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ORIGINAL PAPER

Tongue Schwannoma: A Clinicopathologic Study of 19 Cases

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Abstract
Schwannomas commonly occur in the head and neck but infrequently involve the oral cavity and rarely affect the tongue. The clinical and pathologic features of 19 cases of schwannoma arising in the tongue were analyzed. There were 13 males and 6 females ranging in age from 12 to 82 years (mean 34 years; median 29 years). The majority of tumors presented as an asymptomatic mass localized to the anterior two-thirds of the tongue. Histologically, 18 schwannomas exhibited characteristic Antoni A and B areas with the former pattern predominating. One tumor was composed exclusively of cellular Antoni A tissue and was classified as a cellular schwannoma. Tumor encapsulation was variable with nearly half of the lesions lacking a well-defined fibrous capsule. All were strongly and diffusely positive for S-100 protein. No recurrences were observed on clinical follow-up. Schwannoma of the tongue, although rare, should be separated from other types of lingual nerve sheath proliferations and tumors.

Keywords Schwannoma · Peripheral nerve sheath neoplasm · Neurilemmoma · Tongue neoplasms · Tongue · Lingual · Oral cavity · S100 protein

Introduction

Peripheral nerve sheath tumors commonly occur in the head and neck region but are rarely encountered in the oral cavity. The reported frequency of oral peripheral nerve sheath tumors among all lesions affecting the oral cavity is approximately 0.2%, the majority of which are neurofibromas [1–3]. Schwannomas seldomly involve the oral region. Among intraoral sites, the tongue is the most commonly affected location, but overall lingual examples of schwannoma remain infrequent [4–7]. Due to their rarity, the reported literature documenting schwannoma of the tongue is limited to small series and single case reports [7–11]. In this study, the clinical and pathologic characteristics of 19 cases of schwannoma of the tongue were evaluated. This represents the largest series of this uncommon type of oral peripheral nerve sheath tumor to date.

Materials and Methods

Nineteen cases of schwannoma involving the tongue were identified from the files of the Departments of Pathology, Southern California Permanente Medical Group. Hematoxylin and eosin stained slides from all cases and previously performed immunohistochemical studies were reviewed. Clinical data, treatment, and follow-up was obtained from electronic medical records augmented by the surgical pathology reports. This clinical investigation was conducted in accordance and compliance with all statutes, directives, and guidelines of an Internal Review Board authorization (#5968) performed under the direction of Southern California Permanente Medical Group.

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Results

Clinical features

The clinical data are summarized in Table 1. Thirteen patients were male and six were female. The mean and median ages at diagnosis were 34.4 years and 29.0 years, respectively (range 12–82 years). The average age at diagnosis was 23.7 years for females and 39.4 years for males, but this was not a statistically significant difference ($p = 0.124$). Thirteen tumors involved the anterior two-thirds and six tumors involved the posterior one-third of the tongue. Clinically, all patients presented with a lingual mass or nodule (Fig. 1) of which 11 were noted to be slowly increasing in size. Four patients reported associated tongue pain localized to the lesion. The duration of symptoms ranged from 0.75 to 444 months (mean 43.0 months). Females, on average, experienced symptoms for a longer duration than males (48.7 vs 40.4 months) but without statistical significance ($p = 0.882$). There was no relationship between tumor size and duration of symptoms.

All tumors were completely excised through biopsy or local excision. Outcome information was available for all patients with clinical follow-up ranging from 0.25 to 102 months (mean 29.4 months). None of the patients developed local recurrence and none showed evidence of neurofibromatosis 2 (NF2) or other syndrome.

Table 1 Clinicopathologic features of nineteen cases of tongue schwannoma

Case	Age (years)	Sex	Location	Size (cm)	Follow up (months)
1	80	M	Anterior two-thirds	0.4	9
2	43	M	Anterior two-thirds	0.8	27
3	57	M	Anterior two-thirds	1.0	16
4	29	F	Posterior third	2.0	28
5	40	M	Anterior two-thirds	2.0	0.25
6	12	F	Anterior two-thirds	0.7	48
7	22	M	Posterior third	0.3	0.25
8	12	F	Anterior two-thirds	1.5	9
9	18	M	Anterior two-thirds	0.7	70
10	35	M	Posterior third	0.6	102
11	22	F	Anterior two-thirds	1.0	54
12	50	F	Posterior third	0.7	45
13	30	M	Anterior two-thirds	1.0	25
14	17	F	Anterior two-thirds	3.1	14
15	26	M	Anterior two-thirds	1.8	84
16	27	M	Posterior third	0.5	22
17	35	M	Posterior third	1.2	3
18	82	M	Anterior two-thirds	0.3	1
19	17	M	Anterior two-thirds	0.7	1

