Asymptomatic solitary nodule on the dorsum of the right hand

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A 35-year old Indian male patient presented with skin lesion on left hand since 3 years. The lesion had a gradual onset and slowly progressive course. There were no associated symptoms such as pain, tenderness are limitation of movement of the left hand. There was no previous history of similar lesions or other skin problems. The patient did not complain of any systemic illness and there was no family history of similar lesions.

On physical examination, there was a solitary, subcutaneous nodule with skin colored surface on the dorsum of left hand (Fig. 1a, b). There was no tenderness or pain on palpation. The nodule was firm in consistency and not attached to underlying structures. Routine laboratory investigations including CBC, blood sugar, hepatic and renal profile revealed no abnormal findings. X-ray on the left hand showed no attachment of the lesion to underlying bones. Total excisional biopsy was performed for removal of the tumor and histological analysis. Histological examination revealed exophytic nodule with encapsulated mass, located in the upper dermis and separated from the surrounding stroma by a clear space. There was no residual pathology beneath the excised lesion (Fig.2A). Histologically, the tumor was composed of spindle-shaped cells arranged in two patterns; a predominant dense cellular area (Antoni A) and a hypocellular myxoid zone (Antoni B). The cells were characteristicaally arranged back to back in a parallel pattern (Fig.2B). Immunohistochemically, the tumor cells showed positive reaction for S-100 protein (Fig. 2C) and negative staining for neurofilament (Fig. 2D).

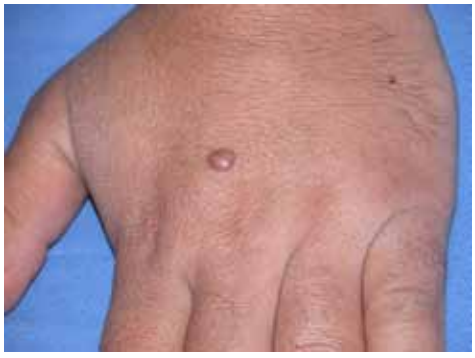

Fig. 1a Solitary subcutaneous nodule on dorsum of the right hand.

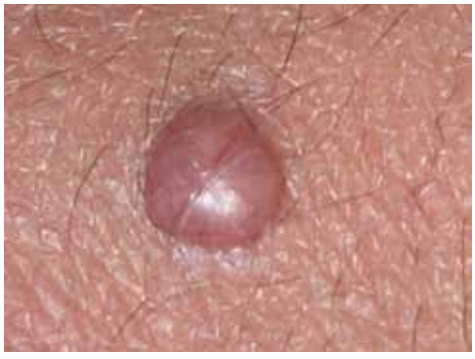

Fig. 1b Closeup

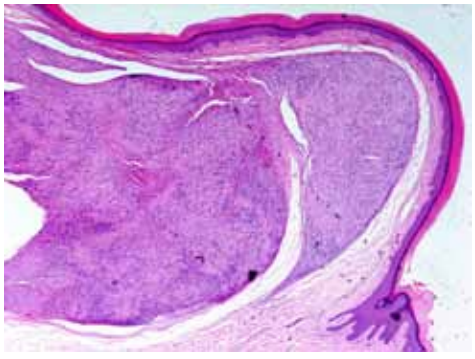

Fig. 2a Exophytic nodule with well-encapsulated dermal mass separated from the surrounding stroma by a cleft.

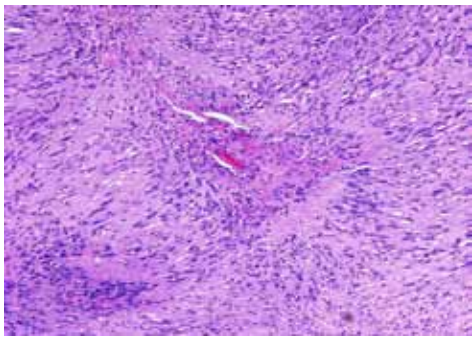

Fig. 2b The mass formed of spindle shaped cells (antoni A) and hypocellar eosinophilic area (antoni B).

