A Case of Neurofibromatosis Associated with Moyamoya Disease

Hyoung-Seob Kim, M.D., Mu-Hyoung Lee, M.D.,
Woo-Young Sim, M.D., Choong-Rim Haw, M.D.

Department of Dermatology, College of Medicine, Kyung-Hee University, Seoul, Korea

Neurofibromatosis produces a broad spectrum of clinical manifestations. Cafe-au-lait spots, cutaneous neurofibroma and tumors of the central and peripheral nervous system are well known manifestations. One of the more serious aspects of the disease relates to the arterial involvement. Renal arterial disease with resultant hypertension has been paticularly well documented. However, cerebrovascular lesions in neurofibromatosis are uncommon. Cerebral arterial occlusive diseases with juxtabasilar telangiectasia (moyamoya disease) associated with neurofibromatosis have been documented in about 40 patients in the world literature. We report a case of neurofibromatosis associated with the moyamoya disease.

(Ann Dermatol 10:(1) 44~47, 1998).

Key Words : Moyamoya disease, Neurofibromatosis.

Neurofibromatosis is an autosomal dominant disorder with varied manifestations in bone, soft tissue, the nervous system, and skin[1]. Neurofibromatosis has been classified into seven types[2]. The unmodified term neurofibromatosis implies the type 1 version. It is the most common form of neurofibromatosis and was formerly known as von Recklinghausen's disease, classic neurofibromatosis, or peripheral neurofibromatosis. Neurofibromatosis type 1 (NF 1) is characterized by café-au-lait macules, neurofibromas, Lisch nodules, optic glioma, bony dysplasia, intertriginous freckling and autosomal dominant inheritance[1,2]. One of the less common but more serious manifestations of NF 1 relates to the peculiar vasculopathy[3]. Despite the fact that renal, aortic, celiac and mesenteric arterial lesions have been described, intracranial vascular lesions have been uncommon and have received little attention[4,5].

Herein, we report a case of neurofibromatosis associated with cerebral arterial occlusive diseases with juxtabasilar telangiectasia (moyamoya disease).

Received Septrmber 23, 1997.
Accepted for publication December 8, 1997.
Reprint request to : Hyoung-Seob Kim, M.D., Department of Dermatology, College of Medicine, Kyung-Hee University, Seoul, Korea

CASE REPORT

A 20-year-old male patient visited our department for the evaluation of skin problems. He had multiple café-au-lait spots on the trunk and extremities, two neurofibromas on the right arm and left wrist and mutiple freckles on both axillary areas(Fig. 1-3). The café-au-lait spots and neurofibromas were present at birth. The axillary freckling developed at the age of 9.

Nine years ago, he was admitted to the neurosurgical department of our hospital for the evaluation of focal seizure, change of mentality and right sided weakness that had suddenly developed. Cerebral angiography showed cerebrovascular occlusive lesions with collateral small vessels. He was diagnosed as having moyamoya disease and then recieved conservative management including antiepileptic drug therapy. His neurological symptoms slowly improved and he had no recurrence of the seizures. Before the attack of moyamoya disease, he had normal intelligence and was healthy except for mild intermittent headaches. When he visited our department, he had mild mental retar-

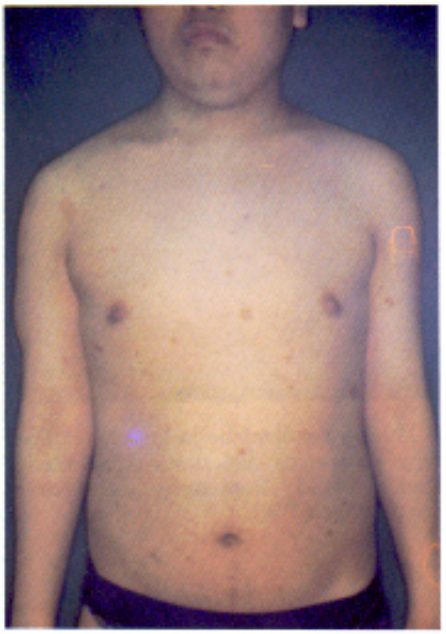

Fig. 1. Multiple cafe au lait spots on the trunk.

