

Oral Schwannoma: A Systematic Review of the Case Reports

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Abstract

Schwannomas are benign neoplasms with unknown etiology, which apparently arise from neural sheath Schwann cells. Intraoral schwannomas are solitary, slow-growing lesions occurring at different ages; these lesions are normally asymptomatic and in some cases, they are accompanied by pain and paresthesia if spotted in the intraosseous regions of the mandibles. Definitive diagnosis of schwannoma is established through histopathological examination and immunohistochemical evaluation, and the first-line treatment involves the surgical excision of the tumor with preservation of neighboring structures. Anti-S100 protein is the most significant antibody used to identify schwannomas. Schwannomas are known to have good prognosis, and if the lesion is completely removed, there is a low risk of recurrence. This systematic review aimed to determine the most significant variables influencing intraoral schwannoma and evaluate effective methods for the diagnosis and treatment of these tumors.

Key words: Intraoral Schwannoma, Benign Neoplasms, Mandible, Histopathological Examination.

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Introduction

Schwannomas, also known as neurilemmoma, neurinoma, or perineural fibroblastoma, are benign neoplasms that commonly appear in the soft tissues of head and neck (25-45%) (1). According to a study by Leu and Chang, intraoral schwannomas were identified in only seven cases among 52 patients presented with schwannoma in the head and neck (2). Oral schwannomas are rare, slow-growing tumors with unknown etiology, which apparently arise from neural sheath Schwann cells. These solitary lesions may occur at different ages (usually within the second and third decades of life), and the prevalence is not significantly different between men and women. Oral schwannomas are normally asymptomatic, while in some cases, they might be accompanied by pain and paresthesia if spotted in the intraosseous regions of the mandibles. In such cases, these tumors may cause bone expansion, pain and paresthesia (3).

In general, schwannomas are solitary lesions; however, they are capable of multiplying when associated with neurofibromatosis. The most frequent sites of intraoral schwannomas are the tongue, palate, mouth floor, buccal mucosa, lips and jaws (4).

Schwannomas could be confused with other benign tumoral lesions, such as fibroma, mucocele, lipoma, neurofibroma and other salivary gland tumors. Immunohistochemical and radiological examinations

are usually performed to determine the extension of these tumors, and immunohistochemical features of these tumors are evaluated in order to verify the neural differentiation of schwannomas.

Anti-S100 protein is the most significant antibody used to identify schwannomas. These lesions have good prognosis, and the first-line treatment involves the surgical excision of the tumor. If completely removed, schwannomas have a low risk of recurrence (4). This systematic review aimed to address the following questions:

1. What are the most influential factors in the occurrence of intraoral schwannoma?
2. What are the most common symptoms and complications associated with intraoral schwannoma?
3. What are the most effective methods used for the differential diagnosis of schwannoma from other lesions?
4. What are the most effective methods for the diagnosis and treatment of intraoral schwannoma?

Materials and Methods

This systematic review aimed to evaluate articles focusing on oral schwannoma via searching in databases such as PubMed and Google Scholar during 2005-2015. Initially, all the articles with related abstracts were assessed by one researcher. Search for related studies was conducted using two key words of intraoral and

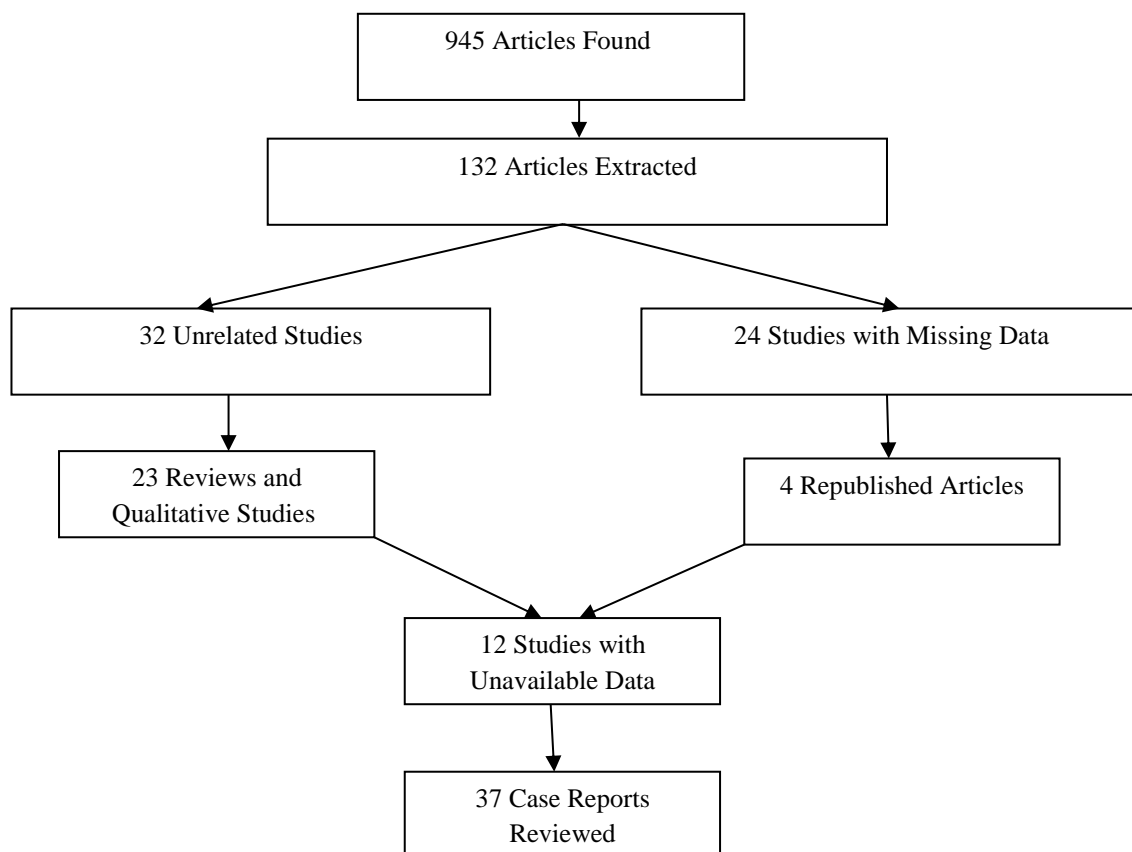
schwannoma. Selected articles were published in English and Persian, and duplicate reports were excluded from the study.

