—Case Reports—

Relationship between Tumor Diameters and Antoni Classification for Schwannoma of the Lower Lip

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Schwannoma is an uncommon benign tumor in the oral and maxillofacial region, and development of schwannoma in the lower lip is rare. Herein, we present the case of a 68-year-old woman who visited Nihon University Itabashi Hospital complaining of a painless mass in the lower lip. The lesion was surgically resected under local anesthesia. On histopathological examination, the resected specimen was a mixture of Antoni types A and B schwannoma. No recurrence has been seen over a postoperative follow-up period of 58 months. In the schwannoma of the lower lip, the mean tumor volume was compared for type A and the mixed type, which tended to be larger in the mixed type. No previous reports have described the relationship between the size of schwannoma in the lower lip and Antoni classification. Therefore, this report discusses the possibility of a relationship between tumor size and Antoni classification for schwannomas in the lower lip. (J Nippon Med Sch 2022; 89: 629–633)

Key words: Antoni classification, lower lip, schwannoma

Introduction

Schwannoma is a benign ectodermal tumor derived from the Schwann cells of the nerve sheath and fibroblasts of the perineural membrane, and mostly occurs in the subcutaneous region of the limbs or head and neck[1,2]. This tumor rarely occurs in the oral cavity, with cases in the lips representing only 0.9% of all cases that develop in the oral cavity[3]. Intraoral schwannoma most frequently arises in the tongue, followed by the palate, floor of the mouth, gingiva, and buccal mucosa[1]. Histopathologically, schwannoma is classified as Antoni type A, Antoni type B, or a mixture of Antoni types A and B. Herein, we describe the case of a woman with a schwannoma in the lower lip and compare the details of this case with previous reports of schwannoma.

Case Report

A 68-year-old woman was referred to Nihon University Itabashi Hospital with a painless swelling in the left side of the lower lip in January 2016. She had first noticed the swelling with no accompanying symptoms about 6 months earlier. Her only significant medical history was allergic dermatitis.

Initial examination revealed swelling of the left side of the lower lip, but her face was almost symmetrical with no apparent swelling of regional lymph nodes. Intraoral examination showed an elastic, hard, mobile mass in the left side of the lower lip with no spontaneous pain or tenderness. No impairment of tongue sensation or signs of infection or inflammation were evident. Ultrasonography revealed a tumor approximately 9 × 4 × 5 mm in size in the subcutaneous fat layer of the left side of the lower lip. The lesion had clear borders with a circular to elliptical shape and uniform internal echogenicity. No blood flow signal was apparent in the tumor.

On magnetic resonance imaging, a well-defined mass measuring 8 × 6 × 6 mm was observed in the left side of the lower lip. The lesion showed hyperintensity on T2-

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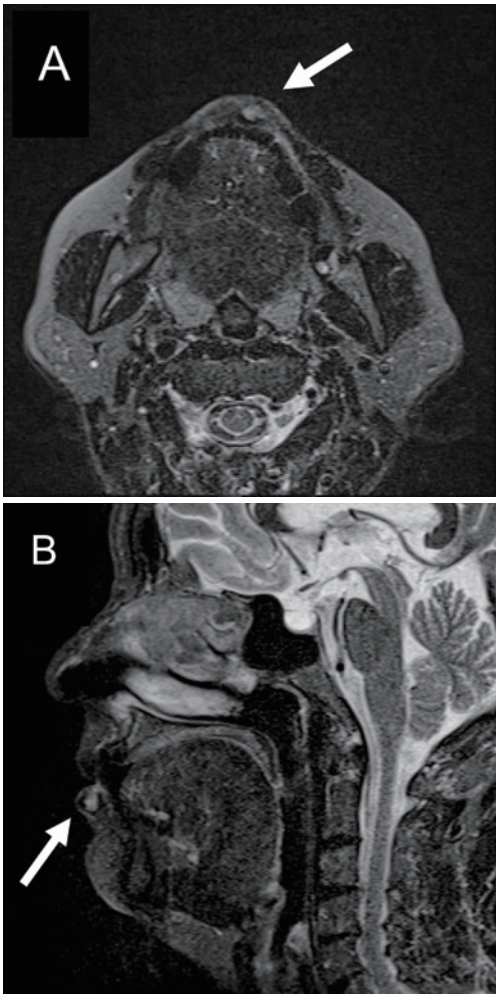

