# Sclerosing perineurioma: a rare benign tumor in a pediatric patient

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## Abstract

A 15-year-old boy presented to outpatient dermatology clinic for evaluation of a lesion on the hand. Originally small and asymptomatic, the lesion had rapidly enlarged in the six months prior to evaluation. A shave biopsy was performed and histopathologic evaluation demonstrated a well-circumscribed nodular proliferation of dense, bland, epithelioid to spindle cells on a fibrillary background. Tumor cells were diffusely epithelial membrane antigen positive; S100 and Melan-A were negative. These findings are consistent with a diagnosis of sclerosing perineurioma. This case illustrates the presentation of sclerosing perineurioma in a pediatric patient and we review the pertinent pathologic and immunohistochemical findings necessary for diagnosis. It is imperative to distinguish this entity from other soft tissue tumors on the hand, both benign and malignant, to avoid overly aggressive surgical intervention.

*Keywords: benign, cutaneous, neoplasm, nerve, perineurioma, sheath, sclerosing*

## Introduction

Sclerosing perineurioma, a benign variant of extraneural soft tissue perineurioma, is an uncommon entity that presents clinically as a skin-colored nodule in adults on acral surfaces [1]. We present a pediatric patient with an enlarging lesion on his hand. Histologic examination revealed a sclerosing perineurioma, which rapidly recurred after shave biopsy.

## Case Synopsis

A 15-year-old boy with no known significant past medical history presented to outpatient dermatology clinic for evaluation of a lesion on his left hand. The lesion, which had present for three years, was originally small and asymptomatic but had enlarged rapidly in the 6 months prior to evaluation. The patient had been applying a homeopathic wart remedy without clinical improvement. Physical examination revealed a 1.5cm flesh-colored nodule on the distal palmar aspect of his left hand (**Figure 1**). Shave biopsy was performed and histopathologic evaluation demonstrated a well-circumscribed nodular proliferation of dense, bland, epithelioid to spindle cells with pale, eosinophilic cytoplasmic processes on a fibrillary background. (**Figures 2A, B**) Tumor cells were diffusely epithelial membrane antigen (EMA) positive (**Figure 2C**) and focally, factor XIII positive. CD99 positivity was present around blood vessels. CD34 and smooth muscle actin (SMA) outlined endothelial cells and CD10 positivity was present within the collagen bundles. S100 and Melan-A were negative. These findings were consistent with a diagnosis of sclerosing perineurioma.

Following shave biopsy, the lesion recurred and grew to its initial size within one month. The patient was referred to an orthopedic hand surgeon for definitive surgical removal.

## Case Discussion

Lazarus and Trombetta first described perineurioma in 1978 [1]. These entities are soft tissue tumors, caused by hyperplasia of the perineural cells and consist of intraneural and extraneural (soft-tissue) subtypes. The intraneural variant will involve a nerve usually resulting in sensorimotor symptoms, whereas the extraneural variant is not associated with nerves and can therefore be asymptomatic [2]. The sclerosing perineurioma is a unique variant of the extraneural perineurioma which was first described in 1997 [1]. Although the pathogenesis of perineuriomas is not fully understood, initial hypotheses suggested they could arise secondary to trauma or injury [2]. Recently, sclerosing perineuriomas have been linked to certain gene deletions in chromosome 10q24 and in chromosome 22 [3,4]. The genes located on the chromosome 10q24 locus include *fibroblast growth factor-8, cyclin M2, nuclear factor-kappa-B2,* and *meningioma-expressed antigen 5* [4]. Abnormalities in chromosome 22 have been tied to nerve sheath tumors. One case of sclerosing perineurioma specifically reported 5'*BRC* and *NF2* gene deletions on chromosome 22, along with clonal changes in chromosome 10 [3]. Aberrations in these genes could begin to explain the tumorigenesis of sclerosing perineuriomas.

