Case Report

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Upper Labial Mucosa Schwannoma: A Rare Case Report

Pathology Section

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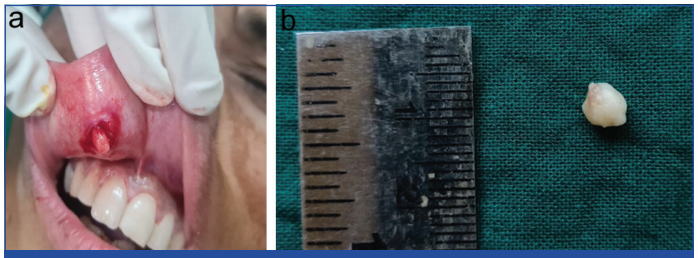
ABSTRACT

An upper lip swelling, asymptomatic, and benign-looking lesion may be attributed to numerous aetiologies. About 25% to 45% of Schwannomas/Neurilemmomas occur in the head and neck region and are seldom seen in oral sites, accounting form only 1% of cases. Herein, the authors presented a case report of a 36-year-old female patient with a clinical appearance of upper labial mucosa swelling is mentioned, which mimicked a mucocele. It was a single, smooth, oval, fluctuant, and non tender swelling. Complete surgical excision was performed following proper protocol, and histological diagnosis revealed a well-outlined lesion enclosed within a fibrous capsule. The connective tissue mass of the tumour consisted predominantly of neural tissue arranged in Antoni A structures, characterised by a palisaded nuclear arrangement and the presence of distinctive eosinophilic Verocay bodies. Another area with a myxoid appearance, representing Antoni B structure, was also present, suggesting a Schwannoma/Neurilemmoma. During follow-up, complete healing with no recurrence of swelling was observed. Schwannomas/Neurilemmomas in the head and neck region are less common, particularly in the oral cavity. According to various studies, the occurrence of neurilemmomas in the intraoral aspect accounts for only 19.24% of cases, specifically involving the mucosa of the lip. Practitioners should consider this rare entity of Schwannoma/Neurilemmoma when evaluating an upper lip swelling routinely.

Keywords: Immunohistochemistry, Neurilemmoma, Upper lip swelling, Verocay bodies

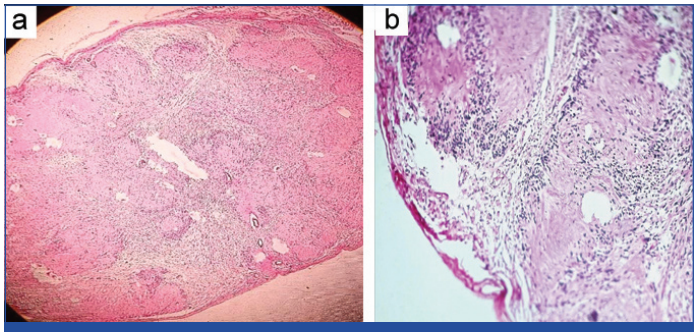
CASE REPORT

A 36-year-old female patient reported to the Outpatients Department (OPD) of Oral Medicine and Radiology with a chief complaint of painless swelling inside her mouth on the right-side of the upper lip. The swelling had been presented for two months. The patient's medical history was unremarkable. Upon examination, no noticeable facial asymmetry was observed, but the patient did experience slight discomfort during normal functions. Intraoral examination revealed a 5x8 mm ill-defined, smooth-surfaced lesion without ulceration, located near the right maxillary central and lateral incisors. The swelling appeared oval in shape and was non pedunculated. Palpation of the swelling revealed it to be non tender, nodular, and fluctuant, with no blanching when the upper lip was stretched [Table/Fig-1a]. A provisional diagnosis of mucocele was made based on the small size, fluctuant nature, and location of the lesion. Routine blood investigations were performed before the surgery, and the results were within normal limits. Excisional biopsy was performed under local anaesthesia with all necessary aseptic precautions. The swelling was completely removed and sent for histological staining and examination. Gross pathology revealed an oval-shaped, whitish lesion with a soft consistency [Table/Fig-1b].



[Table/Fig-1]: a) Oval shaped growth on labial musosa of upper lip; b) Gross pathology.

Histopathological investigation using Haematoxylin and Eosin (H&E) staining demonstrated a well-outlined lesion enclosed within a fibrous capsule. The connective tissue mass of the tumour consisted predominantly of neural tissue arranged in Antoni A structures [Table/Fig-2a,b], characterised by a striking palisaded nuclear arrangement and the presence of distinctive eosinophilic Verocay bodies. Another area with a myxoid appearance, representing Antoni B structures, was also present. Areas of blood vessels with thrombus formation could be seen interspersed throughout the tumour mass. Based on these features, the diagnosis was schwannoma or neurilemmoma of the upper lip.



[Table/Fig-2]: a) Encapsulated lesion with cellular in nature (H&E, 4X). b) Spindle cells with wavy nuclei to round to ovoid nuclei indistinct cytoplasmic borders arranged in interlacing fascicles (H&E, 10X).

There was no requirement for Immunohistochemistry (IHC) markers to be used in the present case. During follow-up, complete healing was observed with no recurrence of swelling.

