CASE REPORT

Schwannoma of the lip: case report and review of the literature

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Abstract

Schwannomas of the lip are rare, benign neoplasms which vary in size. The diagnosis is typically made at the time of surgery following biopsy and surgical resection is the mainstay of treatment. We present one case of lip schwannoma: the patient was 25-year-old and he has presented to otorhinolaryngologist for a non-dolorous tumor on the mucosal side of his inferior lip, which was increasing in size for the last six months. The tumor had a superficial ulceration and infection. Initially it was suspected to be a papilloma. The tumor was radically removed, and the sections were stained with Hematoxylin–Eosin. The tumor was encapsulated and showed two different pattern of growth. Antoni A areas displayed spindle cells closely packed together with palisading of nuclei. Verocay bodies, which were presented in Antoni A areas, are whorled formations of palisading tumor cells. The cells of neoplasm were monotone. Only few spindle cells were moderately pleomorphic, but mitotic figures were unusual. In addition, immunohistochemical labeling was performed for S-100 protein, vimentin, GFAP and NSE and confirmed the diagnosis. This report describes a case of lip schwannoma, which was correctly diagnosed by routine staining and confirmed by immunohistochemical staining for S-100 protein, vimentin, GFAP and NSE.

***Keywords*:** schwannoma, neurilemmomas, neurinoma, immunohistochemistry, S-100, vimentin.

Introduction

The neurilemmoma (schwannoma) is a neurogenic benign tumor that arises from the Schwann cells of the nerve sheath, as both microscopy and immunohistochemistry have established. There is a large variety of terms for schwannomas in the literature, but only three are still in current use: neurinoma, neurilemmoma and schwannoma [1]. Schwannomas are relatively uncommon benign, slow-growing, encapsulated tumors that typically arise in association with a nerve trunk and as it grows it pushes the nerve aside [2]. It may arise from cranial and spinal nerve roots or from peripheral nerves, but has a predilection for sensory nerves [1]. Almost 25–48% of all schwannomas occur in the head and neck region but the development of this tumor in mouth is quite uncommon representing only 1% of all head and neck region tumors [3]. Other common sites include the flexor surface of upper and lower extremities and less often the mediastinum and peritoneum [4]. On occasion, the tumor can arise centrally within bone and may produce bone expansion. Intraosseous examples are most common in the posterior mandible and usually appear as either unilocular or multilocular radiolucencies on radiographs. Pain and paresthesia are not unusual for intraosseous tumors [2].

The tumor can arise at any age but is most common in young and middle-aged adults without a gender predilection [1, 2].

Material and methods

We present a 25-year-old patient with a tumor of the lip. The patient was Caucasian, non-smoker and was admitted in the Otorhinolaryngology Department of the Emergency County Hospital, Timisoara. The tumor was a mucosal lesion, involving left area of the inferior lip. His medical and family history showed no instance of neurofibromatosis and failed to indicate the presence of other central nervous system tumors. He had no known history of medical illness. On physical examination, a whitish bulging mass on left side of the mucosal part of inferior lip was seen, and normal facial function was noted.

At the time of diagnosis, the patient took no medication. His general conditions were satisfactory and his routine blood and urine tests were normal. The thorax radiogram was normal.

Clinical observations came from the original records of the patient, with emphasis on symptoms that brought his to doctor. The primary anatomic site of the tumor, the absence of the pigmentation, the configuration of the tumor and the absence of satellite lesion were noted.

The pathologist complemented these data with the macroscopic and microscopic description.

Specimens

Samples were obtained from fresh surgical specimens of a lip mass after enucleation. Specimens were fixed in 4% w/v buffered formalin, embedded in paraffin. Histological sections, 4 μm thick, were routinely stained with Hematoxylin–Eosin (HE).

Immunohistochemistry

The diagnosis of schwannoma was confirmed using monoclonal antibodies against vimentin, S-100 protein, NSE and GFAP.

Immunohistochemistry was done on formalin-fixed, paraffin-embedded tissue specimens, using the three steps labeled streptavidin–biotin-immunoperoxidase technique (LSAB2, code K0673, DAKO, Denmark).

Sections were dewaxed, rehydrated, washed in distilled water, and then rinsed in PBS (pH 7.2).

Sections were incubated with 3% hydrogen peroxide solution for 5 minutes (step 1, peroxidase block), washed twice with PBS.

After endogenous peroxidase inhibition and antigen retrieval, the sections were incubated with the primary antibodies.

Anti-S-100 antibody (polyclonal, code N1573, ready-to-use) identified S-100 positive cells from normal and neoplastic tissues and was used for the differential diagnosis of melanomas or nerve sheath tumors versus carcinomas. S-100 is a 20–30 kDa calcium binding protein which occurs in three dimeric forms: S-100ao, S-100a and S-100b composed of αα, αβ and ββ subunits. It is expressed by glial cells, neurons, Schwann cells, melanocytes, Langerhans cells and interdigitating reticulum cells.

Formalin-fixed, paraffin-embedded tissues were incubated for 10 minutes at room temperature with the primary S-100 antibody. The negative control reagent used for LSAB2 was Universal Negative Control, Rabbit (code N1699).