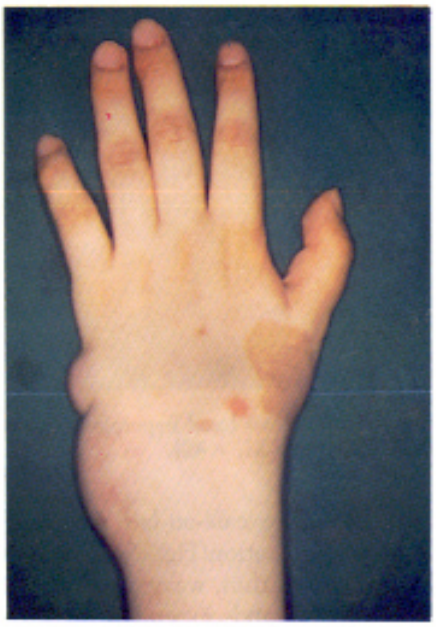

Fig. 2. A skin colored protrudent and folded soft mass on left wrist.

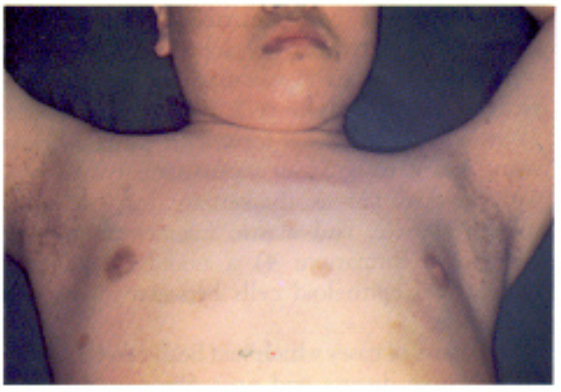

Fig. 3. Numerous tan brown colored small macules on both axilla.

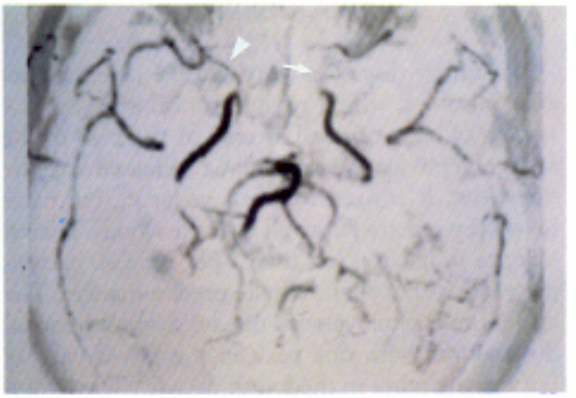

Fig. 4. MR angiography showed partial occlusion of right internal carotid artery(arrow head) and complete occlusion of left internal carotid artery(arrow) and showed collateral 'moyamoya' vessels(M).

dation and right sided weakness that had continued since the attack of moyamoya disease. He had one elder brother in good health, and there was no family history of seizures or neurofibromatosis.

Laboratory studies, including a complete blood count, urine analysis, liver function test, renal function test and VDRL were within normal limits or non-reactive. The ECG was normal and roentgenogram of the chest and skull were insignificant. However, the magnetic resonance(MR) angiography showed small collateral vessels as well as occlusion of both internal carotid arteries(Fig. 4). Brain SPECT(single photon emission computer tomography) showed large perfusion defects at both the parietal and temporal cortex. Psychological tests that were performed by a clinical psychologist showed mild mental retardation and hypochondriasis.

A skin biopsy was taken from the café-au-lait macules on the trunk and subcutaneous mass on

Annals of Dermatology
Vol. 10, No. 1, January 1998

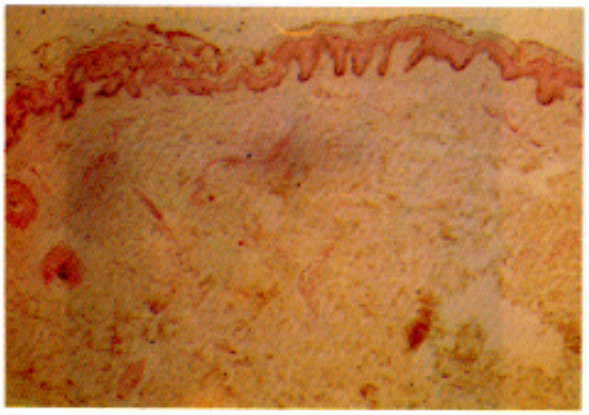

Fig. 5. Epidermis shows basal hyperpigmentation(from cafe-au-lait macule, F-M, ×40).

