Solitary tender erythematous nodule on left knee

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CLINICAL FINDINGS

A 42-year-old man presented with tender bluish red soft to firm nodule on extensor aspect of left knee just below the patella for the last 2 years. It started as an small tender papule and gradually increased in size. There was no improvement with oral antihistamines and topical therapy including topical steroids, pimecrolimus and emollients. There was no past history of similar lesions or other skin problems. The patient had no systemic complaints and there was no family history of similar lesions.

Local examination of the skin revealed well defined soft to firm tender bluish red papulonodular lesion on extensor aspect of left knee. (Fig. 1). Hair, nails and mucous membranes were not affected and showed no significant abnormalities.

Routine laboratory investigations were all within normal limits. Chest x-ray and X ray left knee joint were normal.

What is your clinical differential diagnosis?

Angiolipoma
Eccrine spiradenoma
Angioleiomyoma
Glomangioma
Neurofibroma
Dermatofibroma

Pathological findings

An excision biopsy showed clusters of dilated vascular channels lined by a thin layer of endothelial cells in the dermis. The walls had fibrous stroma containing glomus cells in nests, occasionally containing smooth muscle.[12] Dilated vascular channels lined by endothelial cells were characteristic (Fig. 2, 3). Immunohistochemical staining showed positive staining for alpha smooth muscle actin (Fig. 5) and CD 31 negative (Fig. 4).

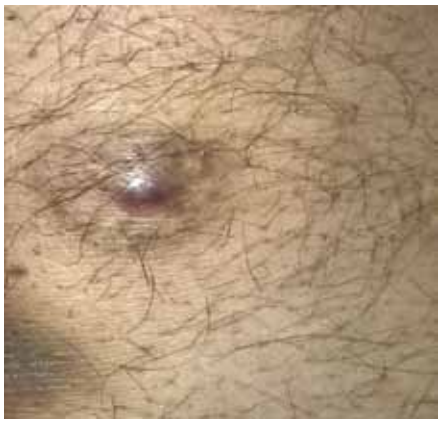

Fig. 1 Well defined erythematous to bluish nodule on left knee

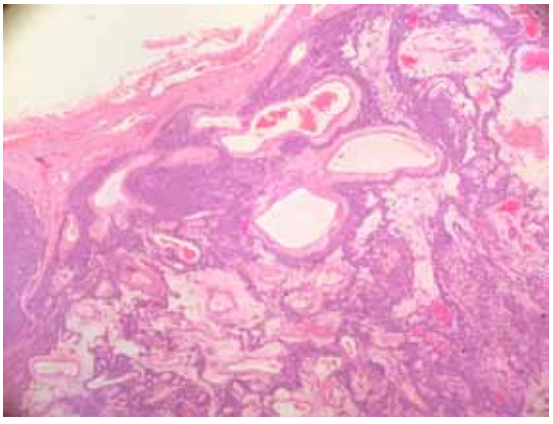

Fig. 2 Branching vascular channels separated by stroma containing glomus cells in nests, aggregates (H&E x40)

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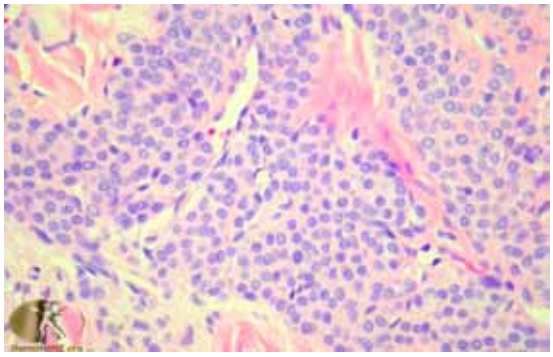

Fig. 3 Showing glomus cells with small, regular, round, indistinct nucleoli (H&E x 100)

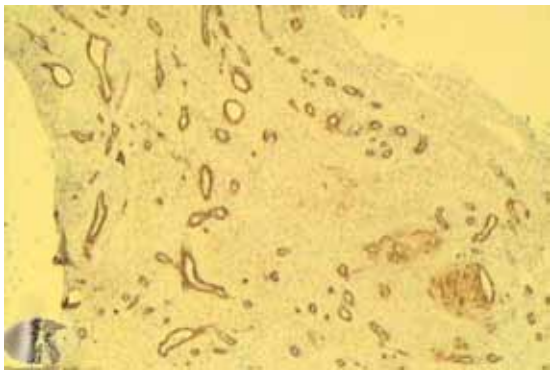

Fig. 4 Immunohistochemistry showing CD31 negative (IHC x400)