Anti-vimentin (clone V9, code N1521, ready-to-use) antibody has been shown to react specifically with the intermediate filament vimentin of molecular mass 57 kDa. Vimentin is one of several intermediate filaments (cytokeratins, desmin, glial fibrillary antigen and others) and occurs primarily in mesenchymal cells, such as fibroblasts, chondrocytes, endothelial cells and vascular smooth muscle cells, where it may be the sole intermediate filament or coexist with other intermediate filaments.

In normal tissue, it has been demonstrated the distribution of vimentin with V9 in most normal mesenchymal cells such as fibroblasts, smooth muscle cells, adipocytes, peripheral nerve (Schwann) cells, vascular endothelial cells, macrophages (including Kupffer cells), as well as myoepithelial cells of sweat and salivary glands and of breast. The cellular vimentin distribution and staining intensity were more variable in the follicular epithelium of the thyroid, adrenal cortex, renal distal tubular epithelium, and mesangial and endothelial cells of the renal glomerulus, as well as in pancreatic acinar cells. Some large lymphocytes also showed cytoplasmic immunoreactivity. It was used as a marker of the optimal fixation and embedding procedures. Monoclonal mouse anti-human vimentin, clone V9 may also serve as an internal control to monitor any antigenic damage suffered by formalin sensitive epitopes on otherwise diagnostically useful molecules.

V9 reacted positively with many melanomas, meningiomas, schwannomas, and sarcomas. Variable V9 positivity (10–57%) has been reported in some mesotheliomas, large cell lymphomas and pleomorphic adenomas, adenocarcinomas, squamous cell carcinomas, small cell undifferentiated carcinomas, carcinoids, paragangliomas, thymomas and neuroblastomas, especially when the tissue was fixed in formalin instead of ethanol.

Formalin-fixed, paraffin-embedded tissues were incubated for 10 minutes at room temperature with the primary antibody. Pretreatment for epitope retrieval is not required. The negative control reagent used for LSAB2 was Universal Negative Control, Rabbit (code N1698).

Monoclonal Mouse Anti-Human Neuron Specific Enolase (NSE, clone: BBS/NC/VI-H141, code N1557, ready-to-use) are homo- or heterodimeric enzymes that catalyze the reaction pathway between 2-phospho-glycerate and phosphoenolpyruvate in the terminal step of anaerobic glycolysis. They are dimmers composed of two of three possible subunits, alpha, beta and gamma. The dimer, NSE, or gamma, gamma-enolase is present in high concentrations in both neuronal and neuroendocrine cells and tumors derived from them. It is also present in non-nervous system tissues such as smooth muscle.

Anti-NSE, H14 reacted with gamma-subunits (46 kDa) of enolase in neurons of the cerebral cortex, brainstem nuclei, in neuronal cytoplasm and processes, in a 1:1 ratio for each gamma-subunit. Because of the staining of numerous neuritic extensions, the cortex and white matter presented a diffuse staining at low magnification. Ganglion cells in the gastrointestinal tract, myelinated and unmyelinated nerve fibers and APUD cells also stained. It did not react with the alpha- or beta-subunit.

Anti-NSE, H14 was shown to stain reactive astrocytes near tumors as well as abnormal astrocytes of tumors of different grades. In mixed tumors (e.g. gangliogliomas), ganglionic cells stained more intensely than the astroglial component. Tumor cells of meningiomas were also frequently reactive with this antibody. Anti-NSE, H14 was also found to be useful in the study of small-cell carcinomas of the endometrium. Abnormal tissue found to be non-reactive for the gamma-subunits of NSE were squamous cell carcinomas, large cell anaplastic carcinomas and adenocarcinomas, neurofibromas, intraductal carcinomas, and lung and large bowel carcinomas.

Formalin-fixed, paraffin-embedded tissues were incubated for 10 minutes at room temperature with the primary antibody. Pretreatment for epitope retrieval is not required.

Monoclonal mouse anti-human Glial Fibrillary Acidic Protein (Clone 6F2, Code M 0761) is an IgG, which labels glial fibrillary acidic protein (GFAP) and may be a useful tool for the identification of astrocytes and astrocytic cells under normal and pathological conditions, staining being confined to the cytoplasm. Differential identification is aided by the results from a panel of antibodies. A qualified pathologist must make interpretation within the context of the patient's clinical history and other diagnostic tests.

GFAP is a 50 kDa intracytoplasmic filamentous protein that constitutes a portion of the cytoskeleton in astrocytes, and it has proved to be the most specific marker for cells of astrocytic origin. In the central rod domain of the molecule, GFAP shares considerable structural homology with the other intermediate filaments. Functionally, GFAP is thought to be important in astrocyte motility and shape by providing structural stability to astrocytic processes.

