Available online at www.sciencedirect.com

ScienceDirect

Annals of Diagnostic Pathology 14 (2010) 235–239

Annals of DIAGNOSTIC PATHOLOGY

Original Contributions

Clinicopathologic analysis of 7 cases of oral schwannoma and review of the literature☆

Pedro Paulo de Andrade Santos, DDS, MSc, Valéria Souza Freitas, DDS, MSc, Leão Pereira Pinto, DDS, PhD, Roseana de Almeida Freitas, DDS, PhD, Lélia Batista de Souza, DDS, PhD*

Postgraduation Program in Oral Pathology, Federal University of Rio Grande do Norte, Natal, RN, Brazil

Abstract Schwannomas, also known as neurilemmomas, are uncommon neoplasms apparently derived from Schwann cells. The growth of these tumors causes displacement and compression of the nerve of origin. Schwannomas are usually solitary lesions but can be multiple when associated with neurofibromatosis. Anti-S100 protein is the most widely used antibody for the identification of this neoplasm. Surgical excision is the treatment of choice for schwannomas, with few and controversial reports of recurrence or malignant transformation. The present article reports 7 additional cases of oral schwannoma, and the literature is reviewed regarding clinicopathologic features, immunohistochemical findings, differential diagnosis, and therapeutic management of this benign neural tumor.

Keywords: Neurilemmoma; Schwannoma; Neural tumor; Benign tumor

1. Introduction

Schwannomas are benign, slow-growing, epineurium-encapsulated neoplasms arising from Schwann cells that comprise the myelin sheaths surrounding peripheral nerves [1]. Schwannomas show 2 histologic patterns: Antoni type A and Antoni type B. Although these tumors may affect any site of the body, 25% to 48% of these lesions are found in the head and neck region [2,3]. Schwannomas of the head and neck occur both intracranially, mainly at the cerebellar pontine angle, and in peripheral soft tissues, mainly the tongue followed by the palate, floor of mouth, oral mucosa, and mandible [4]. Schwannomas involving soft tissues appear as a smooth submucosal swelling, resembling other lesions such as mucocele, fibroepithelial polyp, fibroma, lipoma, and benign salivary gland tumors [5].

Normally, schwannomas are slow-growing tumors that might be present for some years before becoming symptomatic. Swelling is the most common symptom, followed by paresthesia [6]. Over time, schwannomas may grow to large proportions, with their increase in size probably being associated with intralesional hemorrhage [7].

Conservative surgical removal is the treatment of choice, with wide excision not being recommended. If complete enucleation is achieved, no recurrence should be expected [8].

The present article reports 7 additional cases of schwannoma, all of them involving the oral cavity, and the literature is reviewed regarding peculiar clinicopathologic features, immunohistochemical findings, differential diagnosis, and therapeutic management of this tumor.

2. Case report

2.1. Case 1

A 41-year-old woman was referred to our department for evaluation of a painless, smooth, pinkish nodule located in the right posterior region of the hard palate. The nodule had been noted by the patient 5 years earlier. The patient's medical history was unremarkable. An excisional biopsy was performed based on the initial clinical diagnosis of

☆ Conflict of interest: The authors declare no conflict of interest.

* Corresponding author. Departamento de Odontologia, Universidade Federal do Rio Grande do Norte, Natal, RN 59056-000, Brazil. Tel.: +55 84 3215 4138; fax: +55 84 3215 4138.

E-mail address: leliasouza@dod.ufrn.br (L.B. de Souza).

