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Oral plexiform schwannoma: A case report and relevant immunohistochemical investigation

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Abstract

Schwannomas are benign peripheral nerve sheath tumors originating from the Schwann cells. Most schwannomas in the head and neck region are solitary; however, multiple schwannomas affecting one or more nerves suggest a possible association with neurofibromatosis type 2 and schwannomatosis. Plexiform schwannoma is a rare variant of conventional schwannoma that is characterized by intraneural multinodular growth. This grow pattern has also been observed with other neural tumors which may make diagnosis more difficult. Herein, we report the case of a 28-year-old woman who presented a solitary plexiform schwannoma of great palatine nerve. In the present case, we focused on immunohistochemical analysis in daily practice for the differential diagnosis of schwannomas and their mainly morphological mimics, especially with plexiform neurofibroma, granular cell tumor and malignant peripheral nerve sheath tumors. We also discussed on SMARBC1/IN1 marker usefulness in combination with brain magnetic resonance imaging for the distinction of solitary schwannoma from neurofibromatosis type 2 or schwannomatosis.

Keywords

Plexiform schwannoma, benign peripheral nerve sheath tumors, oral cavity, immunohistochemistry, INI1/SMARCB1

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Introduction

Schwannomas are benign peripheral nerve sheath tumors (PNSTs) composed exclusively of Schwann cells. They commonly arise from spinal nerve roots and intracranial nerves of the face. Only 1% of all schwannomas are located in the oral cavity.[1,2] Plexiform schwannoma (PS) is a rare histopathologic variant of schwannoma morphologically characterized by intraneural and multinodular growth.[2] This distinctive subtype of schwannoma is less circumscribed than conventional tumor, or even lack a capsule, which may make the diagnosis more difficult. PS was first described in 1978 by Harkin et al. as solitary and multiple lesions with 5% of reported cases being associated with neurofibromatosis type 2 (NF2) and schwannomatosis.[3] Less than 15 cases of this uncommon histopathologic variant in oral cavity have been reported in the English literature.[4–10]

We report a case of PS of the hard palate depending of the greater palatine nerve. The histological features are presented and we will discuss the usefulness of some immunomarkers in the differential diagnosis and the prognostication of PNSTs.

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Case presentation

A 28-year-old female presented to her private dentist with an asymptomatic slowly growing mass of the left hard palate that had appeared 3 years prior. Extraoral examination was normal. Intraoral examination revealed a well-defined, firm, fixed and sessile nodule, measuring 2.0 × 1.0 cm. The overlying mucosa was normal-appearing, smooth and pale pink. The mass was located adjacent to the left maxillary canine and the first and second premolars (Figure 1(a)). There were no regional lymph nodes, no report of local trauma and no parafunctional habits. The adjacent teeth showed no displacement, no dental decay or tooth mobility and had normal sensitivity, responding within normal limits to thermal and electric pulp testing. Intraoral periapical X-ray was normal. Axial cone-beam computed tomography images showed a radiolucent notch on the palatal aspect of the maxilla at the level of the dental roots. The margins of this radiolucent defect were shown well-defined by a cortical bone outline (data not shown). The main differential diagnoses include focal fibrous hyperplasia, benign soft-tissue neoplasms, peripheral odontogenic tumors and minor salivary gland tumors.

Surgical excision of the whole lesion was performed under local anesthesia. Gross examination showed a multinodular and un-encapsulated tumor (Figure 1(b)). Microscopic examination revealed well-circumscribed nodules predominantly composed of compact spindle cells (Antoni A pattern). Scarce hypocellular and myxoid areas compatible with an Antoni B pattern were also identified. Higher magnification highlighted the presence of Verocay bodies in areas with Antoni A pattern. In areas with Antoni B pattern, hyalinization of the walls of blood vessels was noticed (Figure 2(a)–(d)). Neoplastic cells exhibited diffuse and strong staining for S100 and SOX-10 (Figure 3(a) and (b)). Focal staining for CD34, neurofilament (NFP) and CD117 (c-kit) was also noted (Figure 3(c)–(e)). Immunostaining was negative for desmin, vimentin, epithelial membrane antigen (EMA) and bcl-2 (data not shown). Mitotic activity was low (less than four mitoses per 10 high-power fields) and tumor cells had a low Ki-67/MIB-1 labeling index (Figure 3(f)). Moreover, these tumor cells strongly expressed INI1/SMARCB1 (Figure 3(g)).