Following injury to the human CNS caused by trauma, genetic disorders, or chemicals, astrocytes proliferate and show extensive hypertrophy of the cell body and processes, and GFAP is markedly upregulated. In contrast, with increasing astrocyte malignancy, there is a progressive loss of GFAP production. Thus, malignant astrocytomas have fewer tumor cells that stain positively and intensely for GFAP than do less malignant astrocytomas and normal brain specimens. Outside the CNS, sensitive detection methods may demonstrate GFAP in Schwann cells, enteric glial cells, salivary gland neoplasms, and metastasizing renal carcinomas. Additionally, GFAP has been demonstrated in epiglottic cartilage, pituicytes, immature oligodendrocytes, papillary meningiomas, and myoepithelial cells of the breast.

GFAP was used at a dilution of 1:50, with 20 minutes heat-induced epitope retrieval in DakoCytomation Target Retrieval Solution (code S1700) and 30 minutes incubation at room temperature with the primary antibody. The negative control used was DakoCytomation Mouse IgG1 (code X0931) diluted to the same mouse IgG concentration as the primary antibody. All reagents have been diluted immediately before use. Positive and negative controls have been run simultaneously with patient specimen.

After incubation with the primary antibody, the slides reacted with a labeled streptavidin–biotin system and then treated with 3,3'-diaminobenzidine as peroxidase substrate solution, or chromogen (DAB Tablets, S3000) until color was visualized.

Sections were washed twice in distilled water for 5 minutes to stop the reaction, then counterstained in Hematoxylin for 5 minutes, washed, dehydrated, cleared in xylene, mounted with DPX, and glass cover-slipped. All reagents for the immunohistochemical technique were supplied by DAKO, Denmark.

Sections were examined under oil immersion with a ×100 objective on a Nikon Eclipse E–400 microscope, and images were captured using a Coolpix 995 digital camera and a DN–100 digital imaging system.

Histological sections were reviewed independently by two pathologists, and then discussed for consensus.

Results

The patient, aged 25, presented to the outpatient otorhinolaryngologic ward of our hospital on January 2008.

His main complaint was the presence of a mass on mucosal side of his inferior lip that had been increasing in size for six months. He did not present any other symptoms. On a routine examination, the otorhinolaryngologist found a light grey tumor, involving the inferior lip. A small, painless and slow-growing swelling represented the tumor. The otorhinolaryngologist observed that the lesion of the lip was not pigmented. The lesion, 10×10×10 mm in size, was irregular, vegetative, indurate, tender and ulcerated (Figure 1). No adenopathy was present.

A clinical diagnostic hypothesis of papilloma was put forward.

The patient underwent surgery, which removed the whole tumor mass with a 2 mm normal tissue, in order to decide the specific treatment plan. The tumor was removed without complications. The specimen was sent for histopathological examination. The patient did not have any problem during the postoperative period. The tumor was immediately fixed in 10% v/v buffered formalin and sent for histopathological examination.

Gross pathology

The resected specimen was represented by a well-demarcated solitary tumor measuring 1.0 cm in greatest dimension. The tumor had a tan to pale yellow, lobulated cut surface. Compressed residual lip parenchyma was noted at the periphery of the tumor. The tumor was well circumscribed with smooth borders and had a surrounding fibrous capsule.

Visual inspection of the biopsied specimen, 15×15×12 mm in size, showed the presence of a grey-white vegetative mass, 10×10×8 mm in size. The mass was lined by an eroded oozy mucosa covered by a yellowish slime, had a solid, rather homogeneous grey to white cut surface, was lobulated and lined by a grayish pseudomembrane made up of fibrin and remains of the ulcerated squamous epithelium.

The slides from all tissue fragments were stained with Hematoxylin–Eosin.

Light microscopy

Scanning magnification discloses a raised, dome-shaped tumor, ulcerated on large area. Histologically, the tumor exhibited morphologic features typical of a conventional schwannoma (Figure 2), characterized by a proliferation of spindle cells with uniform cellularity, including cellular Antoni A areas, hypocellular Antoni B areas (Figure 3), and ectatic thick-walled blood vessels.

The tumor was well demarcated from the uninvolved parenchyma by a fibrous capsule and surrounded by a peripheral subcapsular cuff of lymphoid aggregates. The majority of tumor cells displayed elongated, slightly wavy nuclei with evenly dispersed chromatin and tiny nucleoli, with ill defined, lacy cytoplasmic borders. However, scattered tumor cells showed degenerative nuclear atypia characterized by nuclear

enlargement with hyperchromasia and smudging of the chromatin. The spindle cells were arranged in sheets, fascicles, and small whorls. The neoplastic cells were spindle shaped with cytologically bland nuclei. The tumor cells were disposed in short interlacing fascicles or randomly arranged in a loose collagenous matrix. Nuclear palisading was observed in focal areas, well-formed Verocay bodies being identified (Figure 4). Antoni B areas, probably a degenerated form of the Antoni A pattern, showed a loose reticular pattern, with histiocytic proliferation in some areas.

The tumor was associated with a moderate inflammatory infiltrate composed by small lymphocytes, neutrophils and eosinophils. The infiltrate was characterized by patchy nodular aggregates throughout the substance of the tumor in addition to diffuse infiltrates present along the periphery of the neoplasm. Collections of small lymphocytes were scattered throughout the tumor. Hyalinized blood vessels were observed in some areas. The tumor presented no mitotic activity or necrosis.