1092-9134/$ – see front matter.
doi:10.1016/j.anndiagpath.2010.02.009

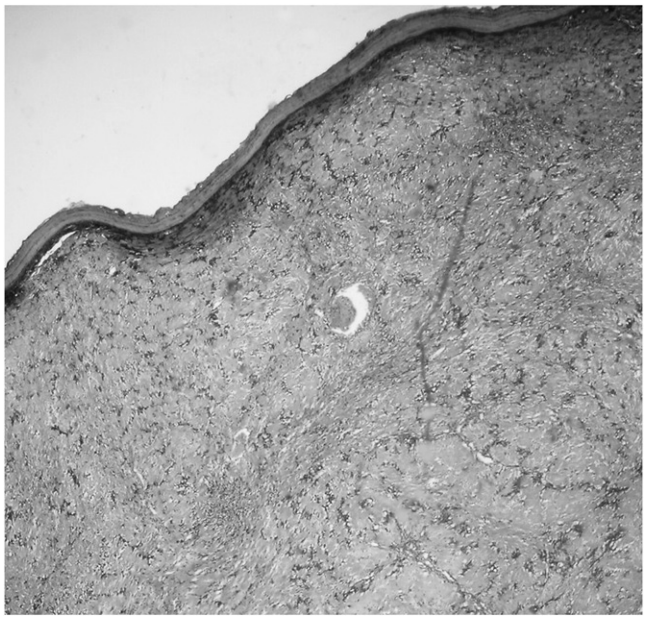

Fig. 1. A thick fibrous capsule surrounding the tumor with predominant Antoni A tissue (hematoxylin-eosin stain, original magnification: ×40).

pleomorphic adenoma. Microscopic analysis of the specimen revealed a benign neural tumor consisting of spindle-shaped cells in a loose texture (Antoni B tissue) and occasional Antoni A tissue. No cytologic atypia was observed.

2.2. Case 2

A 22-year-old man presented with a painless mass located on the right side of the floor of the mouth. His medical history was noncontributory, and the mass had been noted by the patient 8 months earlier. An excisional biopsy was performed based on the initial clinical diagnosis of epidermoid cyst. Histopathologic examination revealed a schwannoma consisting of encapsulated predominantly Antoni B tissue (Fig. 1) and hemorrhagic areas.

2.3. Case 3

An 18-year-old man presented with a 6-month history of a solid, irregularly lobulated yellow-tan nodule in the posterior region of the tongue. An excisional biopsy was performed, and the clinical diagnosis was fibroma. Microscopic analysis of the specimen revealed a pattern of alternating regions of hypocellularity and hypercellularity, known as Antoni A (Fig. 2A) and Antoni B (Fig. 2B), respectively. Cystic degeneration and multinodular features were also observed.

2.4. Case 4

A 46-year-old woman sought a general dentist for evaluation of a painless nodule located in the oral mucosa. The lesion had been noted 1 year earlier. The patient was submitted to an excisional biopsy and microscopic analysis revealed a conventional encapsulated schwannoma mainly consisting of Antoni A tissue. No cytologic atypia was observed.

2.5. Case 5

A 53-year-old woman presented with a swelling in the hard palate that had progressed over approximately 6 months. Clinical examination revealed a pinkish hard nodule measuring 3 cm in diameter. The patient reported no history of pain. An excisional biopsy was performed, and an area of bone erosion was identified beneath the lesion during surgery. Microscopic analysis of the specimen revealed a pattern of alternating regions of Antoni A and Antoni B tissue, cyst formation (Fig. 3A), and areas of epithelioid cells. Immunohistochemistry for protein S-100 Schwann cells was strongly positive and the diagnosis of schwannoma was made (Fig. 3B).

2.6. Case 6

In 2007, a 10-year-old child was referred to our service for evaluation of a 3-month history of a painless,