Full physical examination and magnetic resonance imaging (MRI) of the head and neck region were performed in order to investigate signs or symptoms in favor of neurofibromatosis and were normal (data not shown). Furthermore, no family history of skin or oral mucosa nodules was reported. In the light of these findings (clinical evolution, histology, immunohistochemistry (IHC) and the imaging data), the lesion was diagnosed as solitary PS arising from the greater palatal nerve.

The patient was followed up carefully twice a year, without evidence for local recurrence 5 years after surgery.

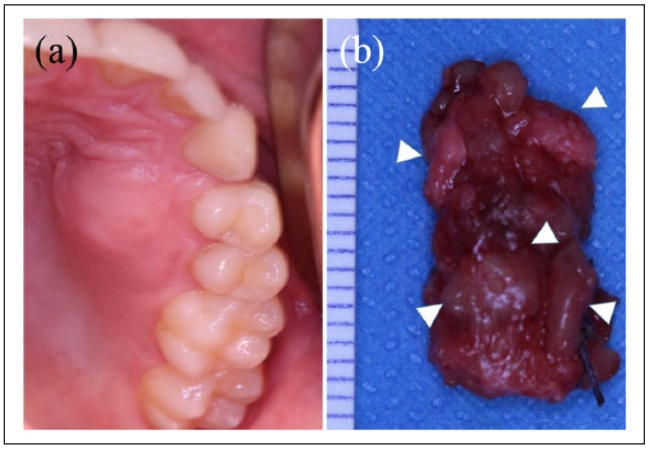

Figure 1. Clinical and macroscopic features. (a) Mass of the hard palate. (b) Macroscopic view of the multilobulated lesion (white arrowheads) removed from the hard palate. The tumor measured 2.0 × 1.0 × 0.7 cm.

Discussion

IHC is a key tool for the diagnosis of PNSTs. Thus, immunohistochemical analysis was performed with a large panel of antibodies. Currently, the most commonly used IHC markers for the diagnosis of schwannomas are S-100 and SOX-10. S-100 and SOX10 expressions are also reported in neurofibroma, malignant peripheral nerve sheath tumors (MPNSTs) and granular cell tumor, but with less uniform patterns than in schwannoma.[2,6,11]

We have also used other markers for discerning schwannoma from other PNSTs, but these markers have low information value because their expression variability is case-dependent. Here, the neural tumor was CD34, NFP and c-kit positive (mainly in Antoni B area) and negative for EMA, confirming the lack of the peripheral capsule surrounding the lesion.[2,12] Recent studies have suggested that podoplanin and calretinin might also be helpful markers for differentiating neurofibromas from schwannomas.[2,12,13] However, due to a lack of specificity, these markers are currently used as part of multi-antibody panels. In contrast, schwannomas are always negative for desmin, vimentin and bcl-2, allowing the exclusion of other benign soft-tissue tumors, such as leiomyomas, granular cell tumors and solitary fibrous tumors.[1,2]

MPNSTs can also exhibit a plexiform pattern.[2] Ki-67/MIB-1 labeling indices ⩾20% or complete loss of S-100 and/or SOX10 immunoreactivity were highly predictive of MPNSTs with high sensibility and specificity.[2] In the present case, a low mitotic activity (less than four mitoses per high-power fields) with an index of proliferation Ki-67/MIB-1 <5% and high S-100 protein and SOX10 expressions were in favor of a benign tumor.[2]

The present case report also highlights the importance of IHC in differentiation between solitary peripheral schwannomas and syndromic schwannomas. Most schwannomas present as solitary tumor, although some patients present with multiple synchronous or metachronous lesions. Multiple schwannomas is one of the major criteria for the diagnosis of

