Solitary neurofibroma of the oral mucosa: a previously undescribed variant of neurofibroma

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Abstract: We report a distinct morphologic type of neurofibroma, lipomatous neurofibroma, arising in the oral mucosa, which has not been described previously in the literature. A 25-year-old female patient presented with a solitary mucosal mass on the palatal gingiva. Although the limited biopsy material was diagnosed as a spindle cell lipoma, characteristic light microscopic neurofibromatous areas, intricately admixed with mature fat, were found in the entire resection specimen. Immunohistochemically, many of the spindle cells were positive, either diffusely or focally, for common neural markers, with patchy staining for CD34 and epithelial membrane antigen. S-100 protein was also positive in adipocytes. Ultrastructural examination confirmed the diagnosis of neurofibroma and suggested an intimate relationship between neoplastic neural cells and adipocytes. (J. Oral Sci., 44, 59-63, 2002)

Key words: differential diagnosis; lipomatous tumor; neurofibroma; spindle cell lipoma.

Introduction

Neurofibroma is a benign tumor originating in the peripheral nerve sheath that may occur as part of neurofibromatosis type 1 (von Recklinghausen’s disease) or, more commonly, as a localized sporadic lesion (1). Solitary lesions occur in most anatomical locations, including the oral mucosa (2). There is a wide spectrum of histological patterns and several distinct variants have been described (1,3,4). Oral neurofibroma is generally a small, well circumscribed, but not encapsulated, tumor (5-8). Tumors with areas of myxoid and/or hyalinized changes are common. Although small amounts of entrapped adipose tissue are interspersed within the oral lesions, no oral neurofibromas with the features of a primary lipomatous tumor have been reported, to our knowledge (5-8).

We report a unique, solitary neurofibroma of the palatal gingiva characterized by an admixture of mature fat, which appears to be an integral part of the tumor. The descriptor “lipomatous neurofibroma” was chosen to include the two principal components of this tumor. Although diagnosis of a conventional neurofibroma is straightforward, this lipomatous variant may be more difficult to diagnose.

Case Report

A 25-year-old woman was referred for evaluation of a painless mass on her palate that had been present for one year. There were no clinical signs or family history of von Recklinghausen’s disease. Intra-oral examination revealed a relatively circumscribed mass (1.2 × 1.0 × 1.0 cm) on the palatal gingiva of the left maxillary, central and lateral incisors (Fig. 1). Radiographs did not show any abnormality. A fibroma was suspected, so we performed an incisional biopsy. A spindle cell lipoma was diagnosed from the histology. Surgery revealed that the mass appeared to adhere tightly to the neurovascular bundle at the incisive canal. There was no sign of a recurrence after two years.

Surgery revealed an ovoid, non-encapsulated mass and the cut surface was greasy and white, with scattered yellow patches (Fig. 2). The histopathological appearance of the specimen removed during the surgery was similar to that...
of the biopsy specimen. The tumor consisted predominantly of fibromyxoid tissue and about 20% adipose tissue. The proliferating spindle cells had slender wavy nuclei and bipolar cytoplasmic processes and they were embedded within a hypocellular myxoid-like stroma that contained loosely textured, fine collagen fibers. There was intralesional mature fat present in the form of small nodular aggregates or individual adipocytes situated away from the periphery. These were evenly distributed throughout the lesion (Fig. 3). There was no evidence of lipoblasts in any of the sections.

An immunohistochemical study showed that most of the spindle cells were positive for S-100 protein (Polyclonal, 1:1200, Dakopatts, Carpenteria, CA, USA) (Fig. 4). The cells were positive, both in patches, and focally, for CD57 (Leu 7, 1:40, Dakopatts, Carpenteria, CA, USA), neuron-specific enolase (N3, 1:100, Dakopatts, Carpenteria, CA, USA), neurofilament protein (NE14, 1:100, Dakopatts, Carpenteria, CA, USA), and the protein gene product 9.5 (1:100, Novocastra, UK). Some of the spindle cells were positive for epithelial membrane antigen (E29, 1:50, Dakopatts, Carpenteria, CA, USA) and CD34 (QBend-10, 1:400, Serotec, Bicester, England), but negative for pankeratin (Polyclonal, 1:50, Dakopatts, Carpenteria, CA, USA). The adipocytes did not react to any of these neural markers except for S-100 protein (Fig. 4).