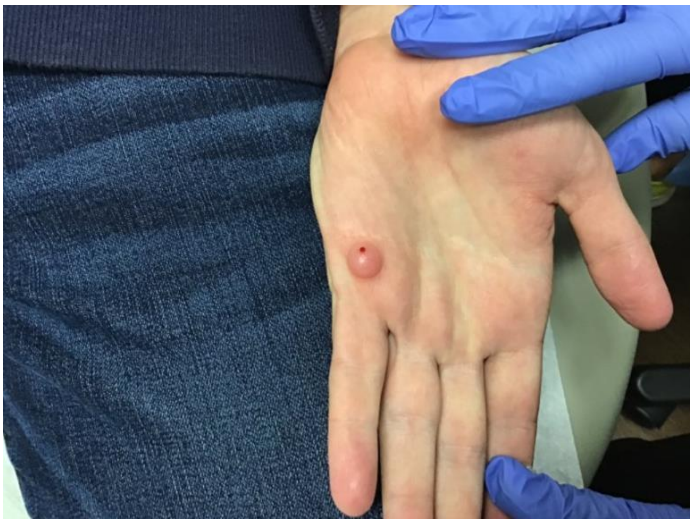

**Figure 1**. *Pink-to-flesh colored nodule on volar aspect of hand.*

Sclerosing perineuriomas commonly present as a single asymptomatic skin-colored to brownish-pink fibrous papule or nodule on the hands or extremities, as it did in our patient. However, there have been reports of sclerosing perineuriomas presenting as multiple lesions and in other locations including the oral cavity, viscera, and scrotum [4,5]. Its prevalence is equal in both men and women and onset usually occurs in young-to-middle aged adults [5]. A review of the literature showed that in pediatric cases, perineuriomas are more likely to present on the subcutis of the hands, face, and scrotum [6]. Sclerosing perineuriomas often demonstrate an indolent growth pattern, although central ulceration of the lesion may be seen [6].

Histologically, sclerosing perineuriomas are generally hypocellular with a sclerotic collagenous stroma admixed with small pale to slightly basophilic epithelioid cells and plump spindle cells showing a characteristic corded or whorled growth pattern [4]. As mentioned previously, sclerosing perineuriomas are a variant of extra-neural perineuriomas, which usually do not contain any nerve elements. However, some studies have reported nerve axons and Schwann cells within sclerosing perineuriomas, indicating this entity may be derived from perineurial cells encircling small nerves. Due to their small size and susceptibility to degeneration, these nerve elements are not evident in all cases [7].

Immunohistochemical (IHC) staining is essential for accurate diagnosis. Perineurial cells classically show membranous immunoreactivity for GLUT-1, claudin-1, vimentin, and EMA [3,4,7]. Perineuriomas should also stain positively for collagen IV and laminin, since normal perineurium has a basal lamina. Perineural cells also normally express CD99 and actin. Importantly, perineuriomas should stain negative for S-100, distinguishing it from schwannomas and neurofibromas, both of which are EMA negative and S-100 positive [7]. However, if the sclerosing perineurioma is surrounding small neural elements, it can have focal S100 positivity [4]. These lesions will usually also have variable CD34 staining, with 30-40% expressing positivity [3]. Sclerosing

perineuriomas should be negative for carcinoembryonic antigen, ER-EP4, B72.3, desmin, NF, CD68, Factor XIIIa, and Factor VIIIrAg [3]. Although rare, malignant perineurial tumors have been described as a variant of malignant peripheral nerve sheath tumors. These malignant forms demonstrate many of the classic perineurioma features, including the EMA positivity and S100 negativity. However, there will be evident cytologic atypia and necrosis [2,6].

Acral lesions can be diagnostically challenging both clinically and histopathologically. Many other tumors can simulate sclerosing perineuriomas, some of which may require additional systemic work-up. For this reason, understanding IHC staining patterns is essential for delineating these entities. Nodules that characteristically present on the hands which could be confused histologically with sclerosing perineuriomas include fibroma of tendon sheath, fibrosing tenosynovial giant cell tumor, and cutaneous sclerotic fibroma. The fibroma of tendon sheath and fibrosing tenosynovial giant cell tumor commonly have giant cells and are EMA negative [3]. Clinically, both of these entities will also be situated more deeply [8]. Cutaneous sclerotic fibromas are EMA negative as well but are generally located on the face and have an association with Cowden syndrome. These fibromas characteristically have fascicles of collagen bundles with a laminated tortuous appearance [3]. Importantly, EMA, GLUT-1, and claudin-1 do not have a 100% sensitivity or specificity in identifying perineuriomas. Additionally, when sclerosing perineuriomas present on non-acral skin and histochemical stains are not conclusive, it can be difficult to distinguish sclerosing perineuriomas from entities like cutaneous sclerotic fibromas [9]. Soft tissue fibrous meningiomas are clinically similar to sclerosing perineuriomas, but histologically differ by the presence of psammoma bodies and intranuclear inclusions besides the positive S100, CD34, and keratin IHC staining pattern [3]. Epithelioid glomus tumors can be morphologically similar. Microscopically, the epithelioid cells will cluster around blood vessels and IHC staining will be negative for EMA and positive for vimentin and SMA [3]. Since multiple lesions can mimic sclerosing perineuriomas clinically and histologically, awareness of this entity could mitigate any misdiagnosis resulting in an unwarranted workup and overtreatment.