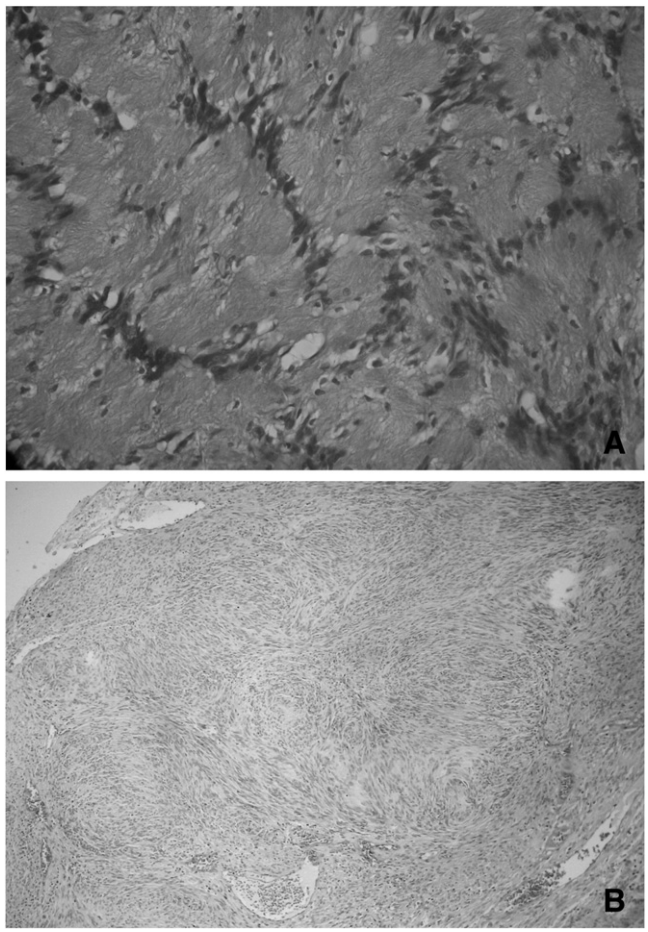

Fig. 2. (A) Antoni A tissue presenting spindle-shaped cells, nuclear palisading, and Verocay bodies in a schwannoma of the floor of the mouth (hematoxylin-eosin stain, original magnification: ×400). (B) Increased cellularity, predominant disorganized Antoni B areas, and scarce Antoni A tissue (hematoxylin-eosin stain, original magnification: ×100).

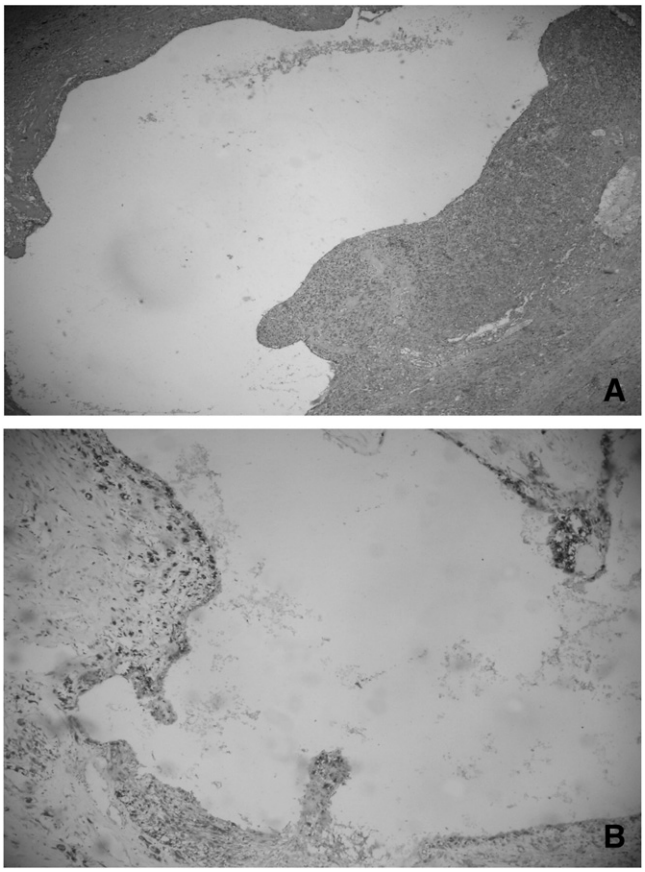

Fig. 3. (A) Cyst formation in a schwannoma of the hard palate (hematoxylin-eosin stain, original magnification: ×40). (B) Strongly positive immunostaining for protein S100 during cyst formation, confirming the neural origin of the tumor, and being consistent with the diagnosis of schwannoma (original magnification: ×100).

hard, irregularly lobulated nodule in the oral mucosa. An excisional biopsy was performed, and the clinical diagnosis of fibrous hyperplasia was made. Microscopic analysis of the specimen revealed a plexiform schwannoma (Fig. 4).