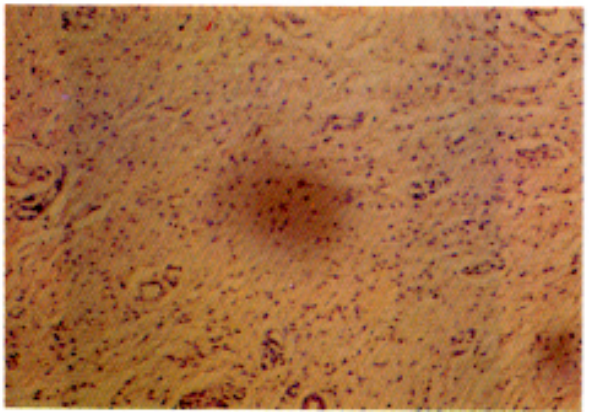

Fig. 6. Thin, wavy fibers lie in loosely textured strands extending in various directions. Most nuclei appear elongated or ovoid. (from subcutaneous mass on the rigth arm, H&E, ×100).

the right arm. The café-au-lait macule showed basal hyperpigmentation(Fig. 5). The subcutaneous mass showed thin, wavy fibers which lay in loosely textured strands extending in various directions. Most nuclei appeared elongated or ovoid(Fig. 6).

DISCUSSION

Moyamoya disease is an occlusive cerebral vascular disorder, which results in occlusion or narrowing of large cerebral arteries at the base of the brain and produces telangiectatic collateral vascular networks[6]. It is most frequent in Japan, but cases have been reported from all over the world[7]. The incidence in Japan is less than 1 per 100,000 persons per year, with a slight female predominance[8]. The age of onset of moyamoya disease shows a bimodal distribution, with one peak in the first decade of life and the other in the fourth decade[9]. The etiology of this disorder is unknown, but the disorder may arise from a variety of causes, including atherosclerosis, meningitis, sickle cell anemia, periarteritis nodosa and radiation therapy[9]. It has also been found in the neurocutaneous disorders such as Sturge-Weber syndrome and neurofibromatosis[5].

In neurofibromatosis, a less commonly recognized finding is the occurrence of vascular disease[10]. Vascular changes in neurofibromatosis may occur in any arterial tree from the proximal aorta to the small arteries, but these changes are most common in the renal arteries, aorta, celiac arteries and mesenteric arteries[3]. The pathogenesis of these arterial lesions in neurofibromatosis is unknown. It has been suggested that these vascular lesions are attributed to proliferation of Schwann cells within the arterial walls, followed by secondary degenerative changes and fibrosis[11]. Detailed histological findings of noncerebral arterial lesions in the neurofibromatosis have been described by Salyer and Salyer[12]. Four patterns of vasculopathy may occur : 1) a purely intimal, small vascular type with intimal proliferation of spindle cells and thinned media; 2) an advanced intimal form with intimal thickening and fibrosis; 3) an intimal-aneurysmal type with marked fibrous thickening, loss of media smooth muscle, and elastic fragmentation with aneurysmal formation; 4) a nodular type with spindle and epitheloid cells between media and adventitia.

In reviews of cases which had both cerebrovascular occlusive disease and neurofibromatosis, most patients were less than 16 years of age and the occlusion of the cerebral arteries did not appear to be progressive[10,13]. Our case also had no progression of moyamoya disease. In general, histopathological studies of the cerebral vessels in neurofibromatosis are few. Reported pathological examination of intracranial arteries in moyamoya disease with neurofibromatosis had shown fibrous intimal thickening and medial fibrosis - changes similar to those seen in vascular complications of neurofibromatosis elsewhere in the body[10,14]. Thus, the cerebrovascular changes of moyamoya disease in neurofibromatosis seem to be a manifestation of vasculopathy in neurofibomatosis[15].