Fig. 1
T2-weighted imaging reveals a well-defined mass confined to the lower lip and in contact with the orbicularis muscle.
A: Axial view
B: Coronal view

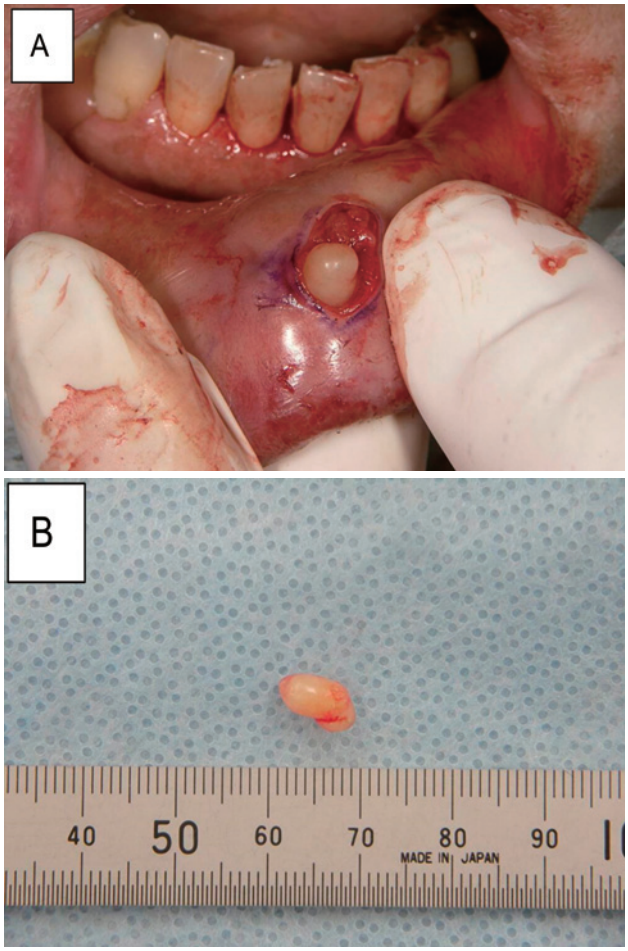

Fig. 2
A: Intraoperative view of removal of the encapsulated tumor in the lower lip.
B: The surface of the extracted tumor is covered with a thin, fibrous coat. The cut surface appears fulminant and yellowish in color.

weighted imaging (**Fig. 1A, B**) and hypointensity on T1-weighted imaging.

The clinical diagnosis was lower lip tumor. Tumorectomy was performed under local anesthesia in February 2016, via a 15-mm-long incision along the intraoral wrinkle line at the transition point of the lip on the left anterior part of the mandible. The tumor was resected en bloc and histopathological examination of the excised material was conducted to reach a diagnosis.

The tumor was found to be covered by a membrane and was easily separated from the surrounding tissue (**Fig. 2A**). The resected tissue measured 8 × 5 × 5 mm in size (**Fig. 2B**). On cross-section, the tumor was solid in texture and yellowish in color.

On histopathological examination, the tumor was observed to be surrounded by a fibrous membrane. The tumor parenchyma consisted of wavy, spindle-shaped nuclei and a complex array of fibrous tumor cells with acidophilic cytoplasm, with scattered fence-like arrays of tumor cells (**Fig. 3A～C**). Immunohistochemically, the tumor cells were positive for S-100 protein (**Fig. 3D**) and negative for both α-smooth muscle actin protein and desmin protein (data not shown). Based on these histopathological findings, mixed Antoni type A and B schwannoma was diagnosed. As of 58 months postoperatively, no signs of recurrence have been observed.

Discussion

Schwannoma is a benign tumor of the ectodermal system derived from Schwann cells. The most common site of the tumor is the head and neck region, and schwannomas frequently affect the lateral neck and auditory nerve[1]. Schwannomas develop infrequently in the oral cavity region, with an extremely low incidence rate of

