

Cutaneous Plexiform Schwannomas in a Patient with Neurofibromatosis Type 2

Joo Yeon Ko, M.D., Ji Eun Kim, M.D., Young Hoon Kim, M.D., Young Suck Ro, M.D.

Department of Dermatology, Hanyang University College of Medicine, Seoul, Korea

Plexiform schwannoma is a rare benign neoplasm of the neural sheath characterized by a multinodular plexiform growth pattern. The tumor usually occurs as an isolated finding, although rare cases have been reported in association with neurofibromatosis type 2 (NF2). A 25-year-old man was admitted for foot drop. He had an asymptomatic skin-colored nodule on his neck that had been present for 10 years. His medical history included local excision of a plexiform schwannoma on his left leg in our dermatology clinic 6 years prior. A histopathological examination of the skin-colored nodule also showed the typical microscopic features of a plexiform schwannoma, including the characteristic Antoni type A areas showing frequent nuclear palisading and Verocay bodies. Magnetic resonance imaging revealed a meningioma and a vestibular schwannoma in the cranium and multiple neurofibromas on the spinal cord. Herein we report a rare case of cutaneous plexiform schwannomas in a patient with NF2. (**Ann Dermatol 21(4) 402~405, 2009**)

-Keywords-

Neurofibromatosis type 2, Plexiform, Schwannoma

INTRODUCTION

Plexiform schwannoma is a rare, benign peripheral nerve sheath tumor composed of Schwann cells arranged in a plexiform pattern^{1,2}. Plexiform schwannomas predominantly affect young adults and occur most commonly as a solitary, slow-growing, asymptomatic nodule on the head,

neck, trunk, or upper extremities¹⁻³. It usually arises in either dermis or subcutaneous tissue, although rare cases originate in skeletal muscle or other deep somatic soft tissue^{1,2}. While sporadic cases of plexiform schwannoma usually present as solitary tumors^{1,4}, the literature includes a few reports on multiple plexiform schwannomas in patients with neurofibromatosis (NF) 2^{2,3,5-8}. Herein we report a rare case of cutaneous plexiform schwannomas that developed in a patient with NF2 who had a unilateral vestibular schwannoma, a meningioma, and multiple neurofibromas.

CASE REPORT

A 25-year-old man presented with an asymptomatic skin-colored nodule on his neck that had been present for 10 years (Fig. 1A). He had been admitted to the department of neurology one day ago for foot drop. His medical history included local excision of a plexiform schwannoma on his left leg in our department 6 years prior (Fig. 1B). He had no family history of neurofibromatosis (NF). On physical examination, a 1.5×0.5 cm-sized, movable, skin-colored, subcutaneous nodule not associated with pain or tenderness was observed on the neck. We found no NF-1-related cutaneous lesions (e.g. neurofibromas, café-au-lait spots, axillary freckling) or Lisch nodules.

An excisional biopsy specimen from the neck showed multiple lobulated tumor masses in the dermis and fatty tissues surrounded by a thin fibrous capsule. The nodules were composed of multiple interlacing and interconnecting fascicles of Schwann cells, which were bordered by delicate rigid reticular fibers (Fig. 2A). Characteristic Antoni type A cellular areas showing frequent palisading nuclear and Verocay bodies were observed (Fig. 2B). Immunohistochemical analysis revealed that the tumor cells were strongly positive for S-100 protein and negative for neurofilaments (Fig. 2C, D), which are typical features

Received February 13, 2009, Revised May 6, 2009, Accepted for publication May 6, 2009

Reprint request to: Young Suck Ro, M.D., Department of Dermatology, Hanyang University Hospital, 17, Haengdang-dong, Seongdong-gu, Seoul 133-792, Korea. Tel: 82-2-2290-8441, Fax: 82-2-2291-9619, E-mail: romio@hanyang.ac.kr