M male, *F* female

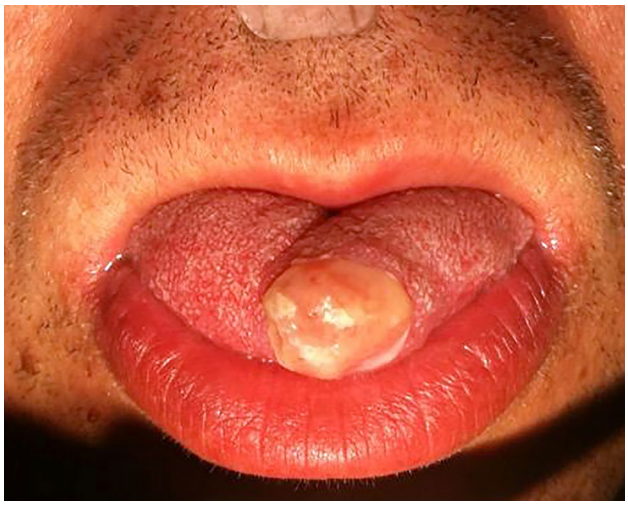

Fig. 1 A partially ulcerated mass identified on the anterior tongue of a male patient (courtesy Dr. B. L. Nelson)

Pathologic features

On gross examination, the tumors were described as nodular with firm, white to tan cut surfaces. Sizes ranged from 0.3 cm to 3.1 cm in maximum dimension (mean 1.1 cm). Females, on average, had larger tumors than males (1.5 cm versus 0.9 cm), but this was not statistically significant ($p = 0.076$). Microscopically, all tumors were sharply circumscribed (Fig. 2a). Ten tumors were surrounded by a thin fibrous capsule (Fig. 2b). The remaining tumors had smooth peripheral contours but were unencapsulated (Fig. 2c). Ulceration of the overlying surface epithelium was present in three cases (Fig. 2d). No nerve association was observed, and thus the myxoid change and nerve edema more frequently associated with painful schwannomas was not identified. Eighteen tumors exhibited the characteristic histologic Antoni A and B patterns of conventional schwannoma. The Antoni A zones were typified by cellular areas of compact spindle cells with elongated nuclei arranged in fascicles, whorls, or palisades. The less cellular Antoni B regions featured cobweb-like arrangements of spindle to ovoid cells in a myxoid stroma (Fig. 3a–c). Antoni A areas predominated in all tumors and well-formed Verocay bodies, characterized by parallel rows of palisaded nuclei separated by their aligned eosinophilic cell processes, were observed in seven cases (Fig. 3d). One tumor was uniformly cellular throughout and entirely composed of spindle cells with thin, elongated nuclei arranged in fascicles and whorls. It lacked Antoni B areas, nuclear palisading, and Verocay bodies and was thus classified as a cellular schwannoma (Fig. 4a). Five tumors showed prominent ectatic and dilated blood vessels with hyalinized walls (Fig. 4b). No cellular