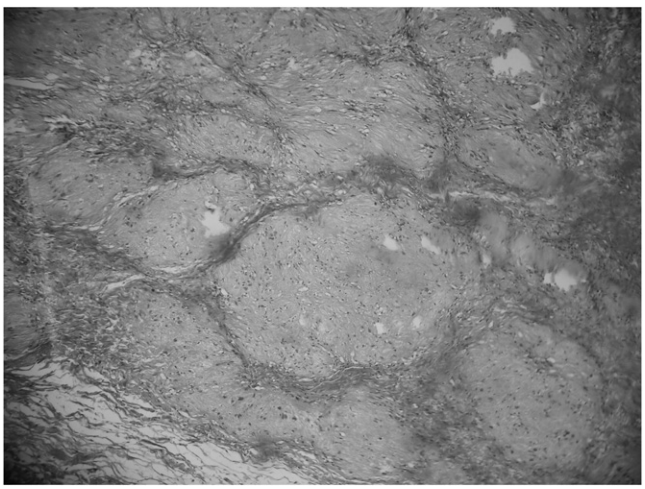

Fig. 4. Plexiforme schwannoma of the tongue. Note the multiple round oval profiles of tumor-affected nerve fascicles with distinct perineural ensheathment (hematoxylin-eosin stain, original magnification: ×100).

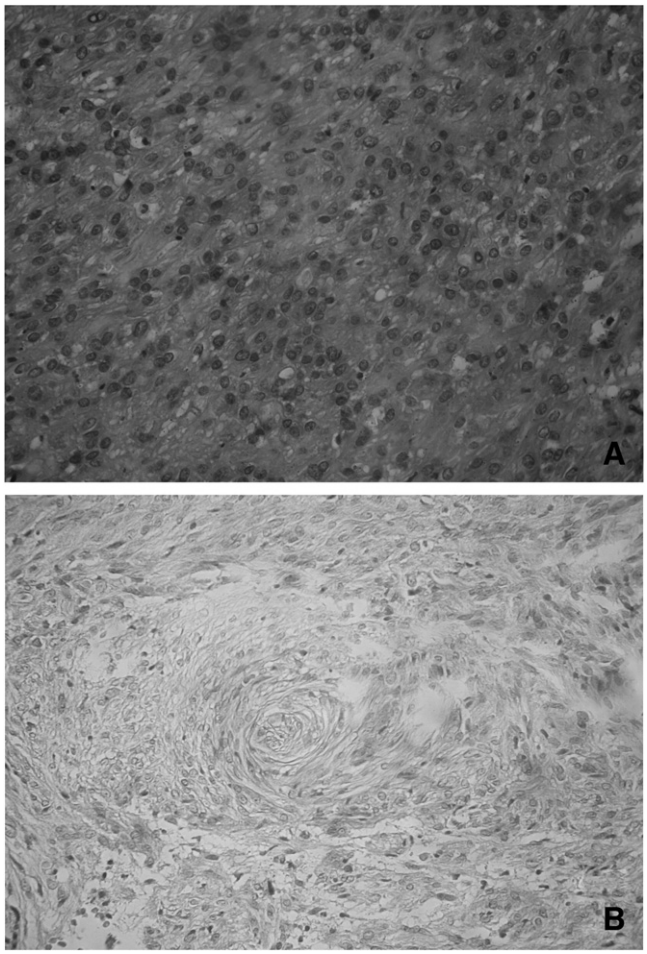

Fig. 5. (A) Neoplasm consisting of epithelioid cells with vesicular nuclei. Note the presence of nucleoli (hematoxylin-eosin stain, original magnification: ×400). (B) "Whorling" of epithelioid cells in a schwannoma of the oral mucosa (hematoxylin-eosin stain, original magnification: ×400).

2.7. Case 7

The most recent case occurred in 2009. A 32-year-old man exhibited painless facial expansion that had progressed over a period of approximately 1 year. Clinical examination revealed a blue hard nodule in the oral mucosa measuring 5 cm in diameter. An incisional biopsy was performed based on the clinical diagnosis of salivary gland tumor. Histopathologic examination revealed a schwannoma consisting of encapsulated predominantly Antoni A tissue and epithelioid cells (Fig. 5A) that presented a "whorled" pattern (Fig. 5B).