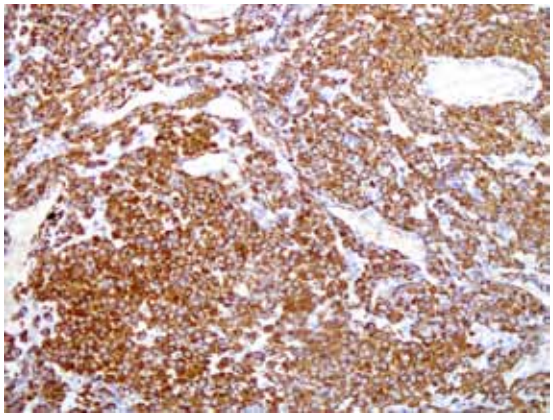

Fig. 5 Immunohistochemistry showing Alpha-smooth muscle actin Positive (IHC x400)

DIAGNOSIS

Glomangioma

(Glomus tumor)

COMMENT

Glomangiomas are benign localized tumors of the skin characterized by abnormal, smooth muscle-like glomus cells.[1] In 1924, Masson[2] described the neuromyoarterial glomus, which he later renamed the neurovascular glomus, and its tumors. The term glomangioma was coined by Bailey[3] in 1935 and is currently applied to lesions with a wide vascular lumen, which are most commonly found in patients with multiple tumors.[4] Glomus tumors arise from modified smooth muscle cells normally found in specialized arteriovenous shunts present in acral sites, especially the fingertips. This location reflects their function, as the arteriovenous anastomoses of these areas, also known as the Sucquet-Hoyer canals, are involved in temperature regulation. Sucquet-Hoyer canals are lined with endothelial cells, contain several layers of glomus cells in their walls, and connect afferent arterioles to efferent venules.[5] Glomus tumors are thought to be hamartomas[6] and account for 1% to 2% of all soft tissue tumors.[5] There are 2 forms of glomus tumors, with the more common solitary variant accounting for 90% of cases and a more rare multiple variant, termed glomangioma, accounting for 10% of cases.[7] The tumors of the solitary variant are small, painful, purple nodules with predilection for acral areas of the extremities, especially the nail beds of the fingers and toes.[8] Aching pain, well-localized tenderness, and temperature sensitivity are the characteristic triad of signs and symptoms.[5] They typically are less than 1 cm in diameter.[8] In contrast, multiple glomus tumors are characterized as glomangiomas because of the angiomatous appearance of the lesions. Glomangiomas often appear during childhood as small bluish nodules situated deep in the dermis, widely scattered over the skin surface. They are rarely subungual and are less likely to be painful.[8] Glomangiomas have a predilection for the upper extremities and occasionally are found on the lower extremities, head, and back. They may

