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Case Report

Plexiform Schwannoma in the Plantar Aspect of the Foot: A Case Report and Review of the Literature

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Abstract

Schwannomas are benign peripheral nerve tumors, presenting as solitary tumors mostly in head and neck region followed by upper and lower extremities. Various variants of Schwannomas have been described as: cellular, plexiform, ancient and psammomatouse. Plexiform Schwannoma (PS) is an unusual and rare variant of Schwannoma. They are usually more cellular and therefore also qualify as cellular schwannomas. Surgical excision with complete tumor removal with safe margin is the usual mode of treatment of PS. Schwannomas, including the plexiform variant, are benign and do not recur when completely excised. PS can be easily confused, and misdiagnosed as plexiform neurofibroma (PN), and thus may be misinterpreted as a sarcoma arising in a plexiform neurofibroma. It is critical to differentiate a PS from a PN because the latter is pathognomonic of Neurofibromatosis (NF) and carries significant risk of malignant transformation. Here we present a case of planter PS and review the literature.

INTRODUCTION

Plexiform schwannoma (PS) is a rare benign tumor of the peripheral nerve sheath, in which Schwann cells exhibit a multinodular or plexiform growth pattern (1). PS classically affects young adults aged 20–50 years and the incidence in men and women is equal (2). They are typically solitary, (but can be multiple in cases of Schwannomatosis) (3), mobile, smooth-surfaced, slow growing (4), uncircumscribed tumors, and often lack a capsule, which can make the diagnosis difficult (5). Almost entirely benign, there have only been a few reports of a possible malignant evolution of PS to angiosarcoma (6). PS often present without pain or neurologic symptoms. If pain or neurologic symptoms are present, they are usually associated with a mass effect (4). In most solitary cases, there are no identifiable risk factors, although multiple tumors are associated with some risk factors including neurofibromatosis type II, trauma, and positive family history (2). PS typically arise from the dermis or subcutaneous tissue (79%), occurring most commonly in the head and neck region (23%), and account for 15% of cutaneous schwannomas (7). Nevertheless, this neoplasm can be found deep to the superficial layers near any peripheral nerve throughout the body (8). Among the deep-seated locations, PS can occur in the deep somatic soft tissues of extremities, retroperitoneum, trunk, parotid, thoracic space and vulva (9). At the time of writing this paper, only 15 cases of PS in the foot have been reported (10). In this case report, we present a rare case of PS found in the left plantar aspect of the foot.

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CASE PRESENTATION

A 49-years-old man presented with left foot mass at the planter aspect measuring 4.5 x 3.0 cm. The patient reported presence of the mass for at least 15 years with only slight increase of the size. Magnetic resonance imaging (MRI) revealed a soft tissue tumor mass from the dermis to the subcutaneous fat of the plantar aspect. The tumor was homogeneously isointense relative to the skeletal muscle on T1-weighted images and hyperintense on T2- weighted fat-suppressed images. The mass was surgically excised with complete safe margins. The tumor mass was well circumscribed and easily separated from the deep fascia and surrounding soft tissue. Histopathologic examination revealed multiple lobulated tumors in the dermis and hypodermis composed of Schwann cells with uniform spindle cells and nuclear palisading, indicative of Antoni A tissue and Verocay bodies (**Figure 1 A, B, C**). Immunohistochemistry results are as follows: strong positive staining with Vimentin, S-100 (**Figure 1D**), and Glial Fibrillary Acidic Protein (GFAP). The tumor cells were negative for Pan keratin AE1/AE3, EMA, SMA and CD34.

Patient received no post-operative treatment, was followed for two years with no evidence of recurrence, and then eventually was lost to follow up.

DISCUSSION

Histologically, schwannomas are divided into the following seven subtypes: classical (Verocay), plexiform, cellular, cranial nerve, melanotic, degenerated (ancient), and granular cell schwannomas (11). PS was first described by Harkin and Reed in 1978 as a rare tumor (accounting for 5% of all schwannomas) composed exclusively of Schwann cells exhibiting a plexiform growth pattern (3). Plexiform refers to the serpentine distortion it imparts to the affected nerve segment.