In this review, we only included case reports and case series studies about oral schwannoma, and other studies were excluded. Additionally, different variables such as age, gender, location and size of schwannoma, duration of disease, associated complications, and type of treatment and diagnosis were evaluated in the present study. Previous reviews, meta-analyses, expert opinions, consensus statements, original articles, editorials, letters and qualitative studies were excluded from this review.

In total, 132 articles were selected out of 945 related studies, and other excluded articles were as follows: 6 reviews and narrative articles, 17 qualitative articles, 32 unrelated studies, 24 studies with missing data, 12 studies with unavailable data, and 4 republished articles. Eventually, 37 case reports were systematically reviewed by the researchers.

Required data were extracted by one researcher, and all the selected articles were reviewed in full text after screening. Moreover, the results obtained by each case report were studied in detail and evaluated based on the objectives of the study. The screening process is depicted in the PRISMA Flow Diagram.

PRISMA Flow Diagram:
Screening Process of Articles in the Current Review 945.



Results

In the present review, different variables such as age, gender, location and size of schwannoma, duration of disease, complications caused by the tumor, type of treatment and diagnosis, and follow-up of the patients were evaluated. The results are shown in (Table 1).

In total, 37 case reports were reviewed in this study, 18 of which were case report reviews, and other articles were case reports only. The majority of these studies focused on one reported case of schwannoma, while a few studies evaluated two cases of these tumors. In

almost all these cases, patients underwent surgical procedures for the tumor resection.

Among the reviewed cases presented with schwannoma, 18 patients were male and 19 were female within different age ranges. These cases were reported in different countries, and among 37 articles, 8 cases were reported in India. In general, several of schwannoma cases were reported in regions of Southeast Asia. In addition, duration of disease ranged between three months and 20 years, and recurrence was observed in none of the studied cases.

Table 1. Evaluation of Variables Associated with Schwannoma based on Literature Review

Authors/ Publication Year (Reference)	Count ry	Age	Gender	Location of Schwannoma	Size	Duration of Disease	Reported Complications	Type of Treatment	Follo w-up	Diagnostic modalities(histopathologic al findings)
Amirchahm et al. (2010) (5)	Iran	14	Male	Gingival, Right Mandibular Canine Tooth	1.5 cm	1 year	Asymptomatic, No tender mass enlargement or mobility	Surgical Excision	Unknown	Loss of crest bone and lamina dura in some teeth/ Immunostaining with Anti-S100 Protein: Positive in cellular areas
Subhashraj et al. (2009) (6)		19	Male	Periapical Region of Left Lower First Premolar	31×2 4×12 Mm	8 Months	Asymptomatic, Enlarging Mass	Surgical Excision using high labial incisions in left mandibular Region	18 Months	Proliferation of spindle cells without atypia arranged in nuclear palisades Degenerative Changes and Hyalinization Detected
Enzo et al. (2006) (7)	Turkey	7	Male	Anterior Mobile Region of Tongue	25 mm	8 Months	Easily visible and palpable, Swelling associated with pain and tenderness	Excision of tumor, capsule and a small border of uninvolved surrounding tissue	5 Years	Immunohistochemical Evaluation: Positive staining for S-100 protein, Leu-7 antigen, vimentin and glial fibrillary acidic protein
Lollar et al. (2009) (3)	USA	33	Male	Midline of Hard Palate	2×2 cm	3 Months	Asymptomatic	Wide Local Excision of Mass	Unknown	Variable cellular proliferation of spindled cells with foci of nuclear palisades Immunohistochemical Evaluation: Positive for S-100 protein and vimentin
Chen et al. (2006) (8)	Taiwan	34	Male	Left Anterior Mouth Floor	3×3× 2.5 cm	18 Years	Asymptomatic	Encapsulated tumor removed by blunt dissection	2 Years	-----
Salehinejad et al. (2011) (9)	Iran	27	Female	Ramus and Angle Region of Left Mandible		2 Years	Asymptomatic	Surgery by retromolar incision and blunt dissection under general anesthesia	9 Months	Schwann cells in fibrous with stromal myxoid changes Clinical Diagnosis: Ameloblastoma and Myxoma Immunohistochemical Evaluation: S-100 protein positive
Bansal et al. (2005) (1)	India	26	Male	Ventral Surface of Right Side of Tongue	3-4 cm	4-5 Years	Gradual growth, paresthesia of tongue, and difficulty in phonation	Excision with adequate surgical margins of resection	2 Years	Spindle shaped cells with long, twisted, curled nuclei, plentiful pale eosinophilic cytoplasm and uncertain cytoplasmic borders