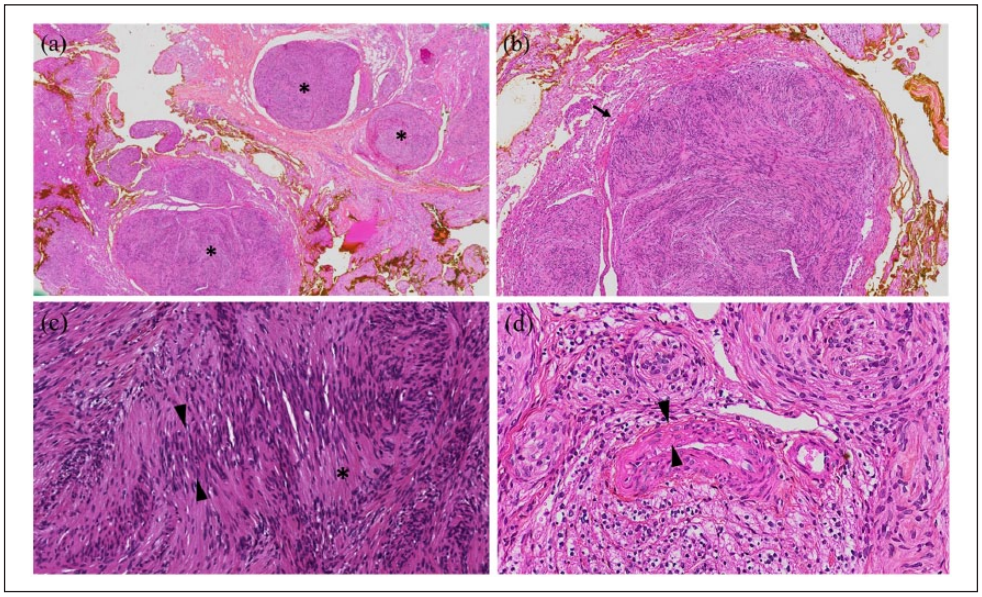

Figure 2. Histological analysis. (a) Unencapsulated tumor composed of multiple round and oval nodules (black asterisk) within the connective tissue. (Hematoxylin and eosin (H&E), magnification ×10). (b) The nodules were surrounded by a thin fibrous capsule (black arrow). The tumor was predominantly composed of areas with compact spindle cells (Antoni A tissue). Antoni B tissues (paucicellular area) are infrequent (H&E, magnification ×66). (c) In Antoni A tissues, Verocay bodies were found (black asterisk), formed by alternating rows of palisading nuclei (black arrowheads) and intervening nuclei-free stroma. Spindle neoplastic cells had wavy and tapered nuclei, elongated eosinophilic cytoplasm and no discernible cell membrane (H&E, magnification ×200). (d) Near Antoni B tissues, blood vessel walls (black arrowheads) were thickened and hyalinized (H&E, magnification ×200) (Product Version Olympus VS ASW 2.9).