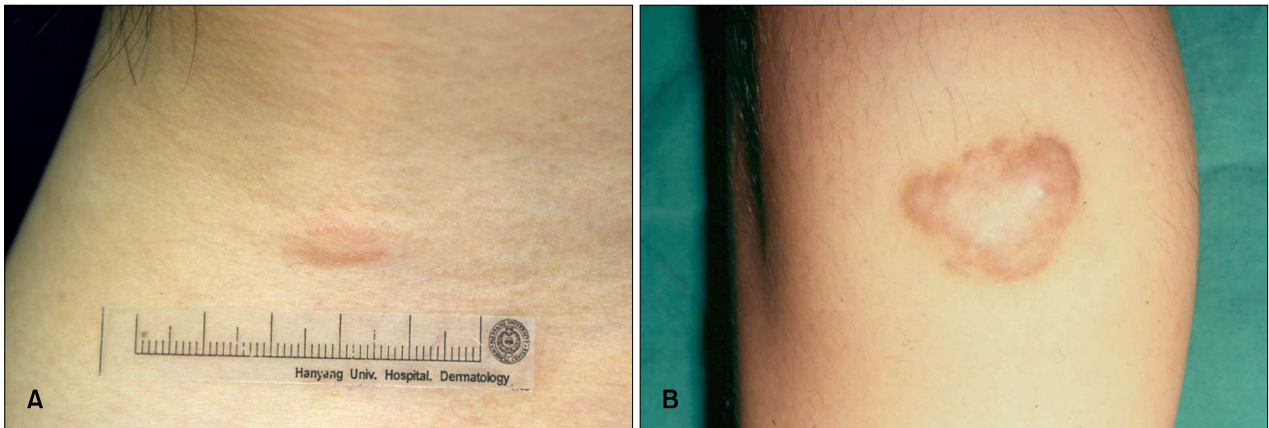


Fig. 1. (A) Skin-colored movable nodule on the right side of the neck, (B) a brown tumor on the left calf.