										Immunohistochemical Evaluation: S-100 protein positive
De Bree et al. (2000) (10)	Netherlands	24	Female	Right Base of Tongue	5×5×3 cm	6 Months	Asymptomatic	Lesion removed using a submandibular approach	Unknown	MRI: Enlarged, Well-circumscribed Solid Mass Histopathological Examination: Schwannoma
Parikh & Desai (2010) (11)	India	64	Female	Anterior Hard Palate	2×2 cm	3 Years	Asymptomatic	Tumor removed with incision of tongue in the midline	Unknown	Well-defined radiolucency with sclerotic lining in palate
Karaca et al. (2010) (12)	Turkey	13	---	Anterior Corpus of Tongue	---	1 Year	Disturbance in mastication and phonation	Surgical Excision	Unknown	Schwannoma/ Histopathological identification of Antoni A and B areas Staining S-100 Protein: Positive
Baranović et al. (2005) (13)	Croatia	53	Female	Lingual Mucosa of Mandible	11 mm	10 Months	Asymptomatic	Surgical Excision	Unknown	Mass with interlacing fascicles of compact spindle cells and twisted nuclei
Kim et al. (2011) (14)	Korea	66	Female	Buccal Region of Left Lower First Premolar Area	2.0×1.3×1.0 cm	13 Years	Asymptomatic	Complete Excision using Intraoral Approach	9 Months	Well-demarcated, unencapsulated lesion, curled form, poorly defined cytoplasm and oval nuclei S-100 Protein: Positive
		35	Female	Left Mandible Body	3.0×1.5×2.0 cm	---	Paresthesia	Incomplete Surgery	Died	Spindle cells in fascicles Immunohistochemical Evaluation: Positive and Negative for Pancytokeratin
Murthy et al. (2009) (15)	Turkey	28	Female	Anterior Hard Palate	1.5×1.5 cm	4 Months	Occasionally bleeding due to pressure with tip of the tongue	Surgical Excision	Unknown	Histopathological Evaluation: Schwannoma
Cohen et al. (2009) (16)	USA	19	Female	Right Posterolateral Border of Tongue	18×13×11 mm	---	Asymptomatic	Transoral Surgery	Unknown	Magnetic Resonance Imaging (MRI): Well-circumscribed mass isointense on T1, hyperintense on T2
		77	Male	Right Lateral of Tongue	7×5×5 mm	---	Asymptomatic	Transoral Surgery	Unknown	----
Patil et al. (2009) (17)	India	23	Female	Right Mandibular Body	2.5×2 cm	6 Months	Asymptomatic	Resection with reconstruction using autologous iliac crest bone graft	Unknown	Unencapsulated lesion, Antoni A and B regions arranged in a palisading pattern Immunohistochemical Evaluation: S-100 protein positive
López-Jornet et al. (2005) (18)	Spain	39	Male	Right Side of Tongue	8×8 mm	5 Months	Moderate Pain	Antibiotic Treatment	One Year	Well-defined neo-formation surrounded by fibrous connective tissues Immunoperoxidase Staining: S-100 protein positive
Naidu et al. (2010) (19)	Nepal	12	Male	Right Side of Tongue	20×10 mm	15 Days	Bleeding, Paresthesia and Dysgeusia	Surgical Excision	3 Months	Predominant spindle cells and mixed inflammatory cell infiltration Immunohistochemical Evaluation: Strong Reactivity
Lacerda et al. (2006) (20)	Brazil	11	Male	Permanent Mandibular Incisors	---	3 Years	Asymptomatic	Surgical Excision	5 Years	Histopathological Examination: Neoplastic connective tissue arranged in short fascicles
Rahpeyma et al.	Iran	12	Female	Soft Palate	3×2×1	3 Months	Asymptomatic	Lesion removed under general	6 Months	Microscopic Evaluation: Encapsulated