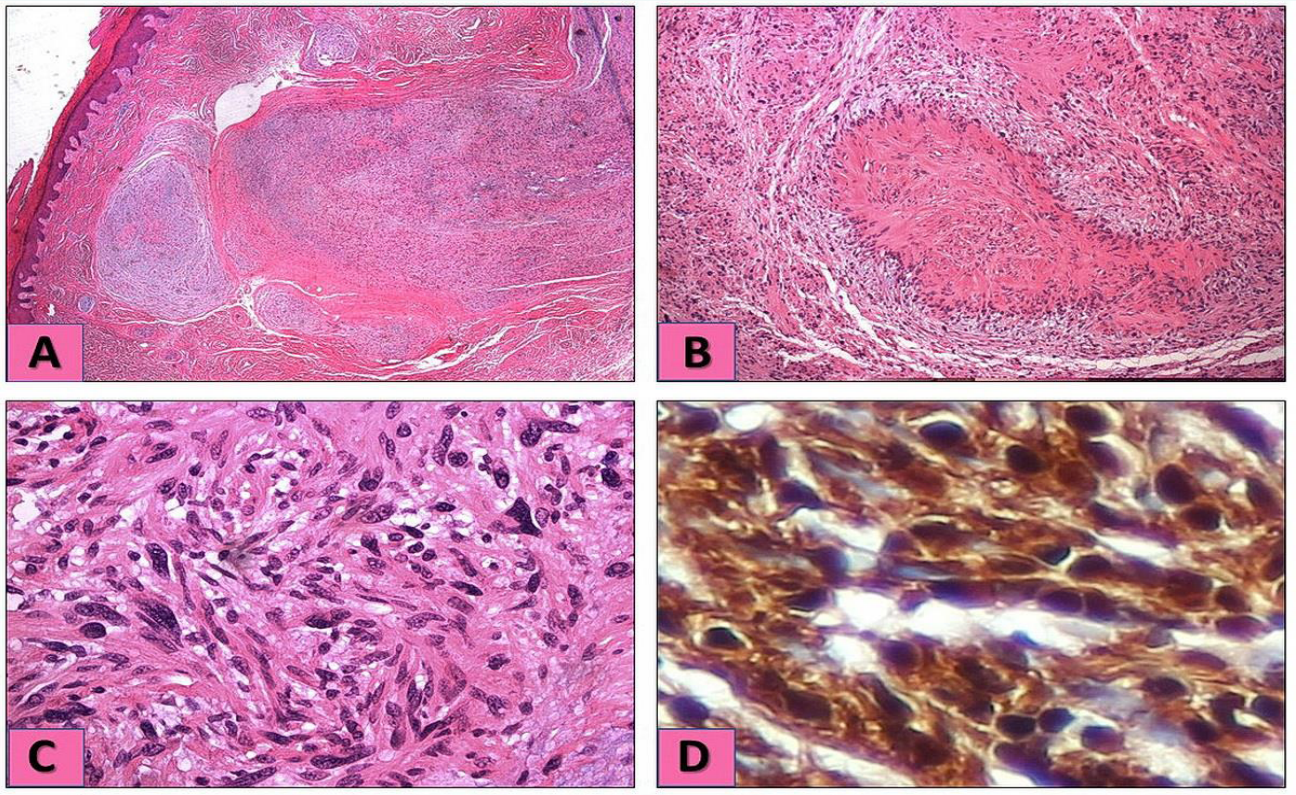

Figure 1 Pathologic examination of the excised Schwannoma
Figure 1A: Multiple lobulated tumors in the dermis and hypodermis (H&E stain X20)
Figure 1B Classical palisading forming Verocay bodies (H&E stain X40)
Figure 1C: Spindle-shaped Schwann cells with mild atypia but no malignant features or abnormal mitosis (H&E stain X60)
Figure 1D: Schwann cells positive for S-100

The diagnosis of schwannomas is typically made by histopathologic examination. PS has several elements found in conventional schwannomas, such as being composed of compact Schwann cells (but arranged as multinodular/plexiform rather than in a globular configuration), Verocay bodies, hyalinized and/or ectatic vessels and collagenous residues (12). Unique to PS are its cytologically bland spindle cells in hypercellular Antoni A and hypocellular Antoni B patterns (13). Recent studies also demonstrated that PS may not always display the Antoni A and B patterns (but when it does, Antoni A is predominant) (12). The Antoni A hypercellular areas primarily consist of monomorphic spindle-shaped Schwann cells with pointed basophilic nuclei and poorly defined eosinophilic cytoplasm. Antoni B areas consist of loosely arranged cells and small cystic spaces (14). PS also shows complex growth and often involves multiple fascicles, and this differs from the single fascicle involvement of conventional schwannoma (15). A precise definition of the histopathological characteristics is extremely important, as it is the best method for differentiating PS from other benign or malignant lesions (16).