The overlying epithelium was thin, effaced, and ulcerated on large area, being replaced on large areas by necrosis, due to the neutrophils influx and presence of the bacteria. At this level, fibrin deposits and inflammatory exsudate were present. The blood vessels were enlarged and the connective tissue presented edema with fluid exudates. The surrounding tissue formed inflammatory granulation tissue about the area of necrosis. The all area was expanded by a dense infiltrate of cells, mostly neutrophils, and a few large mononuclear cells, probably macrophages. The cells were localized within a meshwork of fine threads, probably fibrin. The blood vessels were dilated. The underlying space was occupied by tumor proliferation.

Immunohistochemical findings

The immunoreaction for vimentin was positive, with a strong and diffuse pattern of distribution (Figure 5). The reaction for vimentin was heterogeneous. There were some differences between areas, the reactivity of vimentin immunolabeling decreasing from strongly to weakly positive toward cluster cells. A weaker labeling for vimentin was found mostly in Antoni B areas compared with Antoni A areas. However, the strongest vimentin staining was generally found in the palisading cells of Verocay bodies.

In addition to the diffuse expression of vimentin, the tumor cells also displayed positive immunoreactivity for S-100 protein. The S-100 protein immunolabeling of the tumor cells had a cytoplasmic and nuclear pattern and was more intense than the vimentin labeling. The immunoreaction was homogenous in all tumor areas. All tumor cells presented an intense labeling for S-100 protein (Figure 5).

Even if the intensity of reaction was almost uniform in the tumor cells, there was some small variation of intensity, the spindle cells areas being slightly more positive than myxoid areas. The tumor cells were negative for NSE, even if only few tumor cells presented a granular cytoplasmic positive reaction, mostly with a perinuclear pattern of distribution. As we expected, there was no evidence of positive immunoreaction for GFAP in tumor cells. All these findings supported the diagnosis of benign conventional type schwannoma.

Discussion

Verocay described in 1910 a group of neurogenic tumors and he named them as neurinomas [5]. It was proposed later, in 1935, another term for these tumors: neurilemmomas [6]. In the literature, there is an abundance of terms under which these tumors have been reported but only three are still used: neurinoma, neurilemmoma and schwannoma [1].

The head and neck region is a frequent site for schwannoma as 25–48% of all schwannomas are described here, but mouth is quite an uncommon site for development of schwannoma, responsible for only 1% of all head and neck region tumors [2]. At this level, schwannomas are commonly identified in the mobile position of the tongue, the palate, the cheek mucosa and the lip, with tongue being by far the most common site [4]. One study, in consensus with other authors, reported 146 cases of oral cavity schwannoma, from which 52% occurred in the tongue, 20% in the buccal or vestibular mucosa, 9% in the soft palate and 19% were in the gingiva and lip [7, 8]. Our case has a special localization, because the lip is an uncommon occurring site for schwannomas.

Schwannomas may arise from any peripheral, cranial or autonomic nerve, which has a Schwann cell sheath [9–14]. In the head and neck region, they arise medially from the last four cranial nerves: glossopharyngeal, vagus, accessory and hypoglossal or the sympathetic chain and laterally from the cervical or branchial plexus [15].

Schwannomas have a predilection for the sensory nerves, especially for the eighth cranial nerve [1], but a motory nerve can also be affected - the facial nerve is most frequently involved, how was probably in our case [1]. Schwannomas of the hypoglossal nerve are very rare and they are seldom found in the sublingual space [8]. Although schwannomas originate from the nerve tissue, a direct relation with a nerve can be demonstrated only in 50% of cases [4]. In our case, on slides, there was no relationship between nerves and tumor cells.

The etiology is still unknown and the tumor is generally asymptomatic [3]. Schwann cell tumors can remain quiescent for a long period and sometimes they are found incidentally [15]. The usual presenting symptom is a gradually enlarging mass [15]. Pain and neurological symptoms are uncommon, unless the tumors become larger or if they invade submucosal areas, those leading to pain and discomfort. If the schwannoma involves the tongue, it may include symptoms like dyspnea or dysphagia [3].

Our patient was asymptomatic, and he presented to hospital for a growing, painless mass on his lip, which become larger creating discomfort, without any other symptoms like pain, anesthesia, paresthesia, hyperesthesia or hypersalivation.