(2012) (21)					cm			anaesthesia	hs	Immunohistochemical Evaluation: Positive for S-100 Protein
Pandarakal et al. (2005) (22)	India	25	Male	Gingival	3×2 cm	---	Asymptomatic	Complete Resection	----	Predominant benign spindle cells in several intersecting bundles
Sivasankari et al. 2015 (23)	India	38	Male	Left Side of Palate	5×3 cm	3 Months	Difficulty in swallowing and changes in voice	Complete Resection, antibiotic and anti-inflammatory therapy	One Year	Histopathological Examination: Schwannoma
Shetty et al. (2012) (24)	India	70	Female	Right Posterior Palate	2 cm	2 Years	Discomfort during Mastication	Complete Resection	8 Mont hs	Antoni A type with parallel arrangement of spindle-shaped, curled nuclei
Kumar et al. (2012) (25)	India	18	Male	Left Hard Palate	3×2.5 cm	----	Asymptomatic	Excised under Local Anesthesia	----	Histopathological Examination: Neural lesion surrounded by fibrous capsule
Shah et al. (2011) (26)	India	35	Female	Right Zygomatic Region	5×3×2 cm	2 Years	Asymptomatic	Alkayat Bramley Incision under General Anesthesia	1 year	Tumor composed of interlacing fascicles of compact spindle cells with twisted nuclei
Khiavi et al. (2014) (27)	Iran	21	Male	Midline of Palate	2×2cm	2 Months	Asymptomatic	Complete Resection	6 Mont hs	Proliferation of spindle cells with palisaded arrangements around central acellular Immunohistochemical Evaluation: S-100 protein positive
Sardinha et al. (2005) (28)	Brazil	13	Male	Tongue	1.4×0.6 Cm	---	Asymptomatic	Excised under Local Anesthesia	12 Mont hs	Positive for S-100 Protein Histopathological Examination: Proliferation of spindle cells with palisaded arrangements around central acellular
Martins et al. (2009) (4)	Brazil	44	Female	Left Maxillary Vestibule (3×2 cm)	3×2 cm	20 Years	Asymptomatic	Surgical Excision	4 Year s	Diagnosis established based on clinical, histopathological, and immunohistochemical findings
Arda et al. (2003) (29)	Turkey	34	Female	Beneath Tongue on the Left Side	3×3 cm	3 Months	Asymptomatic	Surgical Excision under General Anesthesia	---	Encapsulated lesion Nuclei arranged in a streaming fashion in routine hematoxylin
Salehinejad et al. (2009) (30)	Iran	40	Male	Gingival of Left Mandible	19×17 mm	6 Months	Asymptomatic	Surgical Excision	5 Year s	Immunohistochemical Evaluation: Positive for S-100 Protein Proliferation of spindle cells with palisaded arrangements around central acellular
Pfeifle et al. 2001 (31)	USA	30	Female	Right Tip of Tongue	1.0×0.9 cm	2 months	Asymptomatic	Surgical Excision	---	Confirmatory S-100 Immunoperoxidase Stain: Strongly Positive
		18	Male	Tongue Swelling	2 Cm	2 years	Asymptomatic	Surgical Excision	---	Immunoperoxidase Stain: Positive
Salehinejad et al. (2010) (32)	Iran	23	Female	Lower Mandible	1×3×5 cm	4 Months	Pain	Surgical Excision	10 Mont hs	Proliferation of spindle cells with palisaded arrangements Immunohistochemical Evaluation: S-100 protein positive
Shetty et al. (2011) (33)	India	42	Male	Left Side of Lower Mandible	5×7 cm	4 Years		Resected	6 Mont hs	Spindle cells with elongated nuclei arrangement

Discussion

Schwannomas are normally asymptomatic lesions; however, they might be associated with pain and discomfort, especially while involving the submucosal areas. Etiology of schwannoma is still unknown. These tumors are usually benign with a slow growth rate, starting as capsulated nodules; however, they might be malignant in some cases (8-10%) (7). In general, the majority of extracranial and intracranial schwannomas are benign, and the rate of malignancy is estimated at 5%. Approximately 9-14% of malignant schwannomas are spotted in the head and neck (34), which may cause pain, hoarseness, dysphagia, cranial nerve neuropathies, and even Horner syndrome depending on the site and complications of the lesion (35).

Schwannomas were first discussed by Verocay in 1908 (1). Accordingly, schwannomas originate from the vagus nerve and sympathetic fibers in the extracranial regions of the head and neck, and about 10-40% of these tumors are of unknown origins. In some cases, schwannomas are detected in the peripheral cranial or autonomic nerves. Normally, schwannomas appear on the flexor surfaces of the body, have centrifugal arrangements and are accompanied by pain and paresthesia (29).

According to the literature, about half of schwannomas are directly correlated with a certain nerve, and a quarter of all schwannomas occur in the head and neck. Intraoral schwannomas are rare, with the prevalence rate of 1%, and the majority of these tumors are spotted in the tongue, while the palate, buccal mucosa, lips and gingiva are other regions frequently affected by these lesions (31).