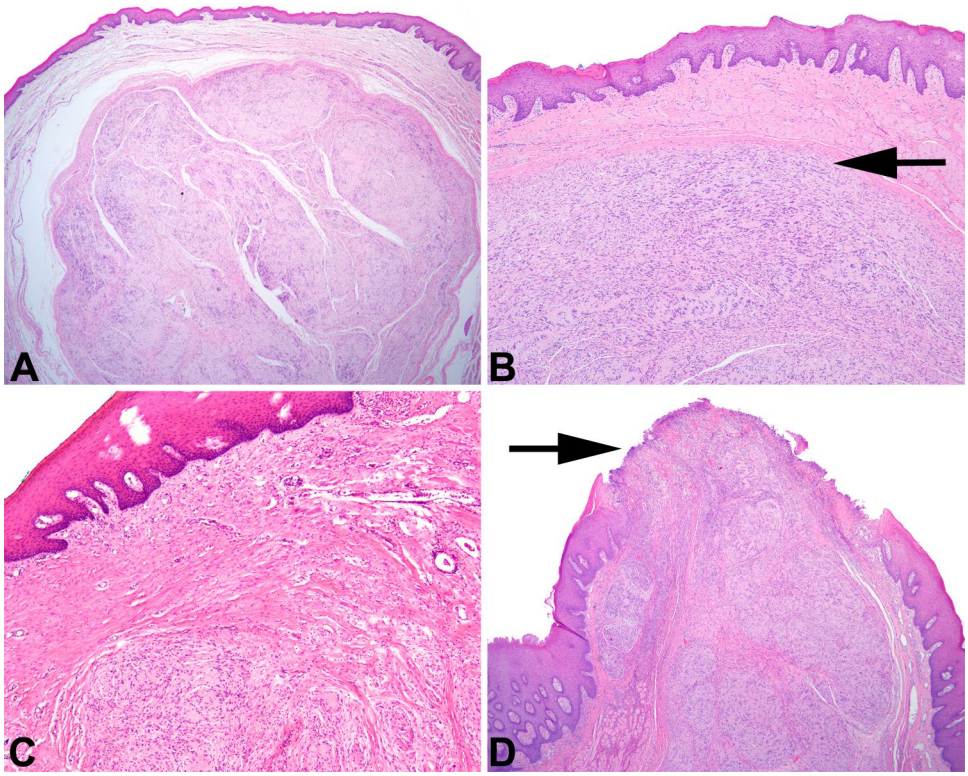

Fig. 2 **a** Schwannoma of the tongue presenting as a circumscribed submucosal nodule. **b** This example of lingual schwannoma is surrounded by a fibrous capsule (black arrow). **c** A subset of schwannomas of the tongue had well demarcated borders but lacked a well-defined capsule. **d** Unencapsulated schwannoma with surface ulceration (black arrow)

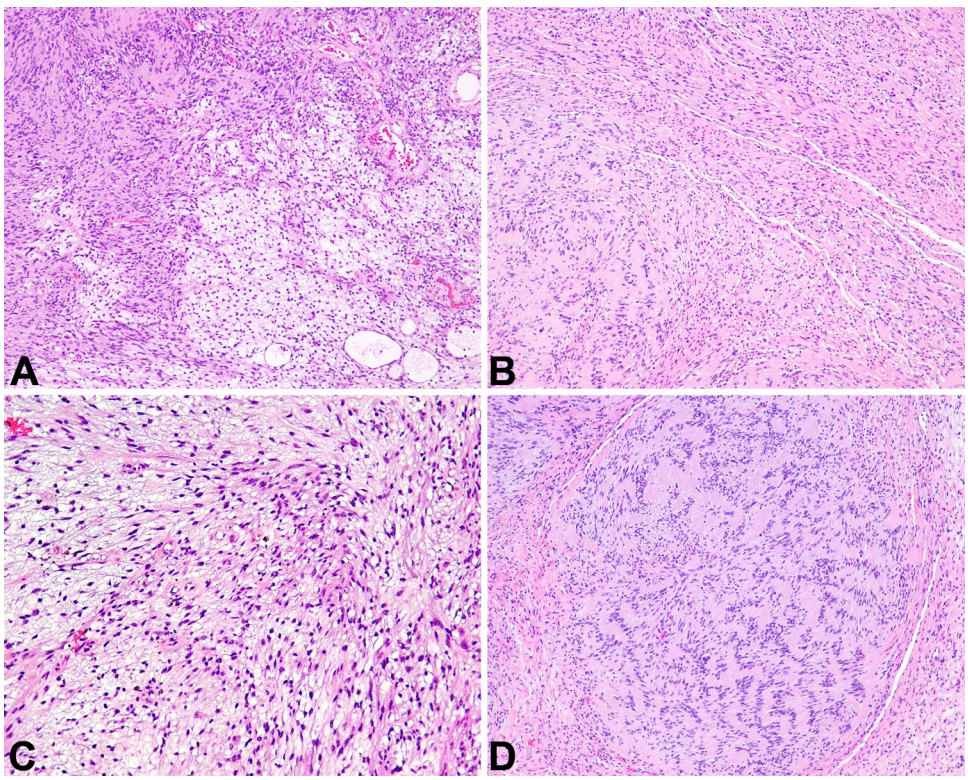

Fig. 3 **a** Typical biphasic histologic appearance of schwannoma of the tongue with compact cellular Antoni A area (left) adjacent to less cellular Antoni B area (right). **b** Antoni A tissue characterized by spindle cells arranged in short fascicles with areas of subtle nuclear palisading. **c** Antoni B tissue composed of loosely arranged ovoid to spindled cells in a myxoid stroma. **d**. Well-formed Verocay bodies

pleomorphism or nuclear atypia was identified in any case. Mitotic activity was not detected with the exception of the cellular schwannoma in which 2 mitoses/2 mm^2 were observed. All tumors exhibited strong and diffuse immunoreactivity for S-100 protein along with SOX10 in cases tested.

