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Benign cutaneous neural tumors

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Benign cutaneous neural neoplasms are one of the most frequent benign mesenchymal tumors in the skin. Because peripheral sheath nerve is composed of different cells, the tumors raised in these structures are varied and usually contain many of these cells. Most of these tumors are easy to diagnose, as usually present characteristic features well-recognized and express -specific immunohistochemical proteins. However, there are so many infrequent variants that many times require distinction from others spindle-cell tumors including melanoma. The tumors differ from one another by displaying a different proportion and arrangement of the various constituents of a peripheral nerve. In this article, we present the most characteristic clinical and histopathological features of many of these frequent benign cutaneous neural tumors including their uncommon variants.

Benign cutaneous conditions of peripheral nerve sheaths are relatively common lesions which show a range of features that mirror the different elements of the nerve including Schwann and perineural cells, neurofilaments, fibroblast, and others. Many of these lesions may occur in superficial soft tissues, but rapidly involve cutaneous structures. In this article, we review the most frequent benign neural lesions observed in a skin biopsy.

Reactive lesions

Most cutaneous reactive neural lesions usually occur after traumatic or inflammatory processes. In this section, 5 different conditions, including rudimentary polydactyly, traumatic neuroma, Morton's neuroma, digital pacinian neuroma, and epithelial sheath neuroma (ESN), are considered.

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Rudimentary polydactyly

Accessory digit or polydactyly is an uncommon neonatal condition characterized by a well-formed extra digit or a miniature fifth digit duplication near their base, along its ulnar border.[1] Isolated and syndromic forms with an autosomal dominant trait have been reported.[2] It has been suggested that this condition is an intrauterine amputation neuroma at the site of supernumerary sixth digit.[3] Microscopically, the lesion is irregular, badly outlined, and located in the dermal papillae and upper dermis. It is mainly composed of a disordered proliferation of nerve fibers and encapsulated Meissner corpuscles embedded in connective tissue. A Merkel cell proliferation in the basal layer of the epidermis is often present.[4] Surgical resection is the usual treatment.

Traumatic neuroma

Amputation or traumatic neuroma is a benign condition secondary to partial or total traumatic section of neural pathway. They can form at any site of trauma, infection, in scars, and amputation stumps. Clinically, the lesion is small, oval,

firm, and occasionally tender or spontaneously painful. Microscopically, the lesion consists of irregular and cross-linked bundles of nerve fascicles embedded in fibrous scar tissue. This tissue usually proliferates around nerve fascicles conferring the appearance of multiple separate nerves. Nerve fascicles contain Schwann cells positive to S-100 protein surrounded by perineural cells positive to epithelial membrane antigen (EMA),[5] which contrast to solitary circumscribed neuroma (SCN), in which only the peripheral capsule contains these cells. Simple excision of the lesion is the usual therapy.

Multiple mucosal neuromas maybe the early manifestation of the multiple endocrine neoplasia syndrome (MEN-IIb), but mucosal neuromas have also been reported isolated. Dermal hyperneury, a hypertrophy of dermal small nerves, may also be present in the normal skin of these patients.

Morton's neuroma

Morton's metatarsalgia is not actually a tumor but represents a degenerative response to chronic low-grade tissue damage. Morton's neuroma usually presents in women who complain of burning pain in the distal sole of the foot that may radiate into the toes, especially when walking or wearing shoes. Night pain is rare. The pain is often localized over the metatarsal heads between the third and fourth toes, usually in response to irritation, trauma, or excessive pressure.[6] The classical microscopic appearance shows a marked fibrosis of the endo-, epi-, and perineurium associated to edema, marked degeneration, and loss of nerve fibers. Fibrosis also involves adjacent subcutaneous tissue and wall of blood vessels. However, some authors support that similar findings are also observed in nerves from the same area of normal specimens excised from autopsy, except for slightly thicker nerves in patients with the condition.[7] Thus, the authors question the value of microscopic study in confirming the diagnosis.

Digital pacinian neuroma

Pacinian corpuscles hyperplasia is an extremely rare and painful condition that usually occurs after local trauma to the finger of adults including dog bite,[8] foreign body reaction, and so on. The lesions are small and have been reportedly associated to Morton's neuroma[9] or Dupuytren.[10] Microscopically, it consists of numerous mature pacinian corpuscles increased in size and number, intermingled with small nerve fibers embedded in a fibrous tissue. Pacinian neuroma is diagnosed when the typical histopathological features are associated with a discrete pain-producing mass.[11]

Epithelial sheath neuroma

This is a distinctive benign cutaneous lesion characterized by a superficial dermal proliferation of enlarged nerve fibers ensheathed by squamous epithelium.[12] Clinically, the lesions occur in adults as asymptomatic solitary papules or nodules, mainly on the back. Microscopically, ESN consists of prominent nerves in the superficial dermis encased by a cytologically bland squamous epithelium with scattered isolated dyskeratotic cells (Figure 1). It also frequently shows the presence of fibroplasia, mucin, and sparse inflammatory infiltrate of lymphocytes and plasma cells around some of these neuroepithelial aggregations (Figure 2). There is no connection to the overlying epidermis or neighboring adnexal structures. Differential diagnosis of ESN is perineural invasion by a previous squamous cell carcinoma or keratoacanthoma with partial regression. However, the absence of histopathological feature of regression, as well as the presence of enlarged nerve fibers in superficial dermis support the diagnosis.[13] The exact histogenesis is not yet established, but the most accepted hypothesis is that ESN represents an entrapped hyperplastic infundibular epithelium in association with hyperplastic nerve bundles. Treatment consists of simple excision.[14]

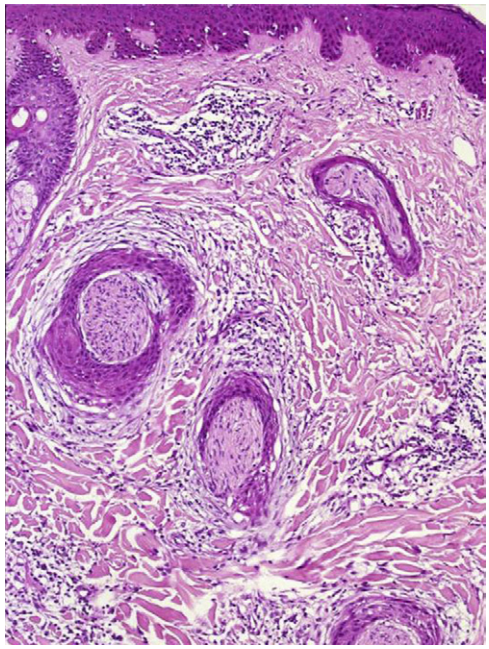

Figure 1 Panoramic view of epithelial sheath neuroma. Prominent nerves surrounded by bland squamous epithelial sheaths in superficial dermis are evident.

Hamartomatous lesions

Lipofibromatous hamartoma

Neural fibrolipoma is a rare hamartomatous condition characterized by an excessive infiltration of the epi- and perineurium by fibroadipose tissue. The process usually involves the volar regions of the hands, wrists, and forearms of young patients. It clinically consists of a soft slowly growing mass surrounding and involving major nerves and their branches, mainly the median nerve.[15] Sometimes, patients complain of pain, paresthesias, or trauma. One-third