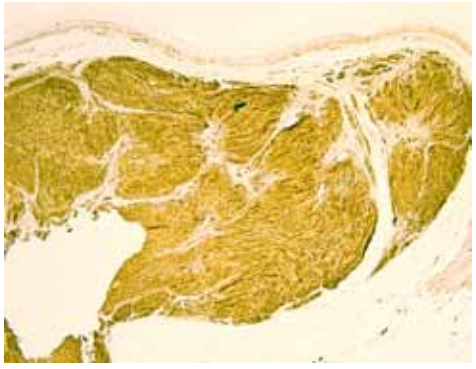

Fig. 2c The tumour cells sowed positive reaction for S100

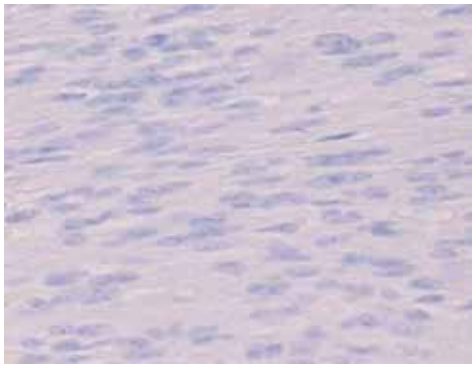

Fig. 2d The tumor cells showed negative reaction for neurofilament.

What is the clinical diagnosis?

1. Ganglion
2. Neuroma
3. Collagenoma
4. Adenxal tumour

The diagnosis is schwannoma

DISCUSSION

Schwannomas are known by a variety of terms, such as neurilemmomas and anaxonal, intraneural Schwann cell tumors. Neurilemmomas have a predilection for the head, neck, and the flexor surfaces of the upper and lower extremities. One rare case report described subungual (under the nailbed) schwannoma.[1] The feet are usually spared. The most common affected nerves include the cervical, sympathetic, vagus, peroneal, and ulnar nerves. Superficial neurilemmomas in the skin may display a prominent plexiform (nodular) growth pattern. Deep-seated tumors are found most commonly in the posterior mediastinum and the retroperitoneum. Intracranial neurilemmomas comprise approximately 8% of all primary tumors of this region. Sensory nerves tend to be affected selectively. The auditory nerve is overwhelmingly the most frequently involved. Acoustic neurilemmomas, also known as vestibular schwannoma, acoustic neuroma, or acoustic neurinoma, arise from the vestibular nerve, and they are observed in the setting of NF2. Patients with NF2 and acoustic neurilemmomas may present with bilateral hearing loss. Neurilemmomatosis or schwannomatosis, a variant of NF2, is an autosomal dominant disorder with full penetrance. Although very few familial cases of neurilemmomatosis have been reported, most of them are multiple, encapsulated, and located in the subcutaneous tissue, while some have a plexiform pattern, and involve the neck, trunk, and extremities.[2]

Tumor that involves small nerve is freely mobile, while tumor that involves large nerves, is movable but moves along the long axis of the nerve where the attachment restricts mobility. Most neurilemmomas are asymptomatic, nontender, and not associated with neurologic signs or symptoms. A special form of inherited neurilemmoma (psammomatous melanotic variant) occurs in the

setting of Carney complex. It is an autosomal dominant disorder characterized by the combination of spotty pigmentation (lentigines), cardiac myxomas, and endocrine overactivity. More than 50% of patients with a psammomatous melanotic neurilemmoma (schwannoma) have Carney complex. In contrast to the conventional neurilemmoma, the melanotic variant is not associated with NF2; thus, conventional neurilemmomas are not observed in association with Carney complex. Another difference between the two variants is that approximately 10% of melanotic tumors are malignant, whereas conventional neurilemmomas almost never undergo malignant change.[3]

The etiology of neurilemmomas is uncertain. Most tumors have shown genetic aberrations (ring chromosome 22).[4] The NF2 gene has been localized to band 22q12. Alteration or loss of the NF2 gene product (also designated as Merlin), a presumed tumor suppressor gene, is postulated to be involved in neurilemmoma formation.[5] Partial or complete monosomy of the chromosome occurs (loss or mutation of both NF2 alleles and mutation of the NF2 gene protein). The negative staining of neurilemmoma cells by immunohistochemical stain for NF2 protein suggests that loss of NF2 protein function is a prerequisite for neurilemmoma formation. More than 150 cases of radiation-induced intracranial and peripheral neurilemmomas have been reported.[6] The mean latency period is approximately 20 years, and most of these are solitary tumors. Bilateral eighth cranial nerve schwannomas indicate neurofibromatosis of NF2 type. Unusual locations and associations with meningeal proliferation are also seen with NF2.[7]

