Cutaneous Plexiform Schwannomas in a Patient with Neurofibromatosis Type 2

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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.

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...
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, ×400), (C) tumor nodules strongly positive for S-100 protein (S-100, ×40), (D) tumor nodules negative for neurofilament (Neurofilament, ×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. 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, non-tender, and sometimes painful nodules ranging from 0.5 cm to 2.5 cm in diameter. Histopathological analysis of the tumor showed multiple intradermal or subcutaneous nodules composed primarily of cellular Antoni type A regions with palisading nuclear and Verocay bodies. As noted by Fletcher and Davies,

![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.](image)

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

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

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 pathognomonic of NF1 and carries significant risk of malignant transformation. Plexiform schwannomas can be distinguished by their greater cellularity, nuclear palisading (with or without Verocay bodies), and degenerative features, such as hyalinized blood vessels.

NF2 is an autosomal dominant disease caused by mutations in a tumor suppressor gene on chromosome 22q12. 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 VS, or posterior subcapsular lenticular opacities; or E. any two of the following: meningioma, schwannoma, glioma, neurofibroma, or any two of the following: meningioma, schwannoma, glioma, neurofibroma, or cataract. Because our patient had unilateral VS without associated clinical symptoms, his case corresponded to diagnostic criteria C.

Most reported cases of plexiform schwannomas were solitary lesions, while a few studies reported that tumors can multiply in NF2 patients. To our knowledge, since Val-Bernal et al. 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). 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 imbalance. 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