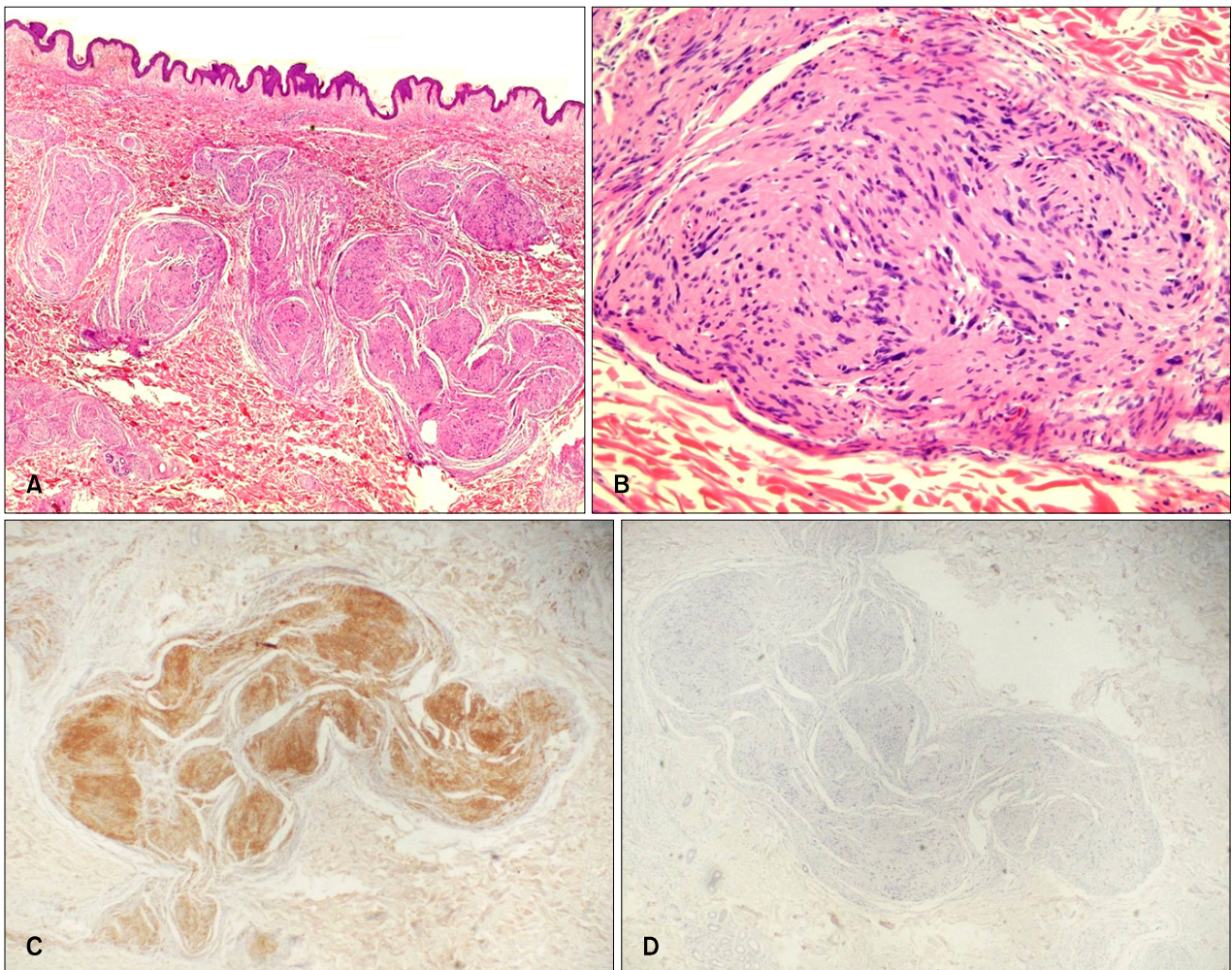


Fig. 2. (A) Multiple lobulated nodules in the dermis (H&E, Scanning view), (B) Antoni type A areas showing frequent nuclear palisading and Verocay bodies (H&E, $\times 400$), (C) tumor nodules strongly positive for S-100 protein (S-100, $\times 40$), (D) tumor nodules negative for neurofilament (Neurofilament, $\times 40$).

of plexiform schwannomas. Magnetic resonance imaging (MRI) with gadolinium enhancement revealed a unilateral vestibular schwannoma (Fig. 3A). It also showed well-enhancing calcified masses in the cranium (Fig. 3B), and multiple masses highly suggestive of neurofibromas of the spinal cord (Fig. 3C). After resection, the calcified masses were proven to be meningiomas histopathologically. Based on these findings, we diagnosed him as having two cutaneous plexiform schwannomas associated with NF2.

DISCUSSION

In 1978, Harkin et al.⁹ described a benign peripheral nerve sheath tumor composed of Schwann cells arranged in a plexiform pattern, which they called a plexiform schwannoma. The tumors presented as single, soft to rubbery, movable, non-tender, and sometimes painful nodules ranging from 0.5 cm to 2.5 cm in diameter¹. Histopathological analysis of the tumor showed multiple intradermal or subcutaneous nodules composed primarily of cellular Antoni type A regions with palisading nuclear and Verocay bodies¹. As noted by Fletcher and Davies¹⁰,



Fig. 3. MRI view, (A) vestibular schwannoma in the left internal acoustic canal, (B) meningioma involving the vertex of the superior sagittal sinus, (C) multiple neurofibromas from vertebral levels T11 to L4.

Table 1. Cases of multiple plexiform schwannomas associated with NF2 reported in the literature

References	Sex/Age (yrs)	Family history of NF2	Location of plexiform schwannoma	Concomitant CNS tumor
Val-Bernal et al. ⁷	F/19	Unknown	Lt. preauricular region, occipital region, Lt. gluteal region, Rt. calf	Bilateral VS, astrocytoma, meningioma
Reith and Goldblum ⁶	M/16	Unknown	Nose, temple, forehead, pre- & postauricular area	Bilateral VS, ependymomas
Sheikh et al. ²	M/37	Unknown	Spinal cord, chest wall, esophageal & paraesophageal region	Bilateral VS, meningioma
Ishida et al. ⁵	F/24	-	Upper lip, forearm, abdomen, foot	Bilateral VS
	M/28	+	Generalized (cutaneous, visceral)	Bilateral VS, meningioma, choroid plexus papilloma, atypical glial cell nests, subependymal glial fibrillary nodules
Lim et al. ³	M/20	-	Scalp, upper eyelid	Bilateral VS, meningioma
	M/18	-	Abdomen (triple)	Bilateral VS
	M/10	-	Lt. hand, scalp, Lt. postauricular area	Bilateral VS, meningioma, bilateral petroclival and upper cervical meningioma
Miyakawa et al. ⁸	M/5	-	Lt. abdomen, back, extremities	Bilateral VS
Present report	M/25	-	Lt. leg, neck	Unilateral VS, meningioma, multiple neurofibromas

VS: vestibular schwannomas.

the vast majority of plexiform peripheral nerve sheath tumors are plexiform neurofibromas. It is critical to differentiate a plexiform schwannoma from a plexiform neurofibroma because the latter is pathognomic of NF1 and carries significant risk of malignant transformation⁴. Plexiform schwannomas can be distinguished by their greater cellularity, nuclear palisading (with or without Verocay bodies), and degenerative features, such as hyalinized blood vessels^{7,10}.

NF2 is an autosomal dominant disease caused by mutations in a tumor suppressor gene on chromosome 22q12^{11,12}. The diagnostic criteria for NF2 have undergone various changes over time. The most recent Manchester clinical diagnostic criteria for NF2 are as follows: A. bilateral vestibular schwannomas (VS); or B. first-degree relative family history of NF2 and unilateral VS, or any two of the following: meningioma, schwannoma, glioma, neurofibroma, or posterior subcapsular lenticular opacities; or C. unilateral VS and any two of the following: meningioma, schwannoma, glioma, neurofibroma, or posterior subcapsular lenticular opacities; or D. multiple (two or more) meningiomas and unilateral schwannoma or any two of the following: schwannoma, glioma, neurofibroma, or cataract¹³. Because our patient had unilateral VS, an intracranial meningioma, intraspinal neurofibromas, and two cutaneous plexiform schwannomas, his case corresponded to diagnostic criteria C.