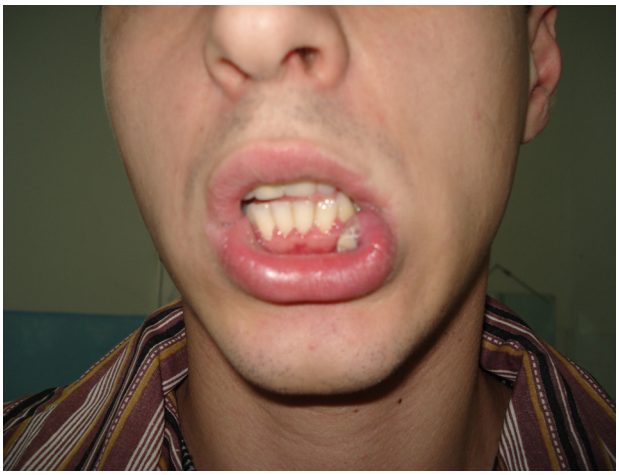

Figure 1 – ***The whitish, small swelling on the lower lip***

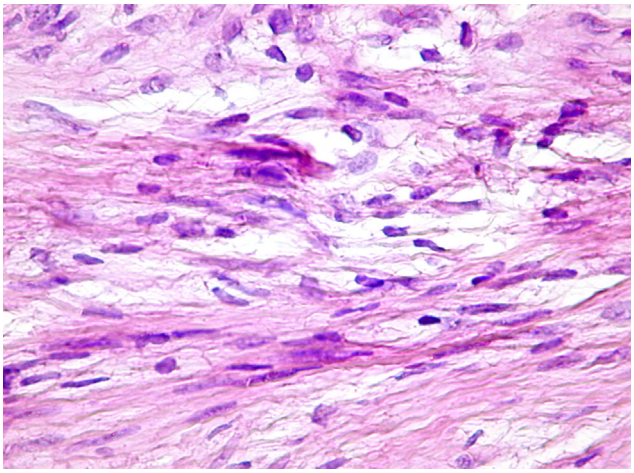

Figure 2 – ***Hypercellular areas (Antoni A) composed of interlacing spindle cells (HE, ob. ×40)***

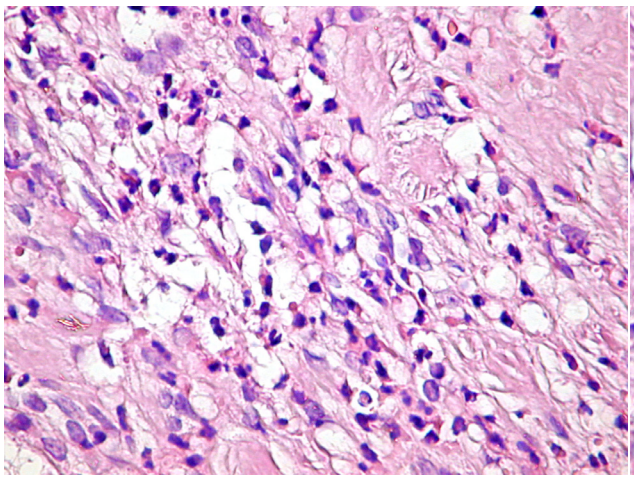

Figure 3 – ***Myxoid pattern of Antoni B areas (HE, ob. ×20)***

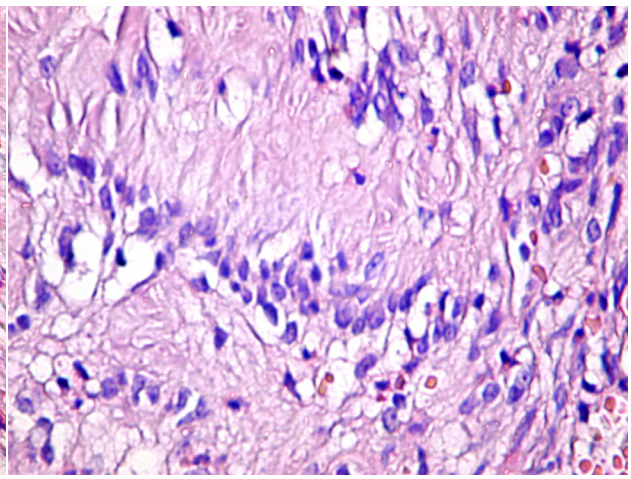

Figure 4 – ***Verocay bodies with the nuclei arranged in a palisading fashion (HE, ob. ×10)***

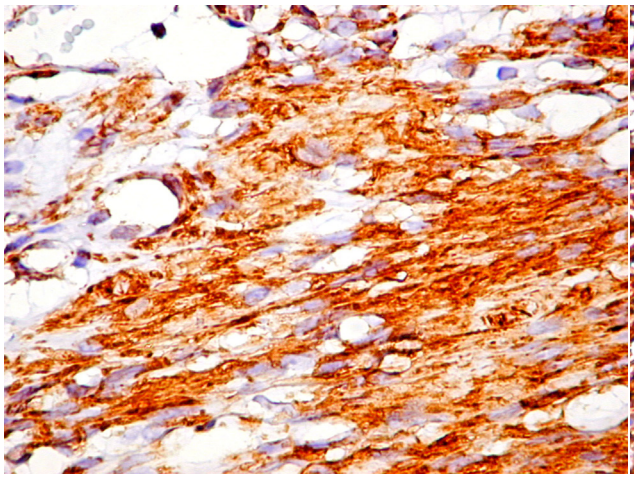

Figure 5 – ***Heterogeneous reaction for vimentin, with Antoni A areas more positive than Antoni B areas (ob. ×40)***

