of melanotic cells in the meninges. In their review of the literature, Kadonaga<sup>1</sup> found that 62% of these lesions undergo malignant changes and show evidence of a leptomeningeal melanoma.

If we can include cases of primary localized malignant melanoma without diffuse leptomeningeal melanosis into the category of NCM<sup>4</sup>, the prognosis of the cases may be better through early operation. The prognosis of the localized cases may reflect on the malignant nature of the tumor.

Although no treatment has so far proved to be effective in prolonging life or providing more than a transient relief of symptoms, dermatologists should be aware of this lethal syndrome in their follow-up of

patients with large or multiple congenital melanocytic nevi so as to watch for the usual signs of IICP and to take prompt palliative measures. Besides, the necessity of early operation of the congenital pigmented nevi<sup>13</sup> may be altered in the presence of symptomatic NCM.

In conclusion, our patient is unique in that he had lived a normal life without neurological symptom until his forties, and he had a large malignant melanoma of the right temporal lobe with malignant melanocytosis of the adjacent leptomeninges.

Tumor resection and shunt operation had no effect on survival of the patient because of the rapid leptomeningeal seeding in cerebrospinal fluid and subsequent increased intracranial pressure after only a few weeks.

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