Histologically, most tumors are unilocular masses surrounded by a fibrous capsule composed of epineurium and residual nerve fibers. While this capsule is evident in most tumors, those arising in mucosa (eg, nose, nasopharynx), the central nervous system, and viscera often lack a capsule. Intradermal neurilemmomas and the plexiform or multinodular growth pattern similar to a plexiform neurofibroma are rare. Histologically, the characteristic feature of a neurilemmoma is the pattern of alternating Antoni type A and B areas. Antoni type A areas (a consist of compact, spindle-shaped cells with twisted nuclei, indistinct cytoplasm borders, and occasionally clear intranuclear vacuoles).The cells are arranged in short bundles or interlacing fascicles with nuclear palisading, whirling of the cells, and Verocay bodies. Verocay bodies are formed by 2 compact rows of well-aligned nuclei and cell processes that are arranged in a roughly oval shape. Antoni type B areas are composed of hypocellular myxiod zone. Verocay bodies are more distinctive of schwannomas than the Antoni A and Antoni B patterns, but they are not seen in all schwannomas. Mitotic figures are rare. S-100 is demonstrated in neurilemmomas, particularly in the Antoni type A areas. Antoni B areas are less cellular and are often disorderly. The spindle or oval cells are arranged haphazardly in the loose matrix with microcystic changes, inflammatory cells, and delicate collagen fibers. Prominent, irregularly spaced blood vessels are present in the stroma.[8,9] The psammomatous melanotic neurilemmoma (schwannoma) shows, in addition to the above features, melanin deposition and concentric calcified bodies (psammoma bodies).[10]

Schwannomas have been variably observed to be glial fibrillary acid protein (GFAP) and occasionally keratin positive, with antibodies reacting with multiple keratins (pankeratins, keratin cocktail (CK) (AE1/AE3). Both markers highlighted the cellular Antoni A areas, particularly adjacent

to the capsule, myxoid or degenerative areas, and perivascularly.[11] Schwannomas contain Leu7 and S-100 protein.[8]

Ultrastructural examination of the tumor reveals almost exclusively a single cell type (Schwann cells). They have characteristic thin cell processes that arrange in undulating layers and are continuous from the cell body. The Schwann cell surface is coated with basal lamina composed of electron-dense material measuring approximately 50 nm.

The basal lamina lies in stacks between the cells along with typical and long-spacing collagen fibrils with a 130-nm periodicity. These collagen fibrils are often referred to as a Luse body.The basal lamina lies in stacks between the cells along with typical and long-spacing collagen fibrils with a 130-nm periodicity. These collagen fibrils are often referred to as a Luse body.[8]

The histological differential diagnosis includes palisaded and encapsulated neuronal (PEN), neurofibroma and leiomyomas. Neurofibroma, the loose, myxomatous Antoni type B tissue of a neurilemmoma may mimic a neurofibroma. However, neurofibromas lack the thick collagenous capsule of neurilemmomas and instead are surrounded by a variably thickened perineurium and epineurium. Neurofibromas also lack the Antoni type A and B patterns and Verocay bodies typical of neurilemmomas. Neurofibromas are composed of a mucinous matrix containing scattered, myelinated, and nonmyelinated axons along with a heterogeneous cell population including Schwann cells, fibroblasts, and perineural cells. Consequently, immunoreactivity for S-100 protein is observed in only a portion of the cells comprising a neurofibroma, as opposed to uniform reactivity throughout a neurilemmoma. Palisaded encapsulated neuroma: This is an uncommon, generally solitary, asymptomatic intraneural neuroma that may arise in early childhood or adulthood. It appears as a firm, rubbery, skin-colored or pink papule commonly affecting the "butterfly area" of the face. Palisaded encapsulated neuromas are bulbous expansions of a peripheral nerve. They appear as well-circumscribed, ovoid, or rounded nodules in the dermis, which, in contrast to neurilemmomas, contain a greater number of axons and Schwann cells in interlacing fascicles along with characteristic cleft like spaces. Leiomyomas are benign smooth muscle tumors. They are not derived from neural tissue and generally lack the thick, hyalinized capsule and vasculature of a neurilemmoma. Palisading resembling Verocay bodies may be observed. The blunt-ended nuclei and densely eosinophilic cytoplasm of smooth muscle cells showing distinct cell borders and perinuclear halos help distinguish them from Schwann cells (with their more tapered, spindle-shaped nuclei).

