□ Case Report □

A case of congenital neurocutaneous melanosis

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Neurocutaneous melanosis is a rare congenital syndrome characterized by the presence of large or multiple congenital melanocytic nevi and benign pigment cell tumors of the leptomeninges. Neurocutaneous melanosis is thought to represent an error in the morphogenesis of embryonal neuroectoderm. We experienced a neonate who presented with giant, dark colored pigmented nevi covering chest, abdomen, neck and arms, with satellite lesions. Magnetic resonance image showed a nodular hyperintense lesion in the amygdala of the right temporal lobe, and T1-weighted images showed hyperintensities in the adjacent leptomeninges. We report a rare case of neurocutaneous melanosis with a brief review of related literature. **(Korean J Pediatr 2006;49:212-216)**

Key Words : Neurocutaneous melanosis, Newborn

Introduction

Neurocutaneous melanosis (NCM) is a rare congenital disorder defined as the syndrome of giant or multiple benign nevi on the skin accompanied by leptomeningeal melanosis or melanoma without evidence of malignant melanoma other than of the meninges[1]. The pathogenesis of this disorder is presumed to involve a developmental error in the morphogenesis of the embryonal neuroectoderm[1-5]. A giant nevus is seen at birth and preferred sites include the back of the trunk, the "bathing trunk" region, and the scalp, and neck[2, 6, 7]. Most of patients develop neurologic manifestations before 2 years of age, and the majority die within 3 years of presenting neurological symptoms[2, 4, 5, 7].

It is recommended that giant congenital melanocytic nevus (GCMN) be removed soon after diagnosis due to cosmetic problems and its propensity for malignant change[2, 4-6, 8, 9].

GCMN occurs approximately in one per twenty thousand people and about a hundred cases had been reported prior to the year 2000 worldwide[3, 4, 10]. In Korea, NCM is a rare disease, which has been reported by Won et al.[6] and Hong et al.[11]. We report another case of NCM including a literature review.

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Case report

A 1 day-old male neonate was born by vaginal delivery at the gestational age of 38 weeks and 2 days. There was a premature rupture of membrane 32 hours before delivery without meconium staining. His Apgar score was 8 points after 1 minute of delivery, and 9 points after 5 minutes. His head circumference was 34.5 cm (75-90 percentile), height 48.0 cm (25-50 percentile) and body weight 2,870 g (25-50 percentile). There was nothing remarkable about his family history of disease. His mother was a 31-year-old healthy woman who had received no medication during pregnancy.

He was admitted for multiple nevi involving the whole body skin. On the first day of admission, his blood pressure was 63/44 mmHg, heart rate 136 beats/min, respiratory rate 58 breaths/min, and body temperature 36.8℃. There were dark nevi in various sizes on his scalp and entire body (Fig. 1A, 1B), irregularly scattered nodules and partially exudative hemorrhages (Fig. 1C). Especially, the abdomen, chest wall, and arms were entirely covered with black nevi, but these showed no color change or pain on digital compression. There was also no ulceration or necrosis on the nevi. Moro reflex, sucking reflex, grasp reflex, and muscle tone were normal.

We found complete blood cell counts, C-reactive protein and blood chemistry to be normal. Skin biopsy showed