3. Discussion

The term Schwannoma was originally suggested because this neoplasm was thought to be derived from Schwann cells of peripheral nerve sheaths. These cells were named after the German anatomist, physiologist, and cofounder of

Table 1
Clinicopathologic features in 7 cases of intraoral schwannomas

Case	Year	Age (y)	Sex	Location	Duration	Size	Clinical findings	Biopsy	Configuration	Encapsulation	Antoni A/B	Cyst formation
1	1972	41	F	Hard palate	5 y	NA	Painless swelling	Excisional	Conventional	Absent	B > A	Absent
2	1979	22	M	Floor of mouth	8 mo	NA	Swelling	Excisional	Conventional	Present	B > A	Absent
3	1995	18	M	Tongue	6 mo	1.7 cm	Painless swelling	Excisional	Plexiform	Present	B > A	Present
4	1997	46	F	Buccal mucosa	1 y	1 cm	Painless swelling	Excisional	Conventional	Present	A > B	Absent
5	2002	53	M	Hard palate	6 mo	3 cm	Painless swelling	NA	Conventional	Absent	A > B	Present
6	2007	10	M	Buccal mucosa	3 mo	1 cm	Painless swelling	Excisional	Plexiform	Present	B > A	Absent
7	2009	32	M	Buccal mucosa	1 y	5 cm	Painless swelling	Incisional	Conventional	Present	A > B	Present

NA indicates not available.

the cell theory, Theodor Schwann (1810-1882) [9]. In 1908, José Verocay provided the first microscopic description of this tumor and suggested the designation neurinoma [10]. In 1935, Arthur Stout [11] proposed the term neurilemoma and further elaborated on the histopathology of this entity. In 1940, on the basis of light microscopy studies, Isadore Max Tarlov [12] proposed this tumor to be of fibroblastic origin and coined the term "perineural fibroblastoma." Today, most pathologists consider the terms schwannoma, neurinoma, neurilemmoma, and perineural fibroblastoma to be synonymous and distinguish this lesion from neurofibroma [13].

In 1985, Erlandson [14] classified Schwannomas into 7 subtypes: classical (Verocay), cellular, plexiform, cranial nerve, melanotic, degenerated (ancient), and granular cell schwannoma [15,16]. Conventional and plexiform schwannomas often arise in superficial soft tissues, particularly of the head and neck region, which is rich in superficially situated peripheral nerves [17].

In the present study, schwannomas involved the oral mucosa in 3 cases (42.8%), hard palate in 2 (28.7%), floor of the mouth in one (14.3%), and tongue in one (14.3%).

There are 3 mechanisms by which schwannomas may involve bone: (1) they may arise centrally within bone, (2) they may arise within the nutrient canal and produce canal enlargement, or (3) a soft tissue or periosteal tumor may cause secondary erosion and penetration into bone. No case of intraosseous schwannoma was observed in the present study [18].

Analysis of the 7 cases studied (Table 1) shows a wide range in patient age for oral schwannomas, which can affect from newborns [13] to the elderly [7,19] (mean age, 31.7 years). Although previous studies have reported a male predominance, a review of the cases published so far revealed a slightly higher frequency of schwannomas among females (53.6%). No sex preference was observed in the present study, with 4 cases in males and 3 in females.

Intraoral schwannomas usually measure 1.0 to 5.0 cm in diameter (mean, 2.34 cm). The reported duration of these tumors ranges from 3 months to 5 years. Recurrence of schwannomas usually occurs only after incomplete excision, with the aim of treatment being complete surgical removal of the tumor [1,8]. The prognosis is good and malignant transformation of benign schwannoma is controversial, although a few isolated cases have been documented [20]. Six of the present cases were treated by excisional biopsy, and no recurrence was observed.

The clinical differential diagnosis of schwannomas includes any other benign tumor lesion such as fibroma, lipoma, neurofibroma, or salivary gland tumor. However, the histologic differential diagnosis includes other lesions of neural origin, such as neurofibroma, neuroma, and tumors of muscular or fibroblastic origin [20]. In the present cases, the main initial clinical diagnosis of schwannoma was pleomorphic adenoma (3 cases) or fibroma (3 cases). However, in 1 case, the clinical diagnostic hypothesis was epidermoid cyst located in the floor of the mouth.

The essential features of conventional schwannoma include (*a*) exclusive composition of Schwann cells; (*b*) arrangement of cells in a compact, often palisade fashion (Antoni A tissue) and, occasionally, in a loose texture in which multiple processes are evident (Antoni B tissue); (*c*) Verocay body formation; (*d*) presence of hyalinized and/or ecstatic vessels, often accompanied by hemosiderin deposits; and (*e*) encapsulation of affected fascicles by residual collagenous perineurium. The degenerative changes frequently seen in large longlasting lesions include hemorrhage, infarction, cyst formation, and dystrophic calcification [17].

