

Palisaded encapsulated neuroma clinically mimicking a mucocele: report of a case

Neuroma encapsulado em paliçada mimetizando mucocele: relato de caso

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ABSTRACT

We report the case of a 21-year-old female patient with the chief complaint of a small tumor on the lower left lip. Intraoral examination revealed a two-month evolution nodular lesion on the left labial mucosa, of resilient consistency and asymptomatic. A history of prior trauma was reported by the patient. A provisional diagnosis of mucocele was established, and an excisional biopsy was performed. The diagnosis was palisaded encapsulated neuroma (PEN). As PEN is considered underdiagnosed by many authors, a discussion on the morphologic diagnostic criteria of this lesion will be provided.

Key words: soft tissue neoplasms; peripheral nerves; neuroma; lip.

INTRODUCTION

The palisaded encapsulated neuroma (PEN) or solitary circumscribed neuroma (SCN) is a benign tumor of neural origin, uncertain etiology, firstly described in 1972 by Reed *et al.* (1972)⁽¹⁾. PENS tend to occur in adults between the fifth and the seventh decades of life and do not show sex predilection⁽²⁾. Most of the lesions occur on the skin, especially of the face, with the oral cavity being the second most frequent site of involvement, and the hard palate, the most common intraoral site of occurrence⁽³⁾.

Clinically, oral lesions present as a small (< 1 cm) movable submucosal, single, pink, slow-growing asymptomatic nodule⁽⁴⁾. PENS are rarely multiple lesions⁽⁵⁾. Patients generally deny any previous traumatic episode. Other rare reported sites include trunk⁽⁶⁾, nasal cavity⁽⁷⁾, and eyelids⁽⁸⁾. No case was associated with neurofibromatosis type 1 (NF1) or multiple endocrine neoplasia type IIb (MEN IIb syndrome).

Histologically, the lesion consists of a proliferation of Schwann cells with variable dimensions and variable number of axons. A delicate capsule, in general, partially involves the lesion⁽²⁾. Cells show positive reaction to S-100 protein. However, unlike other neural tumors, they are negative for glial fibrillary acidic protein (GFAP). Moreover, immunopositivity of capsule cells is also noted for the epithelial membrane antigen (EMA) and collagen IV⁽⁹⁾.

Conservative surgical excision is the treatment of choice, and prognosis is excellent⁽⁹⁾. The purpose of this paper is to report a rare case of PEN clinically mimicking a mucocele, besides discussing the morphological criteria of differential diagnosis with other lesions derived from the peripheral nerve sheath.

CASE REPORT

A 21-year-old dark-skinned patient presented at the oral medicine service of Universidade Tiradentes (Unit) (Aracaju-SE) complaining of a lesion on the lip. Intraoral examination revealed a fibrous resilient nodular lesion on her left lower lip mucosa, with color resembling normal mucosa, around 1.5 cm large, asymptomatic, with a two-month evolution and history of local trauma (**Figure 1A**). A provisional diagnosis of mucocele was given, and excisional biopsy was performed (**Figure 1B**). The surgical specimen was referred to the oral pathology service of the dentistry course at Tiradentes University.

The hematoxylin-and-eosin (HE)-stained sections revealed well-circumscribed proliferation of spindle-shaped and ovoid cells, with well-stained nuclei, sometimes slightly wavy, organized in short interlacing fascicles. Presence of palisading arrangement could be observed, but without the architectural formation typical of Antoni A pattern (**Figure 2A-C**). Immunohistochemical

analysis revealed strong positive staining for S-100 protein, negative staining for GFAP protein and focal positive staining limited to the wall of small blood vessels for alpha-smooth muscle actin (α -SMA) (**Figure 2D** and **2E**). The diagnosis was PEN. The patient has been under follow-up, with no signs of relapse two years after surgery (**Figure 3**).

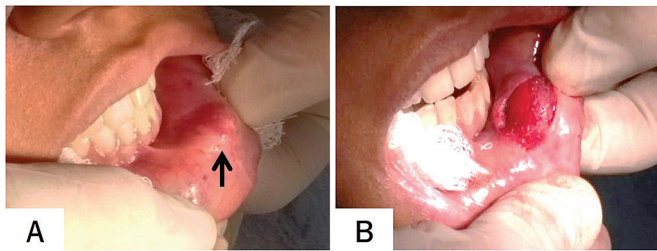


FIGURE 1 – Clinical aspect of the lesion

A) clinical aspect of the lesion. Observe the small nodular sessile lesion, with color resembling the surrounding (arrow) mucosa in lower lip, on the left; B) aspect during surgery, revealing a well-delimited lesion on labial submucosa.