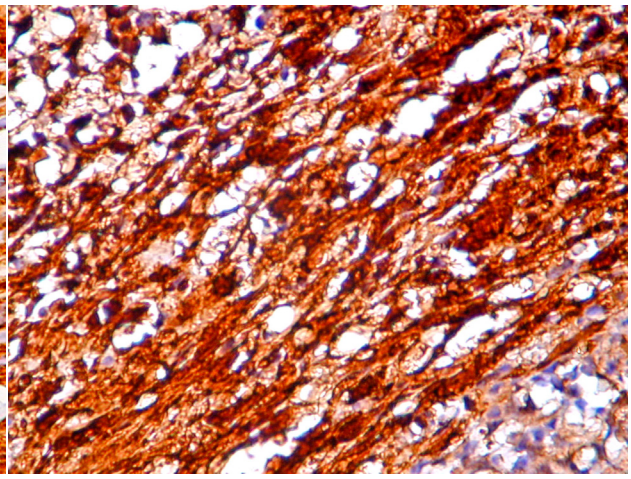

Figure 6 – ***Immunohistochemical stain with S-100 protein antibody shows that the tumor cells are diffusely and strongly positive (ob. ×40)***

There are examples of tumors that arise from the mandibular nerve within the mandible bone, which can display pain and paresthesia [1, 2]. Grossly, schwannomas are surrounded by a true capsule consisting of epineurium, which was also found in our case [2, 4].

On cut surface, the tumor has smooth, glistening, pink, grey-white or yellowish surface; cystic areas and foci of hemorrhage and calcification can also be found. They are variable in size, from a few millimeters to several centimeters, usually less than 5 cm in size. Mediastinal and retroperitoneal tumors are larger,

with more cyst and calcification [2, 4]. Similar with what other authors described, in our case, the tumor had a white-grayish, lobulated cut surface, 10 mm in size in the largest diameter, but there were no evidence of cystic areas, hemorrhage or calcification. Instead, the overlying epithelium was ulcerated and covered by fibrin deposits and collections of granulocytes.

The schwannoma is usually a solitary tumor, or it is associated with von Recklinghausen syndrome and it starts as a capsulated nodule that grows slowly [3]. It may develop at any age but is most common in young and middle-aged adults [2].

Our patient was young, in his twenties, and his main complain was a slowly growing tumor on his lower lip. There were no "café au lait" spots so we consider that tumor as a solitary one, not associated with von Recklinghausen disease.

There is no gender predilection, although there are studies that report a higher incidence of schwannoma in the female population, while others show a male slightly predominance [16].

Microscopically, schwannomas can present two patterns: Antoni type A areas and Antoni type B areas. The Antoni type A areas consists of spindle-shaped Schwann cells fascicles that often form a palisade arrangement around central acellular, eosinophilic areas known as Verocay bodies. Antoni type A zone has parallel formed thin reticulin fibers, fusiform shaped cells and curled nuclei. Antoni type B region is less cellular and less organized. The spindle cells are randomly arranged within a myxomatous stroma [2, 3].

In our case, the inspection of the morphological stained slides revealed all the aspects needed to diagnose a conventional type schwannoma, with both Antony A areas of spindle cells fascicles intricate with more myxoid pattern of Antony B areas, and the presence of Verocay bodies in some hypercellular zones of the tumor.

Immunohistochemically, schwannomas show an intense and relatively uniform staining for S-100 protein, a neural-crest marker antigen, present in the supporting cells of the nervous system. Although it is an important tool for the diagnosis, in malignant schwannomas it may be reactive in only up to half of cases [9]. The cells also express Vimentin, Leu 7 antigen and GFAP, the glial fibrillary acidic protein [19]. In respect with these, in our case, there has been immunohistochemically identified an intense positive response for anti-S-100 protein and anti-vimentin antibodies, but the immunoreaction was heterogeneous, the immunolabeling of the Antony A areas being more intense than myxoid cells of Antony B areas. If we compare the intensity of immunolabeling between these two antibodies, we can admit that the immunoreaction for S-100 protein was more diffuse and more intense than for vimentin. As we expected, anti-NSE and anti-GFAP labeling was negative in most tumor cells, but there were a few cells which presented a granular cytoplasmic positive immunoreaction for anti-NSE antibodies.

Generally, the most common differential diagnosis includes fibroma, neurofibroma, granular cell tumors, lipoma, leiomyoma, rhabdomyoma, neurosarcoma, ganglion cyst, giant cell tumor of tendon sheath [1, 19]. In our case, the architectural aspects of tumors were patognomonic for the conventional type schwannomas so that no differential diagnosis was necessary, the additional immunohistochemical reactions were only useful for the immunophenotypisation of the tumor and for the comparison of the own obtained data with other similar data published in the recent literature.

There are variants of benign schwannomas such as plexiform or multinodular schwannoma, cellular schwannoma, Wagner–Meissner schwannoma, granular cell schwannoma and nerve sheath myxoma-neurothecoma [20, 21], but in this study, we present a conventional type schwannoma with mixed pattern of Antoni A and Antoni B areas and well formed Verocay bodies.

In large tumors, the connective tissue stroma may be more abundant and have dense bands of hyalinised collagen disrupting the cellular pattern. Degenerative changes can be seen consisting of hemorrhage, hemosiderin deposits, inflammation, fibrosis and nuclear atypia [1, 2].