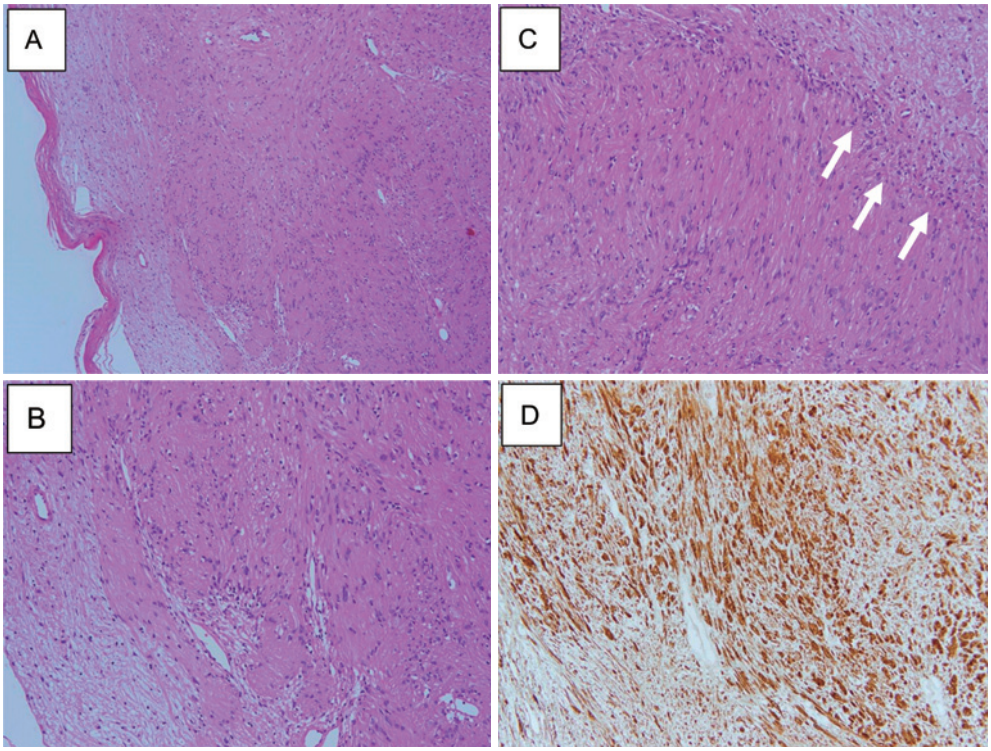

Fig. 3
A: Histopathological examination reveals a well-defined, solid nodular tumor under the lower lip mucosa (hematoxylin and eosin (HE) × 100).
B: Antoni A and B type cells are found mixed together (HE × 200).
C: Antoni A type cells presenting a fence-like arrangement are found (arrow) (HE × 200).
D: Tumor cells are positive for S100 protein (S100 × 200).

0.9% in the lips[3]. Age at onset of schwannoma is most commonly 10-29 years according to Hatziotia and Asprides[1], and 30-40 years according to Willis[2]. Schwannomas have been variously reported as either more common in females[2] or showing no sex predilection[1]. Histopathologically, schwannomas are categorized according to the Antoni classification as Antoni type A and Antoni type B, which display distinct growth patterns. In type A schwannoma, the nuclei show a prominent palisading arrangement due to the dense proliferation of regularly arranged spindle-shaped epithelial cells, also known as a watchtower-like arrangement. Type B tumor cells do not show this characteristic palisading structure of type A tumors. The tumor cells are instead sparsely and irregularly distributed, with hemorrhage, mucous degeneration and a cystic structure often being observed. Mixed-type tumors demonstrate a combination of both arrangements of tumor cells. Type A has been described as occurring most commonly in the jaw and oral cavity, while type B and mixed-type schwannomas are less common in this region[1].

A search of the literature identified 11 cases of schwannoma of the lower lip, including the present case, and excluding duplicate reports[3–9] (**Table 1**). Age at the time of schwannoma diagnosis ranged from 7 to 69 years (mean, 30.1 years). This result was consistent with the report by Willis[2]. The sex ratio was almost even, with five males and six females, consistent with the report by Hatziotia and Asprides[1]. The interval from initial onset to hospital visit ranged from about 1 month to 10 years, which might reflect the slow growth of this tumor. Most tumors were 10-30 mm in maximum diameter, and all were easily removed en bloc. Histopathologically, five of the cases were Antoni type A, and six were mixed type A and B schwannomas.