According to one study by Sanchis *et al.*, out of 52 reported cases of schwannoma in the head and neck, only seven tumors were detected in the oral cavity (36). Furthermore, only nine intraoral schwannomas were reported in one study performed in two hospitals of Madrid and Bilbao, Spain during 17 years (37). Another study revealed that oral schwannomas constituted 0.04% of all intraoral lesions, so that only 4 cases out of 9000 biopsies were diagnosed with schwannoma during 38 years (38).

Assessment of Age, Tumor Size and Gender in Patients with Oral Schwannoma

Size of schwannomas is approximately 1-4 cm, while they might be larger if located in the mediastinal and retroperitoneal regions. In one study by Arda *et al.*, size of the tumors was larger than the average in a case presented with intraoral schwannoma, It means Extra oral lesions was greater than intra oral ones (29). According to the findings of the present study, size of these lesions ranged between 8 mm and 5 cm in the reported cases.

In the current study, effects of gender in the occurrence of oral schwannoma were not reviewed, and only a few studies have discussed this correlation. According to some of these researches, gender has no significant correlation with the occurrence of oral schwannoma (4,7,12,16,23,31,39,52). Consistent with other studies, frequency of gender was equal in our review, and no differences were observed between male and female patients regarding the incidence of oral schwannoma. However, some of the studies in this regard were conducted on female patients only (5,13,32,36,37).

Schwannomas are caused by the proliferation of Schwann cells from motor and sensory peripheral nerve sheaths and normally occur within the second and third decades of life. However, age distribution of patients with schwannoma is variable since these lesions could be present for several years before becoming symptomatic (31). In the current study, the majority of patients were within the age range of 30-50.

According to a study by Salla *et al.*, risk of schwannoma is comparatively higher in female patients, and the majority of tumors appear within 10-40 years (39). In another study by Chi *et al.*, mean age of the patients with mandibular schwannoma was estimated at 34 years (40), while it was reported to be 23.7 years in patients with intraoral schwannoma in the study by Salla *et al.* (39), 38.2 years in the study by Lacosta *et al.* (41), and 27.1 years in the study by Sanchis *et al.* (36). In the present review, mean age of the patients with schwannoma was 30 years. In these patients, age could be affected by different variables, such as the location of schwannoma. For instance, tongue is most frequently affected by schwannoma in children ageing 10-13 years (19, 42).

Long-standing schwannoma, also known as ancient schwannoma, is usually benign and slow-growing and commonly spotted on the mouth floor (8, 43-45). These lesions cannot be distinguished from other types of schwannoma; therefore, they may be confused with other malignant tumors due to the presence of nuclear atypia and hyperchromasia, or misdiagnosis of myxoid neurofibroma and nerve sheath myxoma (46). Mean age of the patients with oral ancient schwannoma is higher than other types of schwannoma. Ancient schwannomas are usually benign in the oral cavity, while they may be malignant at other locations. Surgical excision is commonly performed for the treatment of ancient schwannomas (8).

Ancient schwannomas may appear in the form of solid masses, fluctuant cysts or a composition of both. In a case report by Chen *et al.*, the studied lesions were reported to be solid and cystic (8). The first case of intraoral ancient schwannoma was reported by Eversole and Howell in 1971 (47), and Chen *et al.* reported a case

of ancient schwannoma located in the oral cavity (8). Unlike Chen *et al.*, all cases of oral ancient schwannoma were reported in female patients in some studies (43-45, 47, 48). Furthermore, the case reported by Chen *et al.* had the longest duration of oral ancient schwannoma (18 years), and diameter of the tumor was between 0.9-5.5 cm (8). Despite the fact that patients with ancient schwannoma are usually older than other cases presented with these tumors, cases ageing above 70 or 80 years are extremely rare (12, 24, 49).

Location and Complications of Oral Schwannoma

For the most part, oral schwannomas are located in the tongue. In their research, Gallo *et al.* estimated the rate of intraoral schwannomas at 11.7%, equally spotted in the tongue and pharynx (50). Occurrence of tongue schwannoma is associated with the hypoglossal nerve; these lesions have a slow growth rate and may cause pain, loss of taste, and motor function disorders. Although these lesions are solitary, multifocal lesions could appear in localized multiple neurilemmomas in association with neurofibroma in Von Recklinghausen's disease and schwannomatosis (1).

In a study in this regard, Bansal *et al.* described a case with schwannoma on the ventral surface of the right side of the tongue. According to their observations, the lesion had been present for 4 years, and the patient was admitted due to paresthesia and difficulty in phonation (1).

In another study by Wright and Jackson, the tongue was involved in almost half the cases of intraoral schwannoma, and either buccal or vestibular mucosa were involved in approximately one-fifth of the cases. In addition, soft palate was involved in 8.9% of the lesions, and one lesion was spotted in the gingiva and lips (51).