DISCUSSION

Schwannomas or neurilemmomas are uncommon tumours that predominantly originate from peripheral nerves, specifically the perineural Schwann cells. They can occur in any type of nerve, including somatic or sympathetic nerves, and are typically found in deeper soft tissues [1]. These tumours are also referred to as neurilemmomas, neurinomas, or perineural fibroblastomas [1]. They often develop in the head and neck region due to the specific anatomy of this area, with the parapharyngeal space of the neck being the most common location [2]. Schwann cells, which envelop neurons and their axons, are usually affected by these tumours, involving the peripheral, cranial (except the optic and olfactory), spinal, and

autonomic nervous systems [2]. While no known predisposing factors exist, it is believed that trauma may be a contributing cause. Recent studies suggest that a defect in the merlin protein may be responsible for both sporadic and genetic schwannomas [2]. Approximately 25% to 45% of schwannomas occur in the head and neck region, and they are rarely seen in oral sites, accounting for only 1% of reported cases [1]. According to various studies, neurilemmomas in the intraoral aspect occur in the lip mucosa in just 19.24% of cases [3]. The present case report described a rare case of schwannoma in the head and neck region, specifically in the upper lip, where the specimen was initially diagnosed as a mucocele.

A literature search from 1966 to 2002 revealed only six documented cases of schwannoma of the upper lip [4]. A recent PubMed search within the last 10 years identified an additional four cases of upper lip schwannomas. Krishnan B et al., reported a case of upper lip swelling in a 28-year-old female patient that resembled an adenoma but was histologically diagnosed as a schwannoma. However, the present case involved the extraoral surface of the lip on keratinised mucosa, in contrast to the present case which involved the intraoral surface on non keratinised mucosa [5]. Hajong R et al., presented a case of a 14-year-old female patient with a swelling on the extraoral surface of the upper lip, initially clinically diagnosed as a lipoma but later confirmed as a schwannoma [6]. The present case also presented on the extraoral surface of the labial mucosa with a firm consistency, similar to the findings reported by Krishnan B et al., [5]. Haigh T et al., reported a similar case in a 23-year-old female patient with a small upper lip swelling, initially clinically diagnosed as a mucocele [7]. Desai J reported a paediatric case of a 14-year-old male patient with a differential diagnosis of traumatic fibroma, labial minor salivary gland tumour, or swelling secondary to trauma. The lesion was located in the intraoral part of the upper lip and had a moderately hard consistency [8]. However, the age group of these two cases did not match the present case. Another case involved a 16-year-old male patient with Neurofibromatosis type 1 (NF-1) who presented with a tumour-like lesion on the upper lip, clinically diagnosed as a neurofibroma. The patient had multiple café-au-lait spots on the entire body and ephelides on the face. Surgical resection of congenital melanocytic nevi on the back and thigh was performed, and histopathological examination revealed a Wagner-Meissner neurilemmoma [9]. Humber CC et al., reported a case of an 82-year-old woman with a long-standing firm swelling on the upper lip. The patient experienced intermittent mild paresthesia in the region, and clinically, the lesion was suggestive of a benign mesenchymal origin [10]. In comparison to the present case, the swelling was firm, and the presence of paresthesia was noted, making it the oldest case reported.

Clinically, benign schwannomas are slowly progressing, encapsulated nodular lesions that are typically solitary. In general, they are symptomless, although pain and paresthesia may occur. As they grow, the lesions can displace adjacent nerves [10]. The clinical symptoms of schwannomas vary depending on the origin of the nerve. Schwannomas can be found spontaneously or in conjunction with familial tumours and syndromes such as NF2, schwannomatosis, and Carney's complex [2]. Schwannomas can occur in individuals of all age groups, but they are most common in the third and fourth decades of life. Various studies have reported different rates of sex predilection, although most indicate an equal sex distribution. Schwannomas are typically not attached to deep tissues and are freely mobile, although movement may be restricted when they are adjacent to a large nerve or trunk [10]. Clinically, differential diagnosis can include other benign lesions such as fibroma, lipoma, neurofibroma, salivary gland tumours, certain dermal cysts, and even lymphatic origin tumours. However, histologically, schwannomas can be differentiated from other neural lineage lesions like neurofibromas and neuromas, as well as tumours of muscular or fibroblastic origin [11].

Radiological examinations such as a Contrast-enhanced Computed Tomography (CECT) scan and Magnetic Resonance Imaging (MRI) are required to assess the extent of the tumour and for histopathological diagnosis. Treatment typically involves surgical excision of the lesion, which has a low but rare recurrence rate. The potential transformation of a benign schwannoma of the oral cavity into malignancy is still a subject of debate but remains a concern [11].

Gross pathology of schwannomas typically reveals smooth, nodular ovals with occasional visibility of the nerve of origin. The cut surface of the tumour appears tan or yellow. Histologically, schwannomas exhibit well-encapsulated lesions with areas composed of fascicles of spindle-shaped Schwann cells (referred to as Antoni A pattern). These areas may merge with or transition to more loosely arranged areas with microcysts (referred to as Antoni B pattern). A common feature of schwannomas is the presence of palisading nuclei, forming parallel nuclear arrays known as Verocay bodies, although this feature is not observed in vestibular area lesions [12]. Large tumours often demonstrate extensive degenerative changes, including thick hyalinisation, thrombosis, ectatic blood vessels, haemorrhagic areas, lipidisation, calcification, and cystic changes. These vascular changes may lead to infarct-like areas of necrosis [12]. Tumours with such extensive degenerative changes are referred to as "ancient schwannomas