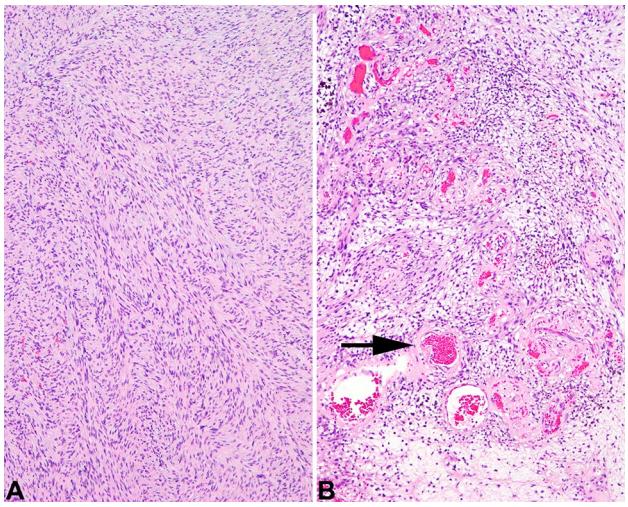

Fig. 4 **a** Cellular schwannoma consisting of intersecting fascicles of spindle cells. **b** Areas of prominent vascularity with ectatic and hyalinized blood vessels (black arrow) were infrequently observed in tongue schwannomas

Discussion

Schwannomas are neoplasms composed entirely or nearly entirely of differentiated neoplastic Schwann cells of the peripheral nerve. They are particularly common in the head and neck region but also seen along the flexor surfaces of the extremities where the vast majority present as solitary, sporadic lesions. Cranial nerve involvement, especially in the ear and temporal bone, is not uncommon especially in NF2 where bilateral lesions are characteristic [12]. Schwannomas rarely arise in the oral cavity, however, and infrequently affect the tongue. Approximately 150 cases of schwannoma of the tongue have been previously documented in the literature, predominantly as single case reports or small series [7–11, 13]. In the present study, nineteen schwannomas of the tongue were analyzed, representing the largest single series of these tumors to date.

While prior reports of lingual schwannoma demonstrated no sex predilection, males were affected twice as often as females in the present series [8–11, 13]. Patients presented at an average age of 34.4 years (median 29 years) which is younger than the peak incidence of 4th to 6th decades for other anatomic sites. The most common clinical presentation was that of a lingual mass or nodule, frequently associated with a history of gradual enlargement over time. Tumors were most frequently localized to the oral (anterior two-thirds) portion of the tongue, an observation congruent with prior reports [7–10]. Patients were generally asymptomatic with only occasional complaints of pain. Interestingly, pain is usually identified in patients with schwannomatosis rather than sporadic cases, and nerve edema and myxoid change have been correlated to this symptom [14]. No nerve association was seen in the present series; thus, the reason for the painful lesions could not be determined histologically. While not observed in the present patient cohort, lingual schwannomas may uncommonly cause dysphagia, dysarthria, or airway comprise which appears to relate to involvement of the base of the tongue [8, 9, 13, 15]. Schwannomas of the tongue are benign neoplasms adequately treated by simple excision. All patients in the current series experienced an uneventful clinical course with no instances of recurrence.

In general, schwannomas affecting the tongue morphologically resemble those occurring in the peripheral soft tissues with some important differences. Typical histologic features of schwannomas include admixed cellular Antoni A areas, composed of compact spindle cells, and less cellular, loosely textured Antoni B areas. Notably, the majority of lingual schwannomas appear to be relatively cellular with Antoni A tissue predominating. While a well-formed fibrous capsule is considered a characteristic feature of most soft tissue schwannomas, nearly half of the lingual schwannomas in the current series were unencapsulated. This observation is consistent with the frequent finding of capsular absence in mucosal based schwannomas of other oral cavity sites [16, 17]. This may be related to the originating nerves lacking an epineurium. Tumors of the CNS parenchyma and other viscera are also usually unencapsulated. Another difference between lingual schwannomas and those of other sites pertains to the vascularity of these lesions. In contrast to soft tissue schwannomas, where conspicuous vascularity in the form of dilated or ectatic hyalinized blood vessels is a typical feature, this was an uncommon finding in lingual schwannomas in this series. As expected of schwannomas of any site, those of the tongue exhibit strong and diffuse nuclear and cytoplasmic S-100 protein expression and extensive nuclear SOX10 in the majority of the lesional cells [18].

Although the presence of typical histologic features allows recognition of lingual schwannoma in most instances, the diagnosis can occasionally be challenging due to overlapping clinical presentations and morphologic features with other peripheral nerve sheath lesions that also occur at this site.