Schwannomas may involve any part of the tongue, as one case was observed in the ventral part of the tongue in a study by Mevio *et al.* (52). Moreover, another case was detected at the base and tip of the tongue by Dreher *et al.* (53) and Robert *et al.* (54), respectively. In several reports, intraosseous schwannoma is described as slightly painful, and without paresthesias (17, 24, 55, 56), which is often detected in the mandible, especially in the posterior segment of the body and ramus (9).

On the other hand, the majority of reported cases of ancient schwannoma were identified on the anterior portion of the tongue (9). Intraosseous schwannoma on the posterior segment of the body and ramus was reported in 28 cases in the study by Chi *et al.* (40). Degenerative changes of ancient schwannoma could be associated with increased size and duration of the tumor (46).

In their research, Salehinejad *et al.* presented a case with large intraosseous schwannoma, which extended

from the lingula to the mandibular second molar (9). In another case reported by Arda *et al.*, submaxillary region was involved (29), and the first case with schwannoma of the submandibular gland was reported by Sodagar and Daneshbod (57). Furthermore, a case of painless sublingual gland schwannoma was described in the study by Arda *et al.* (29).

Swelling and pain are the most common complications caused by intraoral schwannoma (58). In the present review, only 3 cases of painful schwannoma were found in the studied articles (7, 18, 33). However, discomfort caused by swelling of the palate (3, 24) and tongue was reviewed in several cases (19, 42, 59).

Diagnosis and Treatment

Schwannomas could occur in association with different somatic and sympathetic nerves (49). Schwannomas originating from the parasympathetic nerve of the sublingual gland were reported by Arda *et al.* for the first time (29). In another study, Sutay *et al.* detected schwannomas originating from the hypoglossal nerve (60), while they originated from the submandibular gland in the study by Sato *et al.* (61). Based on the aforementioned findings, it could be concluded that diagnosis of schwannoma is relatively easier than similar lesions.

In general, schwannomas are indistinguishable from other encapsulated benign tumors (4, 7). Neurofibroma, traumatic neuroma, fibroma, lipoma and leiomyoma are among the main differential diagnoses of schwannoma (1).

Definitive diagnosis of schwannoma is difficult to establish (62); according to a study by Wang *et al.*, out of 26 biopsied schwannomas, 8 lesions were misdiagnosed as tongue fibromas, dermoid cysts and salivary gland tumors (63). Out of 12 cases described by Sanchis *et al.*, the initial diagnosis was fibroma in four cases, and vascular lesion in two cases (36). Also, eight cases in the study by Lopez and Ballestin were initially misdiagnosed (37).

Many lesions such as lipoma, eosinophilic granuloma, hemangioma, epidermoid and dermoid cysts, epithelial hyperplasia, granular cell tumor, leiomyoma, and lymphangioma may be proposed as the differential diagnoses for schwannoma (64).

Clinically, schwannomas are asymptomatic, slow-growing masses rarely manifested as wounds (64). This is the main reason behind the delayed diagnosis of these tumors, which occasionally takes several years after they appear (59, 65). The results of the current review revealed that the majority of reported schwannomas were diagnosed about one year after they started to grow (4,24,26).

Radiological approaches, such as computed tomography (CT) and magnetic resonance imaging

(MRI), should be used for the differential diagnosis of schwannoma, especially to evaluate different neoplastic processes involving the mouth floor. Panoramic X-ray is a complementary diagnostic measure for oral schwannoma; as such, this method was used in all the reviewed studies (29).

On the same note, MRI is an essential element in the diagnosis of these lesions due to the mucus and exophytic nature of schwannomas and could provide reliable information about these cases. Furthermore, this method could be useful in cases with enlarged tumors or uncertain diagnostic biopsy. However, it is possible that tumor borders are not accurately defined or separated from the peripheral tissue (29).

Schwannomas might be confused with neurofibromas, whereas neurofibromas have a centripetal nature and are typically unencapsulated, originating from different parts of the nervous system, such as Schwann cells, fibroblast, and their neurons. On the other hand, intraosseous schwannoma may be confused with odontogenic cysts or ameloblastoma. While radiological findings cannot distinguish between these lesions, CT-scan could provide an accurate diagnosis (29).

By and large, MRI is the most efficient imaging method to examine the base of the tongue since the resulting image is clear and well-demarcated (7). Through methods such as CT-scan and MRI, valuable data could be obtained for the accurate diagnosis of schwannoma, while biopsy and histopathological examination are essential to the definitive diagnosis of these lesions. A case of schwannoma of the hard palate was reported by Lollar *et al.*, and the diagnosis was confirmed through histopathological and immunohistochemical examinations (3).