Histopathologic analysis of the present schwannoma cases showed encapsulated lesions in 5 cases, conventional schwannoma in 71.42%, and plexiform schwannoma in 28.68%. A predominance of Antoni B tissue was observed

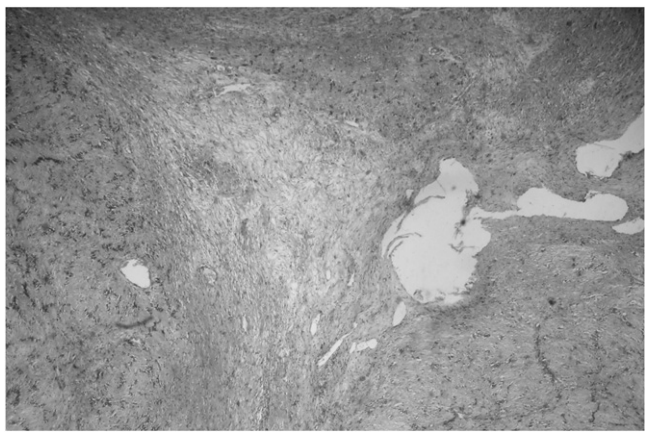

Fig. 6. Myxomatous stroma in an Antoni A schwannoma (hematoxylin-eosin stain, original magnification: ×40).

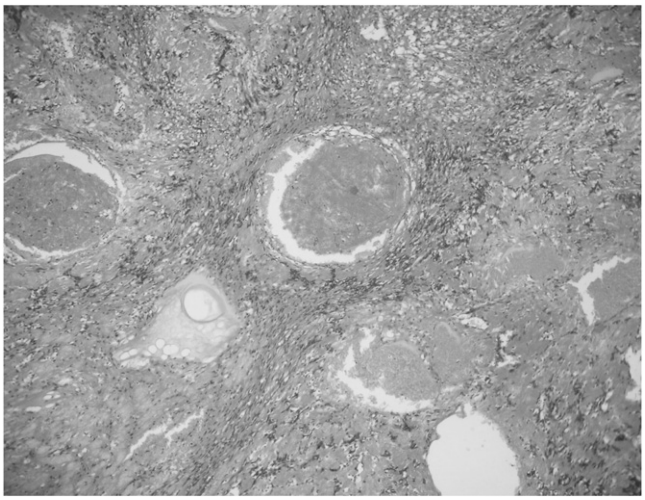

Fig. 7. Dilated and congested vessels and areas of edema and hemorrhage in Antoni A tissues (hematoxylin-eosin stain, original magnification: ×100).

in 57.1% of cases and of Antoni A tissue in 42.9%. The characteristic Verocay bodies were found in 4 cases and the formation of cysts of different sizes was noted in 3 cases (42.9%).

No cytologic atypia was observed, and spindle-shaped cells and frequent epithelioid cells were present in most cases. The latter cells were first described in skin schwannoma by Orosz [21] and pose a challenge in the histopathologic diagnosis [22]. The epithelioid variant of schwannoma is characterized by small and round epithelioid cells arranged as single cells in small clusters and in cords within a collagenous and, at times, myxoid stroma (Fig. 6) [13].

Hemorrhage was a frequent finding in 85.71% of the cases, and no dystrophic calcification was observed (Fig. 7).

Immunohistochemical staining for protein S100 was strongly positive. According to the literature, immunohistochemical analysis is essential for the diagnosis of schwannomas. Most parts of the tumor cells in schwannoma show a positive immunohistochemical reaction to protein S100 [23,24].

4. Conclusions

Schwannomas or neurilemmomas of the oral cavity are rare benign tumors that affect patients of different ages and show no sex preference. No specific site was found to be involved, with the tumors affecting the oral mucosa, hard palate, tongue, and floor of the mouth, sites clinically suggestive of salivary gland or fibroblastic tumors. Although the diagnostic criteria and microscopic features of schwannomas have been relatively well established, microscopic details as demonstrated in this study continue to be scarce in the literature.