Conventional and plexiform schwannomas can be differentiated from other nerve tumors by using immunohistochemical staining. Currently, the most commonly used IHC markers for the diagnosis of schwannomas are S-100 and SOX-10. S-100 and SOX10 expressions are also reported in neurofibromas, malignant peripheral nerve sheath tumors (MPNSTs) and granular cell tumors, but with less uniform patterns than in a schwannoma (5). S-100 is a membrane protein currently considered the most sensitive marker for tumors originating from Schwann cells (7). Schwannomas typically show diffuse, strong expression of S100 protein and abundant pericellular collagen type IV, consistent with the presence of a continuous pericellular basal lamina. Recent studies have suggested that podoplanin and calretinin might also be helpful markers for differentiating neurofibromas from schwannomas (17). However, due to a lack of specificity, these markers are currently used as part of multi-antibody panels. In contrast, schwannomas are always negative for neurofilament, EMA, desmin, vimentin, and bcl-2, allowing the exclusion of other benign soft-tissue tumors, such as leiomyomas, granular cell tumors and solitary fibrous tumors. (5) Other IHC markers that can be used in the diagnosis of schwannomas are CD34, vimentin, and GFAP (18).

It is critical to differentiate a PS from a plexiform neurofibroma (PN) because the latter is pathognomonic of Neurofibromatosis (NF) and carries significant risk of malignant transformation. (19) PS can be distinguished by their greater cellularity, nuclear palisading (with or without Verocay bodies), and degenerative

features, such as hyalinized blood vessels (20). Diffuse strong S-100 cytoplasmic positivity and neurofilament staining limited to subcapsular area favors PS, while focal scattered S-100 positivity in tumor nodules would favor PN (3). Unlike neurofibroma, neurofilament protein staining in schwannomas are usually limited to entrapped axons at the periphery of the tumor, although some recent studies suggest that the presence of intralesional axons is more frequent than previously reported (17). PS with NF2 have been reported in up to 10% of cases. The presence of multiple lesions represents a high risk of having NF2 and is associated with mutations of the NF2 gene on chromosome 22q12.2 (adjacent to the SMARCB1/INI1 suppressor gene). It is important to exclude the presence of associated dermal lesions and neurinoma in patients with PS, particularly in pediatric patients in whom inherited syndromes are more frequent (12). Therefore, careful intracranial and spinal MRI is necessary to exclude potential NF in young patients (10). Genetic studies are useful when there is a positive family history or in case of a certain association with NF-Schwannomatosis (12).

The other differential diagnosis to consider are malignant peripheral nerve sheath tumor (MPNST), which requires wide excision and are malignant, and plexiform fibrous histiocytoma (21). More problematic are the rare plexiform schwannomas that arise in deep anatomic locations, in soft tissue or major peripheral nerves, since they may demonstrate increased cellularity and mitotic activity and thus, may be difficult to distinguish from MPNST. Although these tumors have a negligible malignant potential, local recurrence is high, occurring in approximately half of the cases. Again, the presence of widespread S100, collagen IV immunoreactivity or basal lamina by electron microscopy is reassuring (17).

Imaging such as MRI can also be a useful tool in the diagnosis of PS. On imaging, the rims of PS nodules are smooth, and features of the lesions are similar to those of peripheral nerve sheath tumors, including heterogenous hyper or iso-intensity to subcutaneous fat on T2-weighted MR images. It is reported that multinodular growth patterns in a single lesion and evident cystic degeneration on T2-weighted image are characteristics of PS, which are helpful in the differential diagnosis of these tumors (10).

The overall prognosis of plexiform schwannoma is quite favorable. Conservative surgical removal with a wide excision is the treatment of choice and recurrence is rare (14). However, in 2017, a series of pediatric non-vestibular schwannoma cases indicated the presence of more than four mitoses/ten high-power fields as a slight risk factor for recurrence (22). To note, operative findings and outcomes differ between patients with conventional schwannoma and those with PS located in the spinal cord. Generally, the single fascicle associated with conventional schwannomas can be sacrificed without causing neurological deficit. However, in PS, multiple fascicles are often affected, and it is difficult to completely excise the tumor without damaging multiple fascicles and causing neurological deficits (15).

It is our hope this case report will add to the repertoire of research on this topic and provide clinicians and pathologists with more insight about plexiform schwannoma, allowing for appropriate diagnosis and informed management decisions.

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