Diagnosis of perineuriomas, regardless of subtype, is based on clinical and histologic findings as mentioned previously. Imaging, particularly MRI, may be utilized during preoperative evaluation and can be of diagnostic value in indeterminate cases [10]. Ultrasonography may also be used and will demonstrate fusiform enlargement of the nerve fascicles with hyperechoic perineural tissue [11]. Currently, there is no consensus for the treatment of perineuriomas. Surgical excision seems to provide the best long-term outcomes for patients, especially those under the age of 60, or in cases in which neurologic deficits are present [10]. For these patients, excisional biopsy is performed if the lesion is smaller than 5cm. If greater than 5cm, or if the

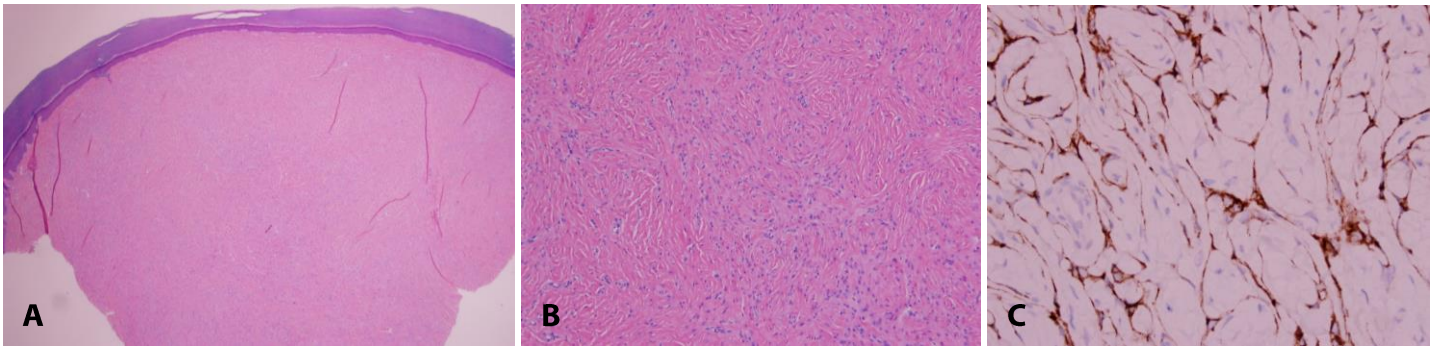


**Figure 2**. ***A)*** *Low-power magnification view of well circumscribed nodular proliferation of epithelioid to spindle cells with dense collagenous stroma, 20×.* ***B)*** *High-power examination demonstrates epithelioid to spindle cells with pale eosinophilic cytoplasmic processes in fibrillary background, 100×.* ***C)*** *Epithelial membrane antigen immunohistochemical analysis demonstrates diffuse positivity, 400×.*

brachial plexus is involved, a nerve graft can be considered [10]. Given the predilection of these lesions to present on acral surfaces and the complex nature of the anatomy of the hands, referral to a hand surgeon is often warranted as in our case.

## Conclusion

Perineuriomas are rare, benign soft tissue tumors derived from hyperplasia of perineurial cells of the peripheral nervous system. Although much remains unknown about the pathogenesis of perineuriomas, alterations of chromosome 10 and 22 and a traumatic etiology are suspected. The diagnosis is confirmed through excisional or shave biopsy for pathologic evaluation. Histologic findings characteristically show small epithelioid and plump spindle cells arranged in a corded or whorled growth pattern surrounded by an extensively collagenized stroma. Given the nonspecific clinical appearance of these lesions, several entities must be considered in the differential diagnosis. Staining with H&E and more specific IHC stains (EMA, GLUT-1, claudin-1) are important in narrowing the number of entities in the differential diagnosis and confirming the correct diagnosis. Treatment is controversial and there remains no consensus. However, studies suggest surgical excision may provide optimal outcomes.

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## Potential conflicts of interest

The authors declare no conflicts of interest.

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