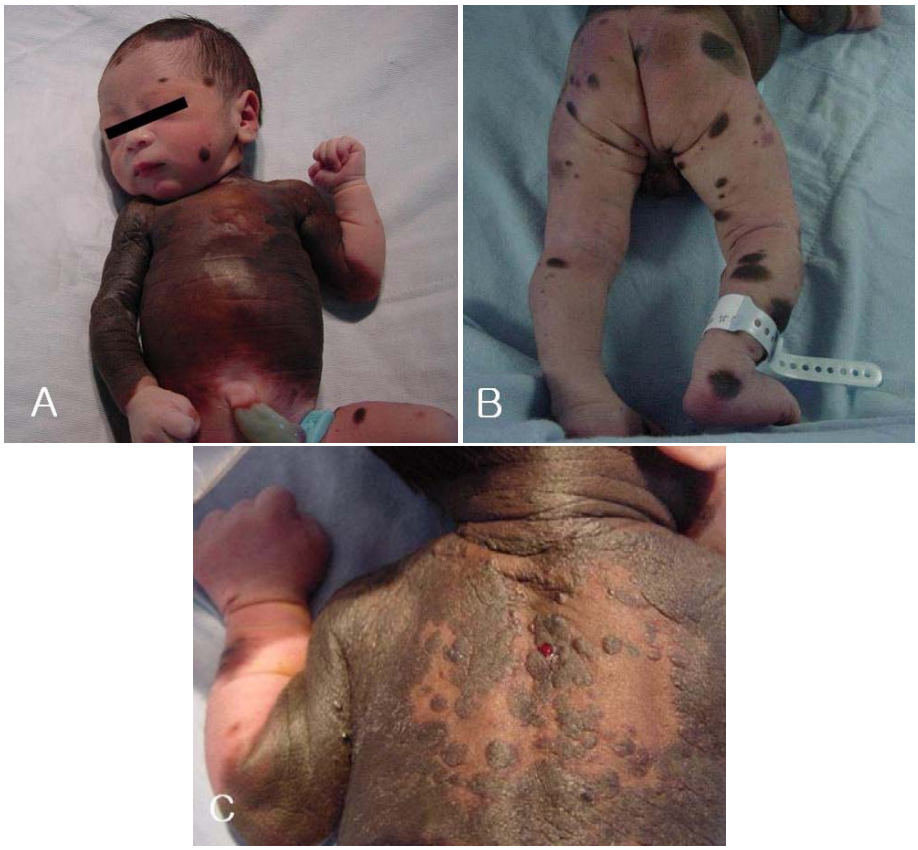

Fig. 1. General appearance. **(A)** A giant dark-colored pigmented nevus covering chest, abdomen, neck and arms with satellite lesions. **(B)** Multiple, small pigmented nevi were seen on buttocks and legs. **(C)** Giant dark-colored pigmented nevus covering neck, back and arm with oozing.

melanocytic nevus cells were present in the deep dermal layer without atypical mitosis or necrosis (Fig. 2). Fat-saturated T1 weighted brain MR images showed melanocytic nevi which was 4 cm in diameter on the right occipital scalp and abnormal high signal intensity lesions in both basal ganglia, anterior commissure, occipital subcortical white matter and nodular high signals in the right amygdala. The leptomeninges under the scalp nevus were thick and hyperintense (Fig. 3).

He underwent curettage and an artificial skin graft at 2, 3 and 4 months of age. He was followed up when he was 7 months of age and his general status was good (Fig. 4). At this time, his body weight was 7.5 kg (10 percentile), height 68.5 cm (10-25 percentile) and head circumference 42 cm (3-10 percentile). He could creep and briefly sit by himself, representing a developmental status of 7 to 8 months of age. He showed no vomiting or convulsion. His skin lesions showed marked improvement and the anterior fontanelle was flat and soft.

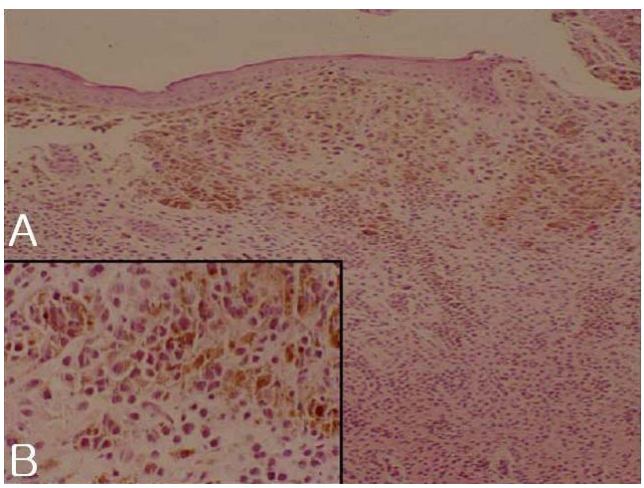

Fig. 2. Skin biopsy. **(A)** The cutaneous lesions consisted of a diffuse infiltrate of melanocytic nevus cells spreading from the papillary dermis to the deep reticular dermis (H&E stain, ×100). **(B)** Nevus cells in the papillary dermis had abundant pigmentation, but this does not imply malignancy in the absence of cellular atypia or mitosis (H&E stain, ×400).