Traumatic neuroma is among the most frequent nerve sheath lesion to involve the oral cavity and commonly affects the tongue [1, 19]. A clinical history of trauma can be helpful but may be absent due to the slight nature of the trauma in some cases. In contrast with schwannoma, which is composed exclusively of Schwann cells, the cellular constituents of traumatic neuroma include axons and perineurial cells as well as Schwann cells. Schwannomas lack the microfascicular cellular arrangement and dense fibrocollagenous stroma characteristic of traumatic neuroma. Also, alternating

Antoni A and B areas and nuclear palisading are not features of traumatic neuroma.

Mucosal neuroma is also a consideration in the differential diagnosis of lingual schwannoma. Unlike schwannomas, mucosal neuromas are characterized by aggregates of prominent, hypertrophic nerves of varying size and shape, comprised of axons and Schwann cells, and often accompanied by a thickened perineurium. Schwannomas typically lack axons, and well-defined palisading is not usually seen in a neuroma.

Ganglioneuroma is a neurogenic tumor consisting of Schwann cells admixed with a variable number of mature ganglion cells. Tumors comprised predominantly of spindled Schwann cells, with a paucity of ganglion cells, can mimic the appearance of a schwannoma. These cases may require careful examination for the presence of a ganglion cell component for correct diagnosis.

Solitary circumscribed neuroma (formerly palisaded encapsulated neuroma) affects various locations within the oral cavity, most often the lips, but may be difficult to distinguish from a lingual schwannoma if located on the tongue [19, 20]. Similar to schwannoma, solitary circumscribed neuroma arises as a well-circumscribed nodule that is often unencapsulated. The tumor is composed of bland spindled cells with wavy nuclei set in a hyalinized collagen background. The spindle cells are arranged in short fascicles often separated by artefactual clefts. In contrast with schwannoma, nuclear palisading is frequently focal and subtle, and well-formed Verocay bodies are rare [20]. Hypocellular Antoni B areas, myxoid stroma, and prominent vessels, if present, are features favoring schwannoma over solitary circumscribed neuroma.

Lingual schwannomas should be distinguished from neurofibroma, as the latter can be potentially associated with neurofibromatosis type 1 [21, 22]. Histologically, the lesional spindle cells of a neurofibroma are uniformly distributed throughout the tumor and set in a collagenous to myxoid stroma. This is in contrast to the biphasic appearance of schwannoma created by the alternating dense cellular Antoni A tissue and less cellular Antoni B tissue. Additional features favoring a diagnosis of schwannoma over neurofibroma include the presence of nuclear palisading, Verocay bodies, and prominent vascularity.

One of the tumors in the present study was classified as a cellular schwannoma. This histologic variant of schwannoma may be difficult to distinguish from a malignant peripheral nerve sheath tumor or spindle cell melanoma. Morphologic features favoring a cellular schwannoma include a well-defined capsule, cellular whorls, collections of macrophages, vascular hyalinization, and minor foci of Antoni B tissue. Conversely, areas of geographic necrosis and increased mitotic activity ($> 10/2\ mm^2$) suggest a diagnosis of malignant peripheral nerve sheath tumor [23]. The presence of diffuse and strong positivity for S-100 protein suggests a cellular schwannoma, as malignant peripheral nerve sheath tumors most commonly exhibit only focal or patchy S-100 protein expression. Loss of H3K27me3 expression by immunohistochemistry also supports a diagnosis of malignant peripheral nerve sheath tumor [24]. Melanoma generally shows infiltration, cellular pleomorphism, prominent nucleoli, intranuclear cytoplasmic inclusions, and reactivity with HMB45, Melan-A and tyrosinase, along with S100 protein and SOX10.

In summary, the present series of schwannomas of the tongue represents the largest clinicopathologic analysis of this uncommon tumor to date. Based on our findings, the typical clinical presentation is that of an asymptomatic lingual mass, with males more commonly affected in the 4^{th} decade of life. The clinical course is benign with no risk of recurrence. Schwannomas arising in the tongue exhibit similar microscopic features to those occurring in other soft tissue sites; however, lingual schwannomas are often unencapsulated and frequently lack the prominent vasculature characteristic of soft tissue schwannomas. Schwannomas of the tongue should be distinguished from other tumors and tumor-like proliferations of peripheral nerves which may also occur at this anatomic site.

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Compliance with Ethical Standards

Conflict of interest All authors declare that they have no conflict of interest as it relates to this research project.

Ethical Approval All procedures performed in this retrospective data analysis involving human participants were in accordance with the ethical standards of the institutional review board (IRB #5968), which did not require informed consent.

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