We did not note any hemorrhage or necrosis, but inflammation and fibrin deposits were identified and a few cells presented nuclear atypia. The degenerative changes have been interpreted as a sign of aging: ancient schwannomas.

We personally cannot support this affirmation, because our patient had a short history of only six months of slow growing tumor. Patchy calcification may also occur. However, these tumors are still benign and should not be mistaken for evidence of sarcoma [1, 2]. Even if a few atypical cells and an ulceration of the overlying epithelium were present we can confirm the benignity of the tumor.

Ackerman LV and Taylor FH first described ancient schwannoma in the thorax in 1951 [22]. This lesion had both Antoni A and Antoni B pattern, pleomorphic nuclei, often hyperchromatic, with mitotic figures and area of hemorrhage. Redman RS *et al.* [20] also reported a case of schwannoma different from the classical type, with an increased cellularity, nuclear pleomorphism and hyperchromasia, which lacked Verocay bodies and had a frequently higher mitotic activity.

Isolated schwannomas hardly ever become malignant but when multiple, they can be associated with neurofibromatosis and a large percentage of patients with neurofibromatosis will present malignant transformation in one or more lesions, contrary to schwannoma [8].

The differentiation between schwannoma from neurofibroma is essential because apparently "solitary" neurofibroma may be a manifestation of neurofibro-matosis [8].

Schwannomas and neurofibromas share a common precursor: the Schwann cell. An interesting report suggested that some nerve sheath tumors might contain components of both neurofibroma and schwannoma in the same specimen. This might explain the confusion in the past between the two tumors [9].

Solitary neurofibromas are relatively uncommon in the orofacial region and tend to affect people in the 20–40-year-age group. They usually form small, painless, expansive submucosal nodule. The tongue is the most common intraoral site, but occasionally they develop on the inferior dental nerve and appear as a fusiform radiolucent area along the course of the inferior dental canal [23]. On the CT, schwannoma appears as a well-circumscribed attenuated homogenous soft-tissue mass that exhibits contrast enhancement. Magnetic resonance images are isointense or hypointense relative to muscle on T1-weighted and hyperintense on T2-weighted images with strong enhancement after contrast administration [24]. MR imaging is superior to other imaging modalities for examination on the base of the tongue [3].

The treatment of a benign solitary schwannoma is enucleation. Although the first diagnostic opinion of the otorhinolaryngologist was a papilloma, during the operation she observed that the tumor was very well encapsulated and she could enucleate it very easy. Being a benign lesion all efforts have to be made to preserve the nerve of origin. In our case, the surgeons did not observe any relationship with the nerve fibers. The relative avascular nature of the tumor allows the dissection within the capsule and the separation from the parental nerve. The surgical treatment for schwannoma consists of a conservative local excision with preservation of neural function via a transcervical approach. If it is not possible to preserve the nerve of origin, an end-to-end anastomosis or interposition nerve graft has to be made [9].

Recurrence is unlikely with complete resection, and until now, our patient had a good evolution, with no sign of recurrence. Malignant transformation is extremely rare in isolated tumors being mentioned in 8–10% of the cases [1, 3, 26–28].

Conclusions

In conclusion, we presented a rare case of schwannoma of the oral cavity.

Although they are rare benign lesions, the unique nature of presentation impose a systematic work-up for an accurate diagnosis and classification, which must integrate the histological analysis with immunohistochemical study and with the clinical data.

Differential diagnosis must be made in relation to numerous benign and malignant tumors derived from epithelial and connective tissue.

Immunohistochemical markers are useful to determine the neural differentiation, the anti-S-100 protein being the main tool of diagnosis in addition with the positive immunoreaction for vimentin.

References

[1] PANDARAKALAM C., SUDHA S., SHAMEENA P. M., VARGHESE V. I., *An unusual presentation of a case of schwannoma,* J Oral Maxillofac Pathol, 2005, 9(1):27–29.

[2] NEVILLE B. W., DAMM D. D., ALLEN C. M., BOUQUOT J. E., Soft tissue tumors. In: NEVILLE B. W., DAMM D. D., ALLEN C. M., BOUQUOT J. E. (eds), *Oral and Maxillofacial Pathology*, 2nd edition, W. B. Saunders, Philadelphia, 2002, 12:456–457.

[3] ENOZ M., SUOGLU Y., ILHAN R., *Lingual schwannoma*, J Cancer Res Ther, 2006, 2(2):76–78.

[4] FLICKINGER F. W., LONZANO R. L., YUH W. T., SACHS M. A., *Neurilemmoma of the tongue: MR findings*, J Comput Assist Tomogr, 1989, 13(5):886–888.

[5] VEROCAY J., *Zur Kenntnis der 'Neurofibrome',* Beitr Pathol Anat, 1910, 48:1–68.

[6] STOUT A. P., *The peripheral manifestations of the specific nerve sheath tumor (neurilemmoma)*, Am J Cancer, 1935, 24:751–796.

[7] WRIGHT B. A., JACKSON D., *Neural tumors of the oral cavity. A review of the spectrum of benign and malignant oral tumors of the cavity and jaws*, Oral Surg Oral Med Oral Pathol, 1980, 49(6):509–522.