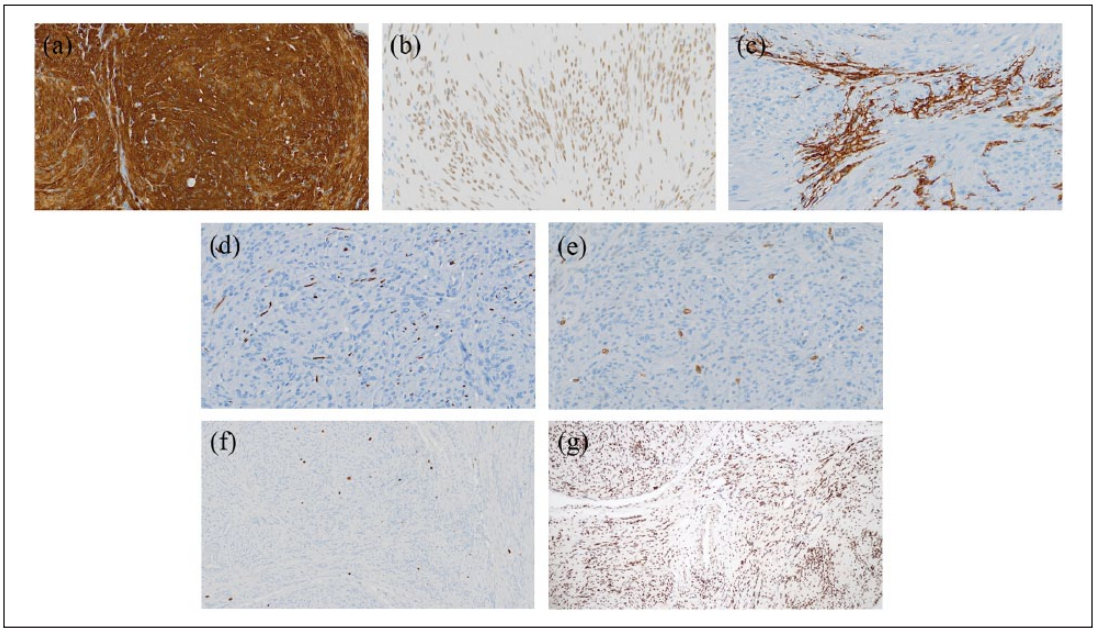

Figure 3. Immunochemistry analysis. (a) Neoplastic cells (both nucleus and cytoplasm) were strongly immunoreactive for S-100 protein (PS100, magnification ×200). (b) Neoplastic cells showed positive nuclear SOX-10 reactivity (SOX-10, magnification ×200). (c) The cytoplasm of neoplastic cells was strongly reactive with CD34, only in areas with Antoni B pattern (CD34, magnification ×200). (d) Neurofilament protein immunoreactivity (NFP) revealed the occurrence of residual axons within tumor nodules (NFP, magnification ×200). (e) Scattered c-kit positive cells were observed in the periphery of nodules and near blood vessels (c-kit, magnification ×200). (f) Ki67 /MIB-1 labeling index was heterogeneous and weak (<5%) showing a low risk of malignant transformation (Ki67/MIB-1, magnification ×100). (g) INI1/SMARCB1 nuclear immunostaining positivity was diffuse (the expression was retained in more than 90% of neoplastic cells) suggesting a solitary peripheral schwannoma (INI1/SMARCB1, magnification ×100) (Product Version Olympus VS ASW 2.9).

NF2 or schwannomatosis. The tumor suppressor genes SMARCB1 or LZTR1 on chromosome 22, adjacent of the NF2 locus, are predisposing genes to the development of schwannomas in schwannomatosis. SMARCB1 mutations were initially described in childhood malignant rhabdoïd tumors. SMARCB1 mutations have also been found in 40%–50% of familial schwannomatosis and less than to 10% of sporadic schwannomatosis. The inactivation of the gene causes a loss of expression of the protein in the tumor cells. Caltabiano et al.[14] have recently demonstrated that solitary peripheral schwannomas and NF2-associated vestibular schwannomas retained the immunohistochemical expression of INI1/SMARCB1 in 97%–100% of neoplastic cells, while those associated with schwannomatosis showed a mosaic pattern ranging in 10%–70% of neoplastic cells. Loss of nuclear INI1/SMARCB1 protein expression is therefore a reliable marker of schwannomatosis regardless of the involved gene (SMARCB, LTZR1, NF2).[14] In the present case, neoplastic cells were uniformly positive for INI1/SMARCB1 which was not in favor of a schwannomatosis.

In addition, NF2 is characterized by the bilateral occurrence of vestibular schwannomas of the eighth cranial nerve. Here, physical examination and MRI of the head and neck ruled out NF2. Recent studies have shown that whole-body MRI can provide a significant advantage for the detection other lesions that may be missed with localized MRI.[15]

The treatment of choice for solitary schwannomas is conservative surgical excision.[2] Although PS is a benign tumor with no malignant potential, a periodic follow-up is essential (at least 2 years) for the early detection of recurrence.[3] Local recurrences may occur after incomplete surgical resection,[3,4] multiple nodules,[6] intraosseous location[1] or in case of malignant transformation.[2] Bony erosion has no prognostic relevance.[1] No evidence of recurrence was noted after 5 years of follow-up, supporting the fact that the lesion had been completely removed during the surgical procedure.

Conclusion

Oral schwannomas are usually indistinguishable from other benign soft-tissue tumors of the oral mucosa based on clinical and imaging findings. Final diagnosis should be done after histopathological examination and in unusual cases after immunohistochemical analysis. INI1/SMARCB1 IHC should be systematically performed when NF2 or schwannomatosis was suspected.

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