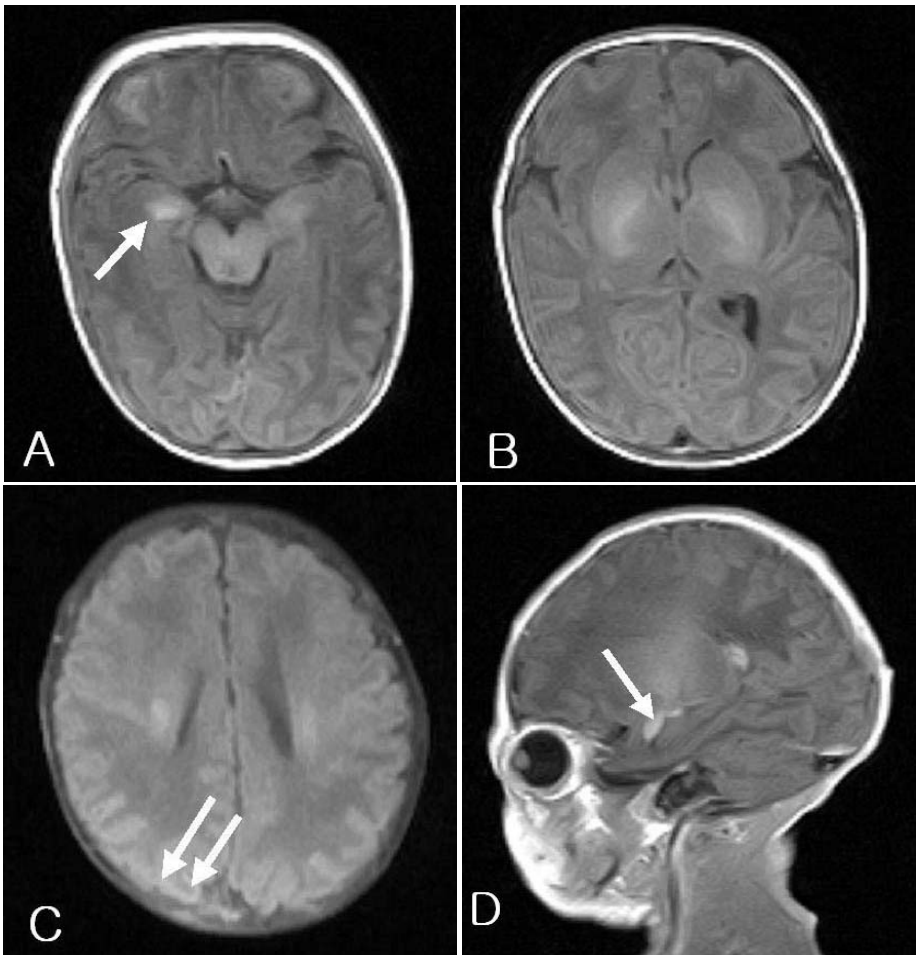

Fig. 3. MR examination. **(A)** Axial T1 weighted image showing an abnormal hyperintense area in the right anterior temporal lobe (arrow). No edema or mass effect was detected. **(B)** Axial T1 weighted image showing hyperintense areas in both basal ganglia. **(C)** Axial Gd-enhanced fat-saturated T1 weighted image showing hyperintense area in the right occipital scalp showing melanocytic nevus and hyperintense thickened adjacent leptomeninges suggestive of leptomeningeal melanosis (arrows). **(D)** Sagittal Gd-enhanced T1 weighted image showing a nodular hyperintense area in the right temporal lobe (amygdala) (arrow).

