MULTIPLE PLEXIFORM SCHWANNOMAS IN A PATIENT WITH NEUROFIBROMATOSIS

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Plexiform schwannomas are unusual benign peripheral nerve sheath tumors, and rare cases have been reported in the setting of "schwannomatosis." We are aware of only a single case having been reported in a patient with neurofibromatosis type 2 (NF-2). We present a case of multiple spinal, chest wall, esophageal, and paraesophageal plexiform schwannomas in a patient with NF-2. Emphasis is placed on correct identification of plexiform schwannoma and its distinction from plexiform neurofibroma and other tumors having a plexiform growth pattern.

A 37-year-old man with NF-2 was referred for treatment of hoarseness and left vocal cord paralysis. Computed tomographic scan and magnetic resonance imaging revealed a mediastinal mass. The patient's history was significant for bilateral acoustic schwannomas, a left parietal meningioma, multiple neurofibromas, and multiple intradural and extradural schwannomas. He underwent a right thoracotomy with resection of paraesophageal, retropharyngeal, and chest wall masses. The postoperative course was uneventful. All three specimens consisted of irregular multinodular masses.

On histologic examination, the specimen consisted of multiple nodules of tumor, each separated by strands of nonneoplastic connective tissue (Fig. 1). Some nodules were highly cellular and composed of spindle cells. Characteristic cellular Antoni A areas with nuclear palisading (Fig. 2), Verocay bodies, and short parallel fascicles of Schwann cells juxtaposed with hypocellular myxoid Antoni B regions were uniformly present. Neither necrosis nor hemorrhage was seen.

Schwannomas are usually solitary neoplasms. Although their most common location is the acoustic nerve, they may arise anywhere along the course of cranial or peripheral nerves. Multiple schwannomas may be noted as an isolated finding but are observed more commonly in patients with NF. Plexiform schwannomas are also benign peripheral nerve sheath tumors. In 1984 Shishiba and associates¹ introduced the term "schwannomatosis" for a syndrome characterized by multiple cutaneous schwannomas, central nervous system tumors, and various neurologic deficits without stigmata of NF.¹ In 1995 Val-Bernal, Figols, and Vasquez-Barquero² summarized 78 cases of plexiform schwannomas already reported in the literature;

eight were associated with clinical schwannomatosis, six with multiple cutaneous schwannoma syndrome, and only three with NF-1. They also reported, for the first time in the literature, a single case of plexiform schwannoma in a patient with NF-2. Rare cases have been reported in association with NF-1 schwannomatosis. In 1996, Reith and Goldblum³ reported a case of multiple cutaneous plexiform schwannomas associated with bilateral acoustic neuromas, as well as other intracranial and intraspinal neoplasms,³ which may represent another example of plexiform schwannoma in NF-2.

Essentially, multifocal Schwann cell proliferation may be separated into three groups²: (1) multifocal microscopic schwannomatosis, (2) clinical schwannomatosis, and (3) multiple cutaneous schwannomas. Patients with multiple cutaneous schwannomas have hyperacusis associated with various intracranial tumors. Clinical schwannomatosis is distinguished from NF-1 by its lack of skin pigmentation, neurofibromas, and autosomal dominant transmission. Multiple cutaneous schwannomas are unassociated with intracranial tumors. Some of these tumors may develop along the course of a large nerve segment. Like those with NF-2, patients with cutaneous schwannomas have loss of heterozygosity of chromosome 22. Because the cutaneous schwannoma locus is present in the NF-2 region, this may well represent a subtype of NF-2.

Plexiform schwannoma consists of multiple intradermal or subcutaneous nodules composed primarily of cellular Antoni A regions with nuclear palisading and Verocay bodies. These tumors, like their more typical counterparts, are composed almost exclusively of Schwann cells without evidence of axons. No malignant transformation has been reported, although local recurrence has been associated with incomplete resection. Plexiform schwannoma must be differentiated from several other entities, including plexiform neurofibroma, plexiform fibrohistiocytic tumor, plexiform malignant peripheral nerve sheath tumor of infancy and childhood, plexiform granular cell tumor, and traumatic neuroma. Plexiform neurofibroma is a plexiform tumor composed of Schwann cells, perineural cells, fibroblasts, and axons admixed with collagen in a loose matrix. The term *plexiform* refers to the serpentine distortion it imparts to the affected nerve segment, which has been likened to a "bag of worms." It is critical to distinguish plexiform schwannoma from plexiform neurofibroma, because the latter is pathognomonic for NF-1 and carries a risk of malignant transformation, in contrast to the former. Plexiform fibrohistiocytic tumor is rare and was first described by Enzinger and Zhang⁵ in 1988. It usually arises in children or young adults, being more common in girls and young women. It is characterized by fibroblasts variably admixed with osteoclast-like giant cells. Although regional lymph node metastases have been reported, neither visceral metastases nor tumor-related deaths have been documented. The so-called plexiform

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Fig. 1. Scanning power view of plexiform schwannoma. Note the multiplicity of lobules of varying sizes with unremarkable connective tissue in between, an appearance imparted by distortion of an affected nerve segment represented in two dimensions.

Fig. 2. Palisaded nuclei are illustrated to their advantage in this field.

malignant peripheral nerve sheath tumor of infancy and childhood was described in 1994 by Meis-Kindblom and Enzinger,⁶ who related the findings in nine cases of a plexiform neoplasm in which there were morphologic features similar to plexiform schwannomas but which differed by having mitoses and lacking Antoni B zones. Although no lesion metastasized, the authors assumed the view that these were malignant neoplasms. Other authors,

however, believe that the lesions described by Meis-Kindblom and Enzinger⁶ are instead examples of plexiform variants of cellular schwannomas,⁷ benign tumors that are known to be cellular, mitotically active, able to erode bone, and frequently congeners of sarcomas.

In summary, we present a case of plexiform schwannoma in a patient with NF-2. In such a setting it is critical to distinguish the plexiform schwannoma from plexiform

neurofibroma, because the clinical and prognostic implications differ substantially for the two.

REFERENCES

1. Shishiba T, Nimura M, Ohtsuka F, et al. Multiple cutaneous neurilemmomas as a skin manifestation of neurilemmomatosis. *J Am Acad Dermatol* 1984;10:744-54.
2. Vai-Bernal F, Figols J, Vasquez-Barquero A. Cutaneous plexiform schwannoma associated with NF type 2. *Cancer* 1995; 76:1181-6.
3. Reith JD, Goldblum JR. Multiple cutaneous schwannomas: report of a case and review of the literature with reference to the association with types 1 and 2 neurofibromatosis and schwannomatosis. *Arch Pathol Lab Med* 1996;120:399-401.
4. Nimura M. Aspects of neurofibromatosis from the viewpoint of dermatology. *J Dermatol* 1992;19:868-72.
5. Enzinger FM, Zhang R. Plexiform fibrohistiocytic tumor presenting in children and young adults: an analysis of 65 cases. *Am J Surg Pathol* 12:818-26.
6. Meis-Kindblom JM, Enzinger FM. Plexiform malignant peripheral nerve sheath tumor of infancy and childhood. *Am J Surg Pathol* 1994;18:479-85.
7. Woodruff JM, Scheithauer BW. Nerve sheath tumors. *Am J Surg Pathol* 1995;19:608-9.