Histopathologically, schwannoma tissues are categorized into two patterns of Antoni A and Antoni B. Antoni A regions have high cellularity and are composed of densely packed, spindle cells arranged in palisades. On the other hand, Antoni B regions have more myxoid structures and *two nuclear palisades* with *nuclear* alignment in *rows* in an eosinophil zone, consisting of frills cytoplasmic, basal lamina, and collagen fibers in between, which are called Verocay bodies (30). (Fig 1 and 2)

Thin reticulin fibres, fusiform cells and curled nuclei are visible in the Antoni A region, consisting of a variety of cells without evident borders. In general, Antoni A region is composed of different cells without apparent borders (3, 7, 8). *In* the Antoni B region, tissues of Shawn cells are spotted in a random arrangement (30). (figure 1 and 2)

In the presence of alternating patterns of Antoni A and B regions, histopathological diagnosis of

schwannoma is usually unequivocal; this finding was observed in all the studied articles. In a study by Bansed *et al.*, schwannoma was diagnosed upon the identification of the cells located under Antoni A and B patterns. In the Antoni A area, cells were in a close arrangement, forming short bundles and interlacing fascicles. In addition, parallel rows were observed around the palisading nuclei (Verocay bodies), and in the Antoni B area, cells were arranged haphazardly within loosely-textured matrixes (1). Similar to other studies, Martins *et al.* reported the histopathological findings as thin fibrous capsules with Antoni A type, and Schwann cells with haphazard arrangement in Antoni B region (4).

Schwannomas rarely occur in the oral cavity; therefore, diagnosis of these lesions should be confirmed through microscopic examination (31). According to one study, intensity scores of tumoral cells with Antoni A type were higher compared to Antoni B type (66). In another article, Attie *et al.* described a case of schwannoma originating from the lingual nerve (67). (Fig 1 and 2)

Definitive diagnosis of schwannoma is established via histopathological examination of the lesion, based on two typical tissue patterns (Antoni A and B) (36). By showing protein S-100 and nuclear export signal, fusiform Schwann cells could be used to identify the neural origin of different lesions. Therefore, immunostaining analysis is essential to the accurate diagnosis of schwannoma (4). According to several studies, protein S-100 (a specific neural tissue marker) is reported to be immunohistochemically positive (9, 36).

Fig 1 and 2 around is here.

In case of solitary, slow-growing lesions, excisional biopsy is recommended as an effective diagnostic measure. In their study, Martins *et al.* evaluated one female patient suspected with schwannoma within the fifth decade of her life. According to the findings, the lesion was accurately distinguished from other benign lesions based on the slow growth rate and circumscribed swelling without any particular features. The patient was referred for biopsy due to the presence of solitary, slow-growing lesions (4).

For the most part, treatment of schwannomas involves the surgical removal of the tumor, with preservation of the neighboring structures (36). If schwannomas are completely excised, there is a low risk of recurrence (4, 7).