References

[1] Sawhney R, Carron MA, Mathog RH. Tongue base schwannoma: report, review, and unique surgical approach. Am J Otolaryngol 2008;29:119-22.
[2] Amir R, Altman KW, Zaheer S. Neurilemmoma of the hard palate. J Oral Maxillofac Surg 2002;60:1069-71.
[3] Salla JT, Johann ACBR, Garcia BG, Aguiar MCF, Mesquita RA. Retrospective analyses of oral peripheral nerves sheath tumors in Brazilians. Braz Oral Res 2009;23(1):43-8.
[4] Ying YLM, Zimmer LA, Myers EN. Base of tongue schwannoma: a case report. Laryngoscope 2006;116:1284-7.
[5] Subhashraj K, Balanand S, Pajaniammalle S. Ancient schwannoma arising from mental nerve. A case report and review. Med Oral Patol Oral Cir Bucal 2009;14(1):E12-4.
[6] Kowatsch E, Feichtinger M, Zemann W, Karpf E, Karcher H. Extraosseous schwannoma of the mental nerve clinically simulating intraosseous. J Oral Pathol Med 2006;35:517-9.
[7] Zachariades N, Skoura C, Papageorgiou G, Chrissomali E. Giant ancient neurilemmoma of the cervical region: report of case. J Oral Maxillofac Surg 2001;59:668-72.
[8] Yang SW, Lin CY. Schwannoma of the upper lip: case report and literature review. Am J Otolaryngol 2003;24:351-4.
[9] Morgan GA, Morgan PR. Neurilemmoma-neurofibroma. Oral Surg Oral Med Oral Pathol 1968;25:182-9.
[10] Schajowicz F. Other tumors. Tumors and tumorlike lesions of bone: pathology, radiology, and treatment. 2nd ed. New York: Springer Verlag; 1994. p. 453-5.
[11] Stout AP. The peripheral manifestations of the specific nerve sheath tumor (neurilemmoma). Am J Cancer 1935;24:751-96.
[12] Tarlov IM. Origin of the perineural fibroblastoma. Am J Pathol 1940;16:33-40.
[13] Chi AC, Carey J, Muller S. Intraosseous schwannoma of the mandible: a case report and review of the literature. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2003;96:54-65.
[14] Erlandson RA. Peripheral nerve sheath tumours. Ultrastruct Pathol 1985;9:113-22.
[15] Kawamura K, Yajima H, Morishita T, Honori K, Takakura Y. Plexiform schwannoma of the ulnar nerve. Scand J Plast Reconstr Surg Hand Surg 2005;39:120-2.
[16] Lobo I, Torres T, Pina F, Dominguez M, Alves R, Barbas do Amaral J, et al. Plexiform schwannoma of the lip mucosa. J Eur Acad Dermatol Venereol 2009;23:570-620.
[17] Berg JC, Scheithauer BW, Spinner RJ, Allen CM, Koutlas IG. Plexiform schwannoma: a clinicopathologic overview with emphasis on the head and neck region. Hum Pathol 2008;39:633-40.
[18] Lacerda SA, Brentegani LG, Rosa AL, Vespúcio MVO, Salata LA. Intraosseous schwannoma of mandibular symphysis: case report. Braz Dent J 2006;17(3):255-8.
[19] Graham RM, Thomson EF, Woodwards RTM. Benign schwannoma of the left cervical phrenic nerve. Br J Oral Maxillofac Surg 2008;46 (2):161-2.
[20] Martins MD, Jesus LA, Fernandes KPS, Bussadori SK, Taghloub SA, Martins MAT. Intra-oral schwannoma: case report and literature review. Indian J Dent Res 2009;20(1):121-5.
[21] Orosz Z. Cutaneous epithelioid schwannoma: an unusual benign neurogenic tumor. J Cutan Pathol 1999;26:213-4.
[22] Gao Z, Palleschi SM, Chen S. Plexiform epithelioid schwannoma: a case report. Am J Dermatopathol 2007;29(1):56-8.
[23] Chrysomali E, Papanicolaou SI, Dekker NP, Regezi JA. Benign neural tumors of oral cavity: a comparative immunohistochemical study. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 1997;84:381-90.
[24] Passador-Santos F, Turatti E, Gorisch MR, Santos E, Sousa SC. Estudo imuno-histoquímico de tumores de origem neural na cavidade oral. RPG Rev Pós Grad 2002;9:277.