Discussion

NCM is a rare congenital disorder that was first described by Rokitansky[12] in 1961 in the 14-year-old girl with GCMN, mental retardation, and hydrocephalus. However, the term NCM was initially used by van Bogaert[13] in 1948 to describe a different clinical entity. In 1972 Fox[1] defined the following diagnostic criteria for NCM : "unduly large or unusually numerous" pigmented nevi in association with leptomeningeal melanosis or melanoma, no evidence of malignant change in any cutaneous lesion, and no evidence of malignant melanoma in any organ apart from the meninges. Giant nevus defined as a lesion greater than 20 cm in diameter in adults or larger than 9 cm for a scalp nevus or larger than 6 cm for a trunk nevus in neonates or infants. In a report by Kadonaga and Frieden[2] more than three lesions were defined. In a review of 289 patients with GCMN, 33 patients (11.4%) had NCM, and all of these patients had posterior axial cutaneous lesions and satellite nevi[7].

About 100 cases were reported worldwide before 2000 [3, 4, 10]. NCM has not been reported in identical twins. GCMN without CNS lesions has no gender predilection, though a higher incidence was reported in Caucasians[2]. About 40 to 50% of leptomeningeal melanomas are known to differentiate to malignant melanomas of the CNS[4].

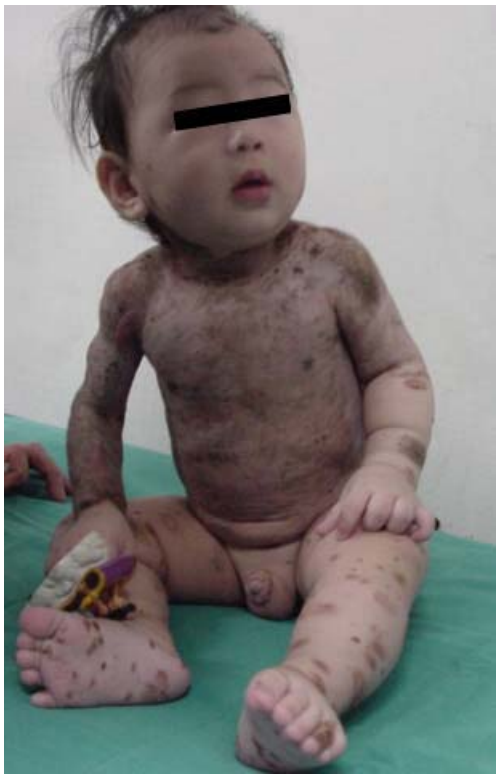

Fig. 4. General appearance after curettage at age 7 months.

The pathogenesis of this disorder is unclear but it is presumed to be due to a congenital error that affects the morphogenesis of the embryonal neuroectoderm[1-5]. Cramer [14] proposed that migration occurs along the autonomic and sensory nerves that supply the epidermis and dermis and along vascular and adnexal structures. This may account for the extension of nevus cells into the reticular dermis. Moreover, Happle[15] proposed that NCM, and a variety of other congenital hamartomas, could result from a dominant lethal gene that survives by mosaicism.

Cutaneous lesions are giant and multiple pigmented nevi. The sites of predilection are the back of the trunk, scalp, neck, and the swimming trunks area, which is why it is often called "bathing trunk". Frequently these lesions appear on the lumbosacral, occipital, and upper back area[2, 6]. The surfaces of nevi are irregular and often covered with hair, and they often have nearby satellite lesions or are associated with a giant nevus and numerous small nevi scattered over the entire body[2, 5, 6]. Our patient had dark nevi over the entire abdomen, chest, and arms, and variously sized satellite lesions over the entire body. Nodules were irregularly dispersed on the surfaces of nevi with exudative hemorrhage but without ulceration or necrosis.

Neurologic symptoms usually develop before 2 years of age, but less frequently in the second or third decades of life. The majority of infants and young children with NCM have symptoms and signs of increased intracranial pressure, such as irritability, headache, lethargy, recurrent vomiting, generalized seizures, an increased head circumference, papilledema, neck stiffness, occasionally cranial nerve VI and VII palsies, an ataxic gait, developmental retardation, voiding and defecation difficulties. In adolescence, psychiatric symptoms, expressive aphasia or dysarthria, focal seizures, or localizing sensorimotor changes may develop, and frequently communicating or noncommunicating hydrocephalus develops[2, 4-7]. Other accompanying clinical manifestations are Meckel's diverticulum, Dandy-Walker syndrome[10, 11], an anomalous urinary tract, sarcoma of striated muscle, syringomyelia, respiratory tract infection, anorexia, angioma, encephalocele, arachnoid cyst, and intraspinal lipoma[2, 5, 6, 8, 10].