Our patient did not have any accompanying intracranial tumors, nor had he received radiation therapy. Thus, our patient, together with the other cases in the literature, support the theory that occlusion of the cerebral arteries in neurofibromatosis is primary.

Although cerebrovascular diseases is not routinely considered in neurofibromatosis patients who have acute neurological deterioration, some previously published case reports and our case strongly suggest this association[16-18]. Therefore, cerebrovascular diseases, including moyamoya disease should be considered when acute neurological deterioration occurs in a patient with neurofibromatosis.

REFERENCES

1. Short MP, Adams RD: Neurocutaneous diseases, neurofibromatosis. In : Fitzpatrick TB, Eisen AZ, Wolff K, Freedberg IM, Austen KF (eds): Dermatology in General Medicine, 4th ed. McGraw-Hill Book, New York, 1993, pp2259-2263.
2. Reccardi VM, Eichner JE: Neurofibromatosis: phenotype, natural history, pathogenesis. John Hopkins University Press, Batimore, pp1-305, 1986.
3. Lehrnbecher T, Gassel AM, Rauh V, Kirchner T, Huppertz HI: Neurofibromatosis presenting as a severe systemic vasculopathy. Eur J Pediatr, 153:107-109, 1994.
4. Bergouignan M, Arne L: A study of cerebral arterial aneurysm associated with other malformations (In French). Acta Neurol Psychiatr Belg 51:529-535, 1951.
5. Hilal SK, Solomon GE, Gold AP, Carter S: primary cerebral occlusive disease in children. Part II. Neurocutaneous syndrome. Radiology 99:87-93, 1971.
6. Suzuki J, Takaku A: Cerebral vascular "Moyamoya" disease. A disease showing abnormal net-like vessels in base of brain. Arch Neurol, 20:288-299, 1969.
7. Suzuki J, Kodama N: Moyamoya disease - A review. Stroke, 14:104-109, 1983.
8. Gray L, Davey NC: Imaging of ischemic cerebral disease, Moyamoya disese. In Wilkins RH, Rengachary SS(eds): Neurosurgery, 2nd ed. McGraw-Hill, New York, 1996, pp2125-2135.
9. Piepgras DG, Ueki K: Moyamoya disese. In Wilkins RH, Rengachary SS (eds): Neurosurgery, 2nd ed. McGraw-Hill, New York, 1996, pp2125-2135.
10. Woody RC, Perrot LJ, Beck SA: Neurofibromatosis cerebral vasculopathy in an infant : Clinical, Neuroradiographic, and Neuropathologic studies. Pediatric Pathology 12:613-619, 1992.
11. Gomez MR: Neurocutaneous disease. In : Bradley WG, Daroff RB, Fenichel GM, Marsden CD (eds): Neurology in clinical practice, 1st ed. Butterworth-Heinemann, Boston, 1991, pp1324-1327.
12. Salyer WR, Salyer DC: The vascular lesions of neurofibromatosis. Angiology 25:510-519, 1974.
13. Taboada D, Alonso A, Moreno AJ, Muro D, Mulas F: Occlusion of the Cerebral Arteries in Recklinghausen's Disease. Neuroradiology 18:281-284, 1979.
14. Lamas E. Diez LA, Cabello A, Abad JM: Multiple intracranial arterial occlusion (moyamoya disease) in patient with neurofibromatosis. One case report with autopsy. Acta Neurochir 45:133-145, 1978.
15. Erickson RP, Woolliscroft J, Allen RJ: Familial occurrence of intracranial arterial occlusive disease (Moyamoya) in neurofibromatosis. Clinical Genetics 18:191-196, 1980.
16. Tomsick TA, Lukin RR, Chambers AA, Benton C: Neurofibromatosis and intracrnial arterial occlusive disease. Neuroradiology 11:229-34, 1976.
17. Gilly R, Elabz N, Langue J, et al: Multiple progressive cerebral arterial stenosis, stenosis of a renal artery and Recklinghausen's disease. A propose of a case of moyamoya in an infant. (In French) Pediatrie 37:523-30, 1982.
18. Sobota E, Ohkuma H, Suzuki S: Cerebrovascular disorders associated with von Recklinghausen's neurofibromatosis: A case report. Neurosurgery 22:544-9, 1988.