For unknown reasons, no cases of Antoni type B schwannoma have been reported in the lower lip. In general, schwannomas have a mixed type, and smaller schwannomas tend to be only type A[10]. Type B schwannoma is also characterized by secondary changes, such as edematous changes in the substrate, and these secondary changes are related to tumor size. As the tumor grows, the blood supply to the tumor becomes compromised, and secondary changes arise in the tumor[10]. We therefore hypothesized that type B schwannoma might not occur in the lower lip due to the physical constraints on tumor

Table 1 Reported cases of schwannoma of the lower lip

	Age	Gender	Evolution	size (mm)	tumor volume (mm^3)	Antoni classification
Yaghoobi et al. 2008[4]	25	M	6 months	10 × 10 × 10 mm	500 mm^3	Antoni A
Yaghoobi et al. 2009[4]	7	M	6 months	7 × 5 mm	87.5 mm^3	Antoni A
Tsushima et al. 2012[3]	69	F	1 year	13 mm	1,098.5 mm^3	mixed
Tsushima et al. 2012[3]	44	F	3 years	3 mm	13.5 mm^3	Antoni A
Shilpa et al. 2012[5]	40	F	10 years	20 × 15 mm	2,250 mm^3	mixed
Gudi et al. 2013[6]	21	F	6 months	10 × 10 mm	500 mm^3	mixed
Dhua 2015[7]	18	F	10 years	30 × 30 mm	13,500 mm^3	mixed
Ravindran et al. 2017[8]	16	M	1 month	20 × 15 mm	2,250 mm^3	Antoni A
Yaghoobi et al. 2019[4]	16	M	1 year	7 × 5 mm	87.5 mm^3	Antoni A
Menezes et al. 2020[9]	7	M	2 months	8 mm	256 mm^3	mixed
Case. 2020	68	F	6 months	8 × 5 × 5 mm	100 mm^3	mixed

size at this location. In previously reported cases, mean tumor diameter was 9.4 ± 5.7 mm for type A, and 14.8 ± 7.9 mm for mixed type schwannomas. Tumor volume was calculated as the major diameter x minor diameter^2 × 0.5. Mean tumor volume was 587.7 ± 846.7 mm^3 for type A and 2,950.8 ± 4,771.5 mm^3 for the mixed type. The mixed type, which includes type B components, thus tends to be larger. Evaluation of cases occurring in tissues of the oral cavity other than the lower lip demonstrated one case with a tumor in the floor of the mouth[3], in which the tumor diameter of 25 mm was larger than the average size of tumors present in other cases. In other words, the lack of previous reports of type B schwannomas in the lower lip might be because schwannomas that develop in the lower lip tend to be small, while type B tumors tend to be comparatively large. However, since the lower lip is relatively easy to observe, tumors in this region might be detected before they grow further, allowing early treatment to be instituted in many cases. This study suggests that a relationship exists between Antoni type and tumor size in schwannomas that arise in the lower lip.

Change in the Antoni classification may be induced by the tumor size. This hypothesis is extremely important when deciding on the timing of a surgical approach. In type A cases, histopathological examination shows characteristic fenestrated nuclear structures. However, in type B, the arrangement is disrupted and the tumor grows randomly. This characteristic of type B may be related to malignant transformation of the tumor. In fact, the pathological findings of type B have much in common with malignant lesions[10]. Performing resection as early as possible, while the tumor is still type A, is therefore important.

The diagnosis of a mass on the lower lip requires the differentiation of several diseases. These include cystic diseases such as mucous cyst, dermoid cyst and epidermoid cyst, benign tumors such as fibroma and pleomorphic adenoma, and malignant tumors such as mucoepidermoid carcinoma and adenoid cystic carcinoma. In particular, mucous cyst occurs most frequently in the soft tissues of the oral region. Mucous cyst must thus be distinguished from other mass lesions of the lips.

Neurological schwannomas are most commonly treated surgically, and symptoms of postoperative neurological nerve damage are often problematic. Identification of the nerve of origin of the schwannoma is reportedly rare. In the current case, the tumor was considered to have arisen from the mental nerve because of its proximity, but no obvious peripheral nerves were identified intraoperatively and no postoperative neurological symptoms were reported. The incidence of malignant transformation of schwannomas is extremely low. However, recurrence of malignant schwannoma has been described, indicating that careful observation of the disease course is warranted[3].

In conclusion, the reason that Antoni type B schwannomas have never been described in the lower lip might involve limits on the size of schwannomas in the lower lip. Schwannomas should be resected as early as possible to avoid progression from type A toward type B.

Conflict of Interest: The authors declare that they have no competing interest.

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