The pathologic findings of skin of NCM are similar to those of other melanocytic nevi. The most commonly affected areas of brain are the temporal lobe, amygdala, brain stem, and cerebellar folia. Leptomeninges may become thickened due to densely pigmented melanin and such pigmentation may be extensively dispersed[3, 4, 7]. Our patient has not yet shown any neurologic abnormality, other clinical manifestations, or hydrocephalus at 7 months.

The histologic characteristics of NCM are; the presence of nevus cells in the deep dermal or subcutaneous fatty layer, nevus cells set in arrays in collagen fibers forming a so called 'Indian file' pattern, and nevus cell invasion to the skin appendages, vessels, and neurons present under the reticular dermis[16].

The signs of malignant change are nodular invasion to the brain parenchyme, destruction, hemorrhage, and microscopically the presence of many atypical mitoses, necrosis, nuclear pleomorphism, hyperchromasia, prominent nucleoli, transparent cytoplasm, and granular brown pigments[4].

CSF findings in NCM are increased pressure, elevated protein, normal or low glucose, and pleocytosis. EEG often shows focal or generalized abnormal waves[2, 9]. Brain MRI is the most reliable modality for the diagnosis of NCM. T1 weighted images usually show high intensity signals due to the presence of melanocytes. T1 and T2 relaxation times shorten, leptomeninges become enhanced, particularly in the anterior temporal lobe and amygdala but may appear in the thalamus, cerebellum, inferior frontal lobe, pons, and cerebral medullary area. High fat signals may mask lesions

and hence fat-suppressing T1 weighted imaging technique may be preferred[2-5, 7, 9].

No satisfactory therapy is available for this disorder although surgical resection is performed to prevent malignant melanoma development or for cosmetic effect. Ventriculoperitoneal shunt, chemotherapy, radiation, and curettage have been tried[2, 4-6, 8, 9]. The treatment of giant nevi requires multiple operations. Moreover, the total excision of wide skin areas may lead to important blood losses, and graft donor site insufficiency problems. Dermabrasion of these nevi was proposed more than 10 years ago, but may result in recurrence if too superficial, or alternatively hypertrophic or depigmented scarring may occur if too deep [17]. Moss[18] proposed an alternative curettage technique. Curettage has the advantages of limiting blood losses, and of a better cosmetic result if performed before 2 weeks of age, which makes it possible to separate the natural cleavage plane between the superficial and deep dermis, allowing the operator to better estimate lesion depth[8, 17, 19].

NCM patients are reported to have a poor prognosis if neurologic symptoms develop[2, 4, 7]. According to Kadonaga and Frieden[2], 70% of patients die before 10 years of age, and over 50% die within 3 years of the development of neurologic symptoms; only 8% of patients survived.

한 글 요 약

선천성 신경피부멜라닌증 1례

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신경피부멜라닌증은 피부와 중추신경계를 침범하는 드문 선천성 증후군으로 연수막에 멜라닌증 또는 흑색종과 동반하여 피부에 거대 또는 다수의 색소성 모반이 존재하며, 피부에서 악성변화의 증거가 없고, 뇌수막 외에 다른 부위에 악성 흑색종의 증거가 없는 경우로 정의된다. 발생기전은 배아신경 외배엽의 형태발생 착오로 생기는 것으로 알려져 있다. 저자들은 복부, 흉부와 팔 전체에 검은색 모반이 덮여있고, 전신에 다양한 크기의 위성병변이 출생시부터 존재한 신생아를 경험하였다. 뇌 자기공명영상은 오른쪽 측두엽의 편도에 결절모양의 고신호 강도를 보였고, 지방억제 T1 강조영상은 연수막 주위의 고신호 강도를 보였다. 저자들은 거대 선천성 색소성 모반을 가진 신생아에서 뇌 자기공명영상으로 진단받고 3차례의 소파술과 인공피부이식술을 받은 드문 선천성 증후군인 신경피부멜라닌증 환자 1례를 경험하고 문헌 고찰과 함께 보고하는 바이다.

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