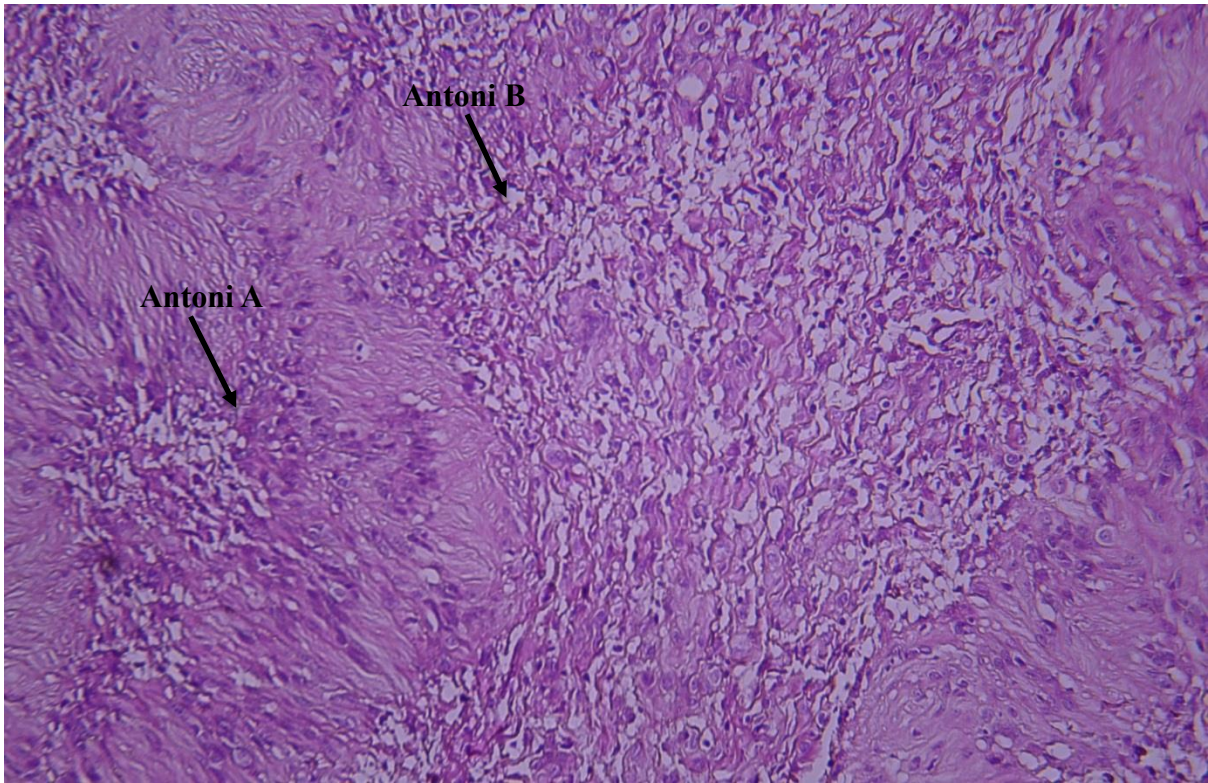


Figure 1. Photomicrograph showing histological section of oral schwannoma cells composed of proliferating groups of Schwann nuclei in Antoni A and Antoni B tissues forming Verocay bodies. (H & E. Original magnification $\times 100$)(Department of Oral and Maxillofacial pathology, Mashhad University of Medical Sciences)

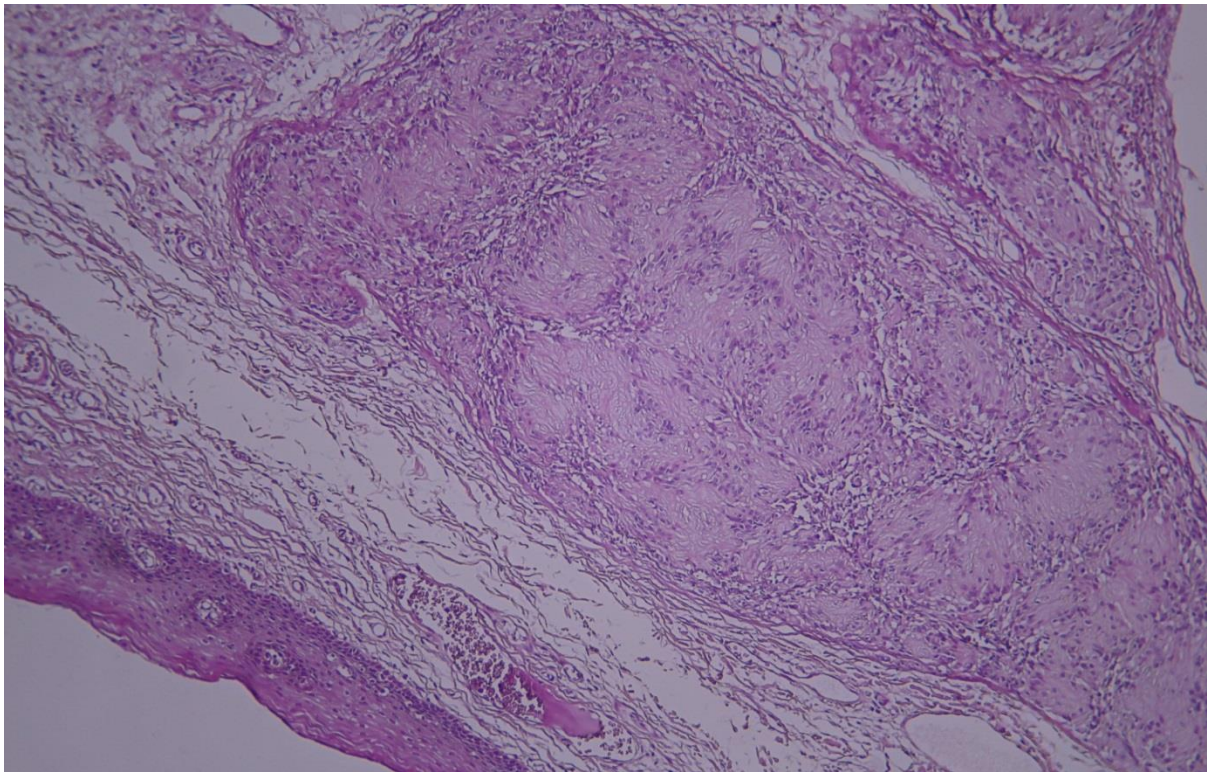


Figure 2. Photomicrograph showing histological section of oral schwannoma cells composed of proliferating groups of Schwann nuclei in Antoni A and Antoni B tissues forming Verocay bodies. Fibrosis (capsulated) tissue separated tumor cells from oral mucosa. (H & E. Original magnification $\times 40$) (Department of Oral and Maxillofacial pathology, Mashhad University of Medical Sciences)

Conclusion

According to the results of this study, evaluation of the differential diagnoses of schwannoma is of paramount importance since these tumors are normally indistinguishable from other benign lesions. In conclusion, histopathological examination and immunohistochemical analysis are essential to the accurate diagnosis of schwannoma. As for the treatment of these lesions, surgical excision of the tumor with preservation of the neighboring structures is the method of choice.

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