Immunohistochemical stains readily distinguish leiomyomas from neurilemmomas, the former staining with myogenic cell markers, such as smooth muscle actin and desmin, and the latter showing positive staining with S-100. Masson trichrome stain may be used to demonstrate the longitudinal striations characteristic of smooth muscle tumors. The ultrastructural features of smooth muscle cells are also highly characteristic, being bounded by a basement membrane and often containing parallel arrays of abundant cytoplasmic microfilaments (actin) with interspersed fusiform dense bodies and pinocytotic vesicles.[12]

Given the benign nature of neurilemmomas, therapy is conservative and directed toward sparing the parent nerve when one is identified. The treatment of choice is gross total resection of the tumor. Although neurilemmomas are benign, incomplete

excision may result in slow local recurrence.[13]

In this case, cutaneous schwannoma presented as a solitary mass on the dorsal aspect of the left hand, which is a very unusual clinical presentation. The lesion was completely excised. Follow up of the patient for one year revealed no reccurence of the lesion.

REFERENCES

1. Huntley JS, Davie RM, Hooper G. A subungual schwannoma. Plast Reconstr Surg. Feb 2006; 117 (2):712-13.
2. Murakami Y, Wataya-Kaneda M, Tanaka M, Myoui A, Sakata Y, Katayama I. Case of schwannomatosis. J Dermatol. Sep 2009; 36 (9):508-11.
3. Plaut J, Galloway M, Childerhouse A, Bradford R. Schwannoma with monoclonal plasma cell infiltration. J Neurosurg. Sep 2009; 111 (3):509-11.
4. Denayer E, Brems H, de Cock P, et al. Pathogenesis of vestibular schwannoma in ring chromosome 22. BMC Med Genet. Sep 22 2009; 10:97.
5. Sainz J, Huynh DP, Figueroa K, Ragge NK, Baser ME, Pulst SM. Mutations of the neurofibromatosis type 2 gene and lack of the gene product in vestibular schwannomas. Hum Mol Genet. Jun 1994; 3 (6):885-91.
6. Carter JJ, Langman G, Orpin SD. A solitary painful papule on the ear Clin Exp Dermatol 2009; 34:125-26.
7. Geddes JF, Sutcliffe JC, King TT. Mixed cranial nerve tumors in neurofibromatosis type 2. Clin Neuropathol. Nov-Dec 1995; 14 (6):310.
8. Kao GF, Laskin WB, Olsen TG. Solitary cutaneous plexiform neurilemmoma (schwannoma): a clinicopathologic, immunohistochemical, and ultrastructural study of 11 cases. Mod Pathol. Jan 1989; 2 (1):20-26.
9. McKeever PE. Immunohistochemistry of the nervous system. In: Dabbs D, ed. Diagnostic Immunohistochemistry. Philadelphia, Pa: Churchill Livingstone Elsevier; 2006:794-95.
10. Peltier J, Page C, Toussaint P, Bruniau A, Desenclos C, Le Gars D. Melanocytic schwannomas. Report of three cases. Neurochirurgie. Sep 2005; 51 (3-4 Pt 1):183-89.
11. Fanburg-Smith JC, Majidi M, Miettinen M. Keratin expression in schwannoma; a study of 115 retroperitoneal and 22 peripheral schwannomas. Mod Pathol. Jan 2006; 19 (1):115-21.
12. Kurtkaya-Yapicier O, Scheithauer B, Woodruff JM. The pathobiologic spectrum of Schwannomas. Histol Histopathol 2003; 18:925-34.
13. Seongmin Noh, M.D., Jeong Eun Do, M.D., Jin Mo Park,M.D., Hyunjoong Jee, M.D.,Sang Ho Oh, M.D. Cutaneous Schwannoma Presented as a Pedunculated Protruding Mass. Ann Dermatol 2011; 23:264-66.