[8] WILLIAMS H. K., CANNELL H., SILVESTER K., WILLIAMS D. M., *Neurilemmoma of the head and neck,* Br J Oral Maxillofac Surg, 1993, 31(1):32–35.

[9] ENZINGER F. M., WEISS S. W., Benign tumors of peripheral nerves. In: ENZINGER F. M., WEISS S. W. (eds), *Soft tissue tumors*, 3rd edition, Mosby–Year Book, Inc., Missouri, 1995, 821–888.

[10] DREVELENGAS A., KALAITZOGLOU I., LAZARIDIS N., *Sublingual hypoglossal neurilemmoma. Case report*, Aus Dent J, 1998, 43(5):311–314.

[11] CARINCI F., CARLS F. P., GRASSO D. L., PELUCCHI S., PASTORE A., *Schwannoma of the parapharyngeal space*, J Craniofac Surg, 2000, 11(4):367–370.

[12] CUNNINGHAM L. L. JR., WARNER M. R., *Schwannoma of the vagus nerve first diagnosed as a parotid tumor*, J Oral Maxillofac Surg, 2003, 61(1):141–144.

[13] LACOSTA J., ZABALETA M., SÁNCHEZ DEL HOYO A., *Extracranial schwannomas. Report of seven cases*, Acta Otorrinolaringol Esp, 1999, 50(7):587–589.

[14] HIBBERT J., Laryngolongy and head and neck surgery. In: KERR A. G. (ed), *Scott–Brown's Otolaryngology*, 6th edition, Butterworth–Heinemann, Oxford, 1997, 16:8–22:6.

[15] COLREAVY M. P., LACY P. D., HUGES J., BOUCHIER-HAYES D., BRENNAN P., O'DWYER A. J., DONNELLY M. J., GAFFNEY R., MAGUIRE A., O'DWYER T. P., TIMON C. V., WALSH M. A., *Head and neck schwannomas – a 10 year review*, J Laryngol Otol, 2000, 114(2):119–124.

[16] CHIAPASCO M., RONCHI P., SCOLA G., *Neurilemmoma (schwannoma) of the oral cavity. A report of 2 clinical cases*, Minerva Stomatol, 1993, 42(4):173–178.

[17] JORDAN R. C., REGEZI J. A., *Oral spindle cell neoplasm: a review of 307 cases*, Oral Surg Oral Med Oral Pathol Oral Radiol Endod, 2003, 95(6):717–724.

[18] FEANY M. B., ANTHONY D. C., FLETCHER C. D., *Nerve sheath tumors with hybrid features of neurofibroma and schwannoma: a conceptual challenge*, Histopathology, 1998, 32(5):405–410.

[19] KUMAR A., RAJAN P., *Schwannoma of the tongue – a case report,* Calicut Med J, 2004, 2(2):e4.

[20] REDMAN R. S., GUCCION J. G., SPECTOR C. J., KEEGAN B. P., *Cellular schwannoma of the mandible: a case report with ultrastructural and immunohistochemical observations*, J Oral Maxillofac Surg, 1996, 54(3):339–344.

[21] LÓPEZ J. I., BALLESTIN C., *Intraoral schwannoma. A clinico-pathologic and immunohistochemical study of nine cases*, Arch Anat Cytol Pathol, 1993, 41(1):18–23.

[22] ACKERMAN L. V., TAYLOR F. H., *Neurogenous tumors within the thorax; a clinicopathological evaluation of forty-eight cases*, Cancer, 1951, 4(4):669–691.

[23] CARDESA A., SLOOTWEG P. J., Benign nerve sheath tumors. In: CARDESA A., SLOOTWEG P. J., *Pathology of the Head and Neck,* Springer Verlag, Berlin–Heidelberg, 2006, 3:95–96.

[24] IIDA S., AIKAWA T., KISHINO M., SAKAI T., NAKANO Y., OKURA M., KOGO M., *Spheric mass beneath the alar base: MR images of nasolabial cyst and schwannoma*, AJNR Am J Neuroradiol, 2006, 27(9):1826–1829.

[25] DE BREE R., WESTERVELD G. J., SMEELE L. E., *Submandibular approach for excision of a large schwannoma in the base of the tongue*, Eur Arch Otorhinolaryngol, 2000, 257(5):283–286.

[26] HARADA H., OMURA K., MAEDA A., *A massive pleomorphic adenoma of the submandibular salivary gland accompanied by neurilemmomas of the neck misdiagnosed as a malignant tumor: report of case*, J Oral Maxillofac Surg, 2001, 59(8):931–935.

[27] ELIAS M. M., BALM A. J., PETERSE J. L., KEUS R. B., HILGERS F. J., *Malignant schwannoma of the para-pharyngeal space in von Recklinghausen's disease: a case report and review of literature*, J Laryngol Otol, 1993, 107(9):848–852.

[28] GREAGER J. A., REICHARD K. W., CAMPANA J. P., DASGUPTA T. K., *Malignant schwannoma of the head and neck*, Am J Surg, 1992, 163(4):440–442.

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