Ultrastructurally, the spindle cells showed features of Schwann cells or perineurial-like cells. The neoplastic Schwann cells had prominent, long, thin cytoplasmic processes coated by a continuous basement membrane. Long cytoplasmic processes with abundant pinocytotic vesicles and a discontinuous coat of basement membrane characterized the perineurial-like cells. The adipocytes were surrounded by an interrupted basal lamina and their cytoplasm was condensed into a thin rim, similar to that found in lipomas. In the transitional areas between the neurofibromatous and lipomatous components, both Schwann cells and perineurial-like cells with variable numbers of different sized lipid droplets in the cytoplasm, were conspicuous (Figs. 5A,B).
Discussion

To our knowledge, oral soft-tissue tumors that show features of both neurofibromas and lipomas have not been described previously. Since neurofibromas are not encapsulated, entrapment of the normal surrounding tissue can occur (1-4). Thus, it could be argued that, in this case, the fatty tissue was entrapped within a normal neurofibroma. This is unlikely for the following reasons: [1] palatal gingiva normally does not contain adipose tissue; [2] even if it were present, entrapment of the “native” fat would also be expected in the peripheral region and the regular distribution and large amounts of mature fat were very unusual; [3] no other entrapped structures, such as salivary glands were seen; [4] the neoplastic neural cells contained intracytoplasmic lipid droplets to varying degrees. For these reasons we concluded that the fatty tissue in our lesion was intrinsic to the structure. The adipose tissue is probably choristoma and, therefore, normal adipose tissue. However, in the case of choristoma tissue, lipid droplets do not occur in the cytoplasm of neoplastic neural cells. Thus this tumor may have been a lipomatous neurofibroma rather than a neurofibroma located within fat.

Differential diagnosis of this lesion included benign lipogenic tumors. Among the ordinary forms and variants of oral lipoma, fibrolipoma (9), myxolipoma (10) and spindle cell lipoma (11) have some common features with our case. In fibrolipoma fatty tissue is replaced by thick septa of richly collagenous fibrous tissue (9). However, unlike fibrolipoma, the spindle cells in the present neurofibroma exhibited a wavy nuclear contour and it was embedded in a more delicate, fibrillar collagenous, or loose mucinous, stroma. The scant areas of myxoid tissue in the present case are not features of myxolipomas (10).

Spindle cell lipoma is quite similar to our lesion histologically, and this made differential diagnosis difficult. Indeed, this case had been misdiagnosed preoperatively as a spindle cell lipoma. Spindle cell lipomas are often confused with neurofibromas (12). Spindle cell lipoma occurs most commonly in the head and neck region of older males and is characterized as a circumscribed lesion with varying combinations of five classic features: mature adipocytes, bland, wavy spindle cells, thick, ropy collagen bundles, mast cells and often myxoid changes (12). Neurofibroma, particularly the diffuse form that infiltrates normal fat, gives the appearance of having mature adipocytes as part of the lesion, and has the same features as spindle-cell lipoma (1,3,4.). Additionally, both tumors exhibit an overlapping immunoprofile including S-100 protein and CD34 immunoreactivity (12-15). However, in our lesion, the positive staining for other common neural markers and epithelial membrane antigens argues against this tumor being a spindle cell lipoma in an unusual site.

Other forms of combined nerve-lipomatous lesions have been described in the literature, and they include lipofibromatous hamartoma of the nerve (16), lipoma of the cranial nerve (17), and nodular neuronal hyperplasia (18). Moreover, a wide variety of other soft tissue tumors occasionally may show lipomatous features, for example, solitary fibrous tumors (19), angiomyofibroblastoma (20), angiomyofibroblastoma-like tumor (21), cellular angiofibroma (22), hemangiopericytoma (23), and sclerotic fibroma (24). Differential diagnosis of these tumors is easy because of their highly distinctive clinicopathologic features.

We are unaware of any other reports describing similar tumors except for a brief mention of one cutaneous neurofibroma with an unusual degree of fatty infiltration (25). The authors postulated that these features are most likely due to alterations in long-standing lesions. Such degenerative fatty changes are probably akin to those seen.
in leiomyoma of the uterus (26). However, this theory fails to explain satisfactorily the presence of fat cells in our neurofibroma, when we consider the patient’s age and the short duration of the condition.

In summary, we have described a case of oral, solitary neurofibroma with histologic features similar to those of spindle cell lipoma. Since the term neurofibrolipoma traditionally has been used for a neurofibroma that invades the surrounding fat (27), we have chosen to designate this lesion as a lipomatous neurofibroma to avoid confusion.

References

spindle cell lipoma. Am. J. Surg. Pathol. 22, 6-16