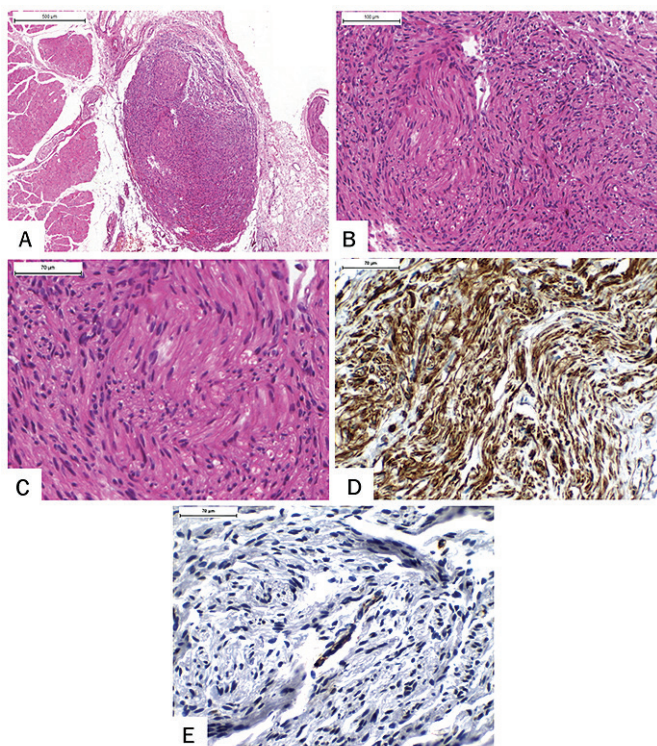


FIGURE 2 – Histopathological and immunohistochemical aspects

A) well-circumscribed spindle-cell lesion located in deep planes; B) proliferation of spindle-shaped and ovoid cells organized in short fascicles, sometimes forming a rudimentary palisading arrangement; C) detail of neoplastic cells, highlighting well-stained wavy nuclei, with imperceptible nucleoli; D) immunohistochemical analysis revealing intense and diffuse positivity for S-100 protein; E) positivity just focal and limited to the wall of small vessels for α -SMA. α -SMA: alpha-smooth muscle actin.



FIGURE 3 – Clinical aspect of the patient's lower labial mucosa two years after surgical removal of the lesion, with no signs of relapse

DISCUSSION

The histopathological differential diagnosis of PEN includes a variety of benign neurogenic and muscle tumors, including schwannoma, neurofibroma, traumatic neuroma, mucosal neuroma, and leiomyoma^(3,4,10). Distinction between those entities, especially neurofibroma and mucosal neuroma, is essential, as they are frequently associated with NF1 and MEN Iib syndrome, respectively⁽⁹⁾.

Histopathological characteristics of PEN include a solitary well-circumscribed, partially encapsulated intradermal nodule, composed of spindle-shaped cells consistent with Schwann cells grouped in interlacing fascicles frequently separated from one another by artifactual clefts. Tumor cells display eosinophilic cytoplasm, and wavy or pointed nuclei. Although nuclei frequently exhibit a parallel orientation within fascicles, a well-defined palisade arrangement and Verocay bodies typical of Antoni A pattern schwannoma are not usually seen. Nuclear pleomorphism, mitotic activity, fibrosis and inflammation are rarely noted^(4,9). The nodular growth pattern is the most frequent, as in the present case, but epithelioid, plexiform, and multinodular types have also been reported. Those morphological variations are neither clinically nor biologically relevant, although familiarity with them minimizes confusion with other tumors of the peripheral nerve sheath, especially schwannoma and neurofibroma⁽⁴⁾.

In general, PEN can be distinguished from schwannomas with no difficulty. Unlike PEN, schwannoma spindle-shaped cells are disposed in two distinct patterns, Antoni A and B, in variable proportions, with no or few intralesional axons, forming

completely encapsulated lesions⁽⁴⁾. In contrast, morphological distinction between neurofibroma and PEN can be difficult, especially with incisional biopsies. The absence of a fibrous capsule and the haphazard distribution of neoplastic cells are the main differential aspects observed in neurofibroma compared with PEN. Mast cells are also rather frequent. Besides, traces of palisade arrangement, typical of PEN, are not observed in neurofibromas. The clinical features of NF1, frequently associated with histopathological findings, make differential diagnosis even easier. There is no association between PENs and neurofibromatosis^(4,9).

From an immunohistochemical point of view, the Schwann cells in PENs are strongly immunoreactive for S-100 proteins and collagen IV. Interestingly, they are consistently negative for GFAP^(3,9), as also observed in our case. In contrast, schwannomas and neurofibromas show frequent staining for this marker (GFAP)^(3,4,9). Thus, GFAP negative staining can be considered a useful distinctive feature between PEN and schwannomas and neurofibromas.

The traumatic neuroma (amputation neuroma) is an exuberant tissue response to neural injury. Clinically, it presents as nodules firm to palpation, causing pain, burn sensation or paresthesia, in most cases. History of trauma and symptoms are important characteristics in the diagnosis of traumatic neuroma^(11,12). In the present case, although there was a prior trauma, no associated symptom was reported. Histologically, traumatic neuromas consist of small and irregular fascicles of nerve bundles separated by a variable amount of collagen or myxoid stroma. The nerve bundles contain Schwann cells positive for S-100 protein surrounded by perineural cells positive for EMA, which contrast with PEN, in which just the peripheral capsule contains EMA+ cells. Besides, the absence of inflammatory cells helps distinguish PEN from traumatic

neuroma^(4,9). Conservative surgical excision of the lesion is the usually employed treatment, and prognosis is excellent^(11,13).

The mucosal neuroma is a non-neoplastic lesion of hamartomatous nature, seen almost exclusively in young patients with MEN IIb syndrome, a rare syndrome with potentially fatal consequences, such as medullary thyroid carcinoma⁽¹⁴⁾. Oral mucosal neuromas are the first sign of the condition, and their correct diagnosis has positive prognostic impact. Clinically, they present as multiple papules or small nodules that affect especially lips and the anterior region of the tongue; other sites include buccal mucosa, gingiva, and palate⁽¹⁵⁾. Histologically, they are composed of bundles of nerve fibers of different sizes, delimited by a prominent perineurium (EMA+) and surrounded by normal conjunctive tissue or conjunctive tissue of loose nature. Moreover, they do not possess nuclei in palisade nor fibrous capsule, different from the typical pattern observed in PENs⁽⁴⁾.

Complete surgical excision is the treatment of choice for PEN, and recurrence is rare⁽³⁾. Given the clinical picture, a provisional diagnosis of mucocele was established, and the patient underwent excisional biopsy. Mucocele is a common lesion of the lip, asymptomatic in most cases, similar to the mucosa in color, clinically resembling a variety of other lesions that affect oral soft tissues⁽¹³⁾. Because it is the most common lesion of the lower lip, it would be always physicians' main choice as a provisional diagnosis.

Although tumors of the peripheral nerve sheath are rare, they must also be included in the list of differential diagnoses of nodular lesions of the lower lip; familiarity with morphological and immunohistochemical aspects of those lesions is essential to avoid diagnostic mistakes and provide a satisfactory therapeutic approach to patients.

RESUMO

Relatamos o caso de uma paciente de 21 anos de idade, com queixa principal de um pequeno nódulo no lábio inferior esquerdo. O exame intraoral revelou lesão nodular na mucosa labial esquerda de consistência resiliente, assintomática, com evolução de dois meses. Histórico de trauma prévio foi relatado pela paciente. Diagnóstico provisório de mucocele foi estabelecido; realizou-se biópsia excisional. O diagnóstico foi neuroma encapsulado em paliçada (NEP). Como o NEP é considerado subdiagnosticado por muitos autores, será fornecida uma discussão sobre os critérios morfológicos de diagnóstico dessa lesão.

Unitermos: neoplasias de tecidos moles; nervos periféricos; neuroma; lábio.

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