The clinicopathological challenges of glomus tumor

Diagnosis	Clinical	Histological
Angiolipoma	• There may be no symptoms, or the lesion may be tender • Clinically, the lesion is a soft skin-colored plaque or nodule resembling lipoma • The most common site is the forearms followed by the trunk and upper arms • Multiple lesions are frequently found	• Shows nonseptate fat with peripheral congeries of small capillaries • Some of the capillaries are plugged with fibrin thrombi • Sometimes, there are only rare adipocytes admixed with numerous capillaries (“cellular angiolipoma”)
Eccrine spiradenoma	• Originates from the eccrine sweat glands • Slow-growing and usually solitary tumor • Occurs as a painful nodule • It is often seen in young to older adults • Can be present anywhere in the body, commonly observed on the head and neck area	• Consist of 1 or more large, sharply delineated, basophilic nodules in the dermis (cannon balls or big blue balls in the dermis) • The nodules are unattached to the epidermis and sometimes extend into the subcutis • The nodules consist of two types of cells: -Small, dark, basaloid cells with hyperchromatic nuclei -Cells with large, pale, vesicular, and ovoid nuclei • Strands of cells are positive for cytokeratin, and the lumina are positive for CEA
Angioleiomyoma	• lt is an uncommon smooth muscle tumor arising from the smooth muscle of the vessel wall • These slow-growing solitary tumors are fairly common • Their presence is felt by a distinct pain in about 60% of the cases • Usually affects the lower limbs • Women in their mid-adult phase are commonly affected	• Scanning magnification view shows a circumscribed tumor nodule arising in the dermis or subcutaneous tissue • The tumor is comprised of densely packed interlacing bundles of smooth muscle which surround small compressed vascular channels • Immunostaining shows positive staining with muscle markers, Smooth muscle actin (SMA) and Desmin
Glomangioma	• Typically solitary, painful 1-2 cm reddish blue papule or nodule • Found on a young adult • They most commonly affect the nail bed or the palm • They are usually tender to touch, but may be extremely painful, particularly following change in temperature or pressure	• There are solid sheets of glomus cells around small blood vessels • Immunohistochemical studies are helpful in diagnosis with cells showing alpha smooth muscle positivity and CD 31 negative
Neurofibroma	• Usually occurs between the ages of 20 and 30 • Presents as papular, nodular or pedunculated lesions and greyish white in colour • It is usually painless, slow growing and soft in consistency	• The lesion is non encapsulated and circumscribed • A grenz zone separates the lesion from the epidermis • The tumor is composed of interlacing bundles of elongated cells with wavy nuclei • Mast cells are present • The stroma is mostly fibromyxoid
Dermatofibroma	• Presents as slow growing, slightly pigmented, solitary nodule • Frequently develops on the extremities (mostly the lower legs) • Usually asymptomatic but may be pruritic, tender or painful • Can occur in patients of any age but more common in adults	• A poorly defined proliferation of “fibrohistiocytic” cells within the dermis • The overlying epidermis may be acanthotic with increased basal layer pigmentation • The infiltrate is separated from the overlying epidermis by clear ‘Grenz’ zone • At the periphery of the lesion there is entrapment of collagen

be slightly larger and less well-circumscribed than solitary glomus tumors.[5] An autosomal dominant inheritance pattern has been described for glomus tumors, with some types being mapped to band 11q23.[6] Familial cases have been reported with incomplete penetrance and variable expression.[7] Glomangiomas have a male predominance, while females more frequently (in 70% of cases) are found to have solitary glomus tumors.[5] Histopathologically, glomus tumors contain dilated vascular channels surrounded by glomus cells. The glomus cells are monomorphic round or polygonal cells with plump nuclei and scant eosinophilic cytoplasm. They are positive for smooth muscle actin, while vascular endothelium is positive for factor VIII and CD34.[9] Choosing the appropriate treatment regimen for glomus tumors and glomangiomas should be individualized to the patient and guided by the clinical presentation. Treatment is not always indicated, particularly in asymptomatic cases of glomangioma. Surgical intervention, when needed, typically is excision with primary closure. Laser treatment, electromagnetic radiation, and sclerotherapy also have been used.[5] Blue Rubber Bleb Nevus Syndrome-It is important to distinguish glomangioma from blue rubber bleb nevus syndrome (BRBNS), which is associated with venous malformations on both the skin and gastrointestinal tract. The BRBNS venous malformations of the gastrointestinal tract can be associated with clinically significant gastrointestinal bleeding.[10] Lesions of BRBNS can be macular, papular, or nodular, and usually are multiple, varying in diameter from a few millimeters to several centimeters. The cutaneous lesions usually are asymptomatic and the overlying skin may show increased sweating. These lesions may appear at birth or in early childhood, and they tend to increase in size and frequency with age. Although they may occur anywhere, they are principally located on the upper limbs, trunk, and perineum. Acral lesions are unusual and the lesions have no evidence of malignant change.[11] Cutaneous lesions of BRBNS are blue, soft, and nipplelike, easily compressing and refilling slowly.[12] On the other hand, glomangiomas are noted for a distinct raised, often hyperkeratotic, cobblestone like appearance, and could not be completely emptied by compression.[13] Glomangiomas generally do not extend into deep structures.[14] Histologically, glomangiomas contain clusters of dilated vascular channels lined by a thin layer of endothelial cells in the dermis or subcutaneous fat. The walls are a fibrous stroma, occasionally containing smooth muscle.[12] Dilated vascular channels lined by endothelial cells are characteristic of both diseases. Therefore, biopsy results confirming the presence of glomus cells lining the dilated vascular channels characterize glomangiomas.[10]

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