Most reported cases of plexiform schwannomas were solitary lesions^{1,4}, while a few studies reported that tumors can multiply in NF2 patients^{2,3,5-8}. To our knowledge, since Val-Bernal et al.⁷ reported a single case of plexiform schwannoma in a patient with NF2 in 1995, only nine cases of multiple plexiform schwannomas associated with NF2 have been reported to date (Table 1)^{2,3,5-8}. In contrast to NF1, NF2 does not involve prominent external cutaneous lesions (e.g. neurofibromas, café-au-lait macules, and axillary freckling). The majority of initial clinical symptoms of NF2 are related to bilateral VS, such as hearing loss, tinnitus, dizziness, and imbalance¹⁴. However, our patient had unilateral VS without associated clinical symptoms. His first clinical manifestation of NF2 was a plexiform schwannoma on his left leg, which had been locally excised at our clinic 6 years prior. In theory, many cutaneous manifestations offer clues to the diagnosis of internal diseases. Although plexiform schwannoma is not a pathognomonic tumor for NF2, our case supports the hypothesis that the presence of two or more cutaneous plexiform schwannomas may reflect underlying NF2. Although the clinical course of NF2 is extremely variable depending on the internal tumor burden, surgical management, and

complications, we suggest that clinicians should keep in mind the possibility of NF2 in patients with two or more plexiform schwannomas.

REFERENCES

1. Kao GF, Laskin WB, Olsen TG. Solitary cutaneous plexiform neurilemmoma (schwannoma): a clinicopathologic, immunohistochemical, and ultrastructural study of 11 cases. *Mod Pathol* 1989;2:20-26.
2. Sheikh S, Gomes M, Montgomery E. Multiple plexiform schwannomas in a patient with neurofibromatosis. *J Thorac Cardiovasc Surg* 1998;115:240-242.
3. Lim HS, Jung J, Chung KY. Neurofibromatosis type 2 with multiple plexiform schwannomas. *Int J Dermatol* 2004;43:336-340.
4. Woodruff JM, Marshall ML, Godwin TA, Funkhouser JW, Thompson NJ, Erlandson RA. Plexiform (multinodular) schwannoma. A tumor simulating the plexiform neurofibroma. *Am J Surg Pathol* 1983;7:691-697.
5. Ishida T, Kuroda M, Motoi T, Oka T, Imamura T, Machinami R. Phenotypic diversity of neurofibromatosis 2: association with plexiform schwannoma. *Histopathology* 1998;32:264-270.
6. Reith JD, Goldblum JR. Multiple cutaneous plexiform schwannomas. Report of a case and review of the literature with particular reference to the association with types 1 and 2 neurofibromatosis and schwannomatosis. *Arch Pathol Lab Med* 1996;120:399-401.
7. Val-Bernal JF, Figols J, Vazquez-Barquero A. Cutaneous plexiform schwannoma associated with neurofibromatosis type 2. *Cancer* 1995;76:1181-1186.
8. Miyakawa T, Kamada N, Kobayashi T, Hirano K, Fujii K, Sasahara Y, et al. Neurofibromatosis type 2 in an infant with multiple plexiform schwannomas as first symptom. *J Dermatol* 2007;34:60-64.
9. Harkin JC, Arrinton HJ, Reed RJ. Benign plexiform schwannoma, a lesion distinct from plexiform neurofibroma [abstract]. *J Neuropathol Exp Neurol* 1978;37:622.
10. Fletcher CD, Davies SE. Benign plexiform (multinodular) schwannoma: a rare tumour unassociated with neurofibromatosis. *Histopathology* 1986;10:971-980.
11. Honda M, Arai E, Sawada S, Ohta A, Niimura M. Neurofibromatosis 2 and neurilemmomatosis gene are identical. *J Invest Dermatol* 1995;104:74-77.
12. Trofatter JA, MacCollin MM, Rutter JL, Murrell JR, Duyao MP, Parry DM, et al. A novel moesin-, ezrin-, radixin-like gene is a candidate for the neurofibromatosis 2 tumor suppressor. *Cell* 1993;72:791-800.
13. Evans DG, Baser ME, O'Reilly B, Rowe J, Gleeson M, Saeed S, et al. Management of the patient and family with neurofibromatosis 2: a consensus conference statement. *Br J Neurosurg* 2005;19:5-12.
14. Evans DG, Sainio M, Baser ME. Neurofibromatosis type 2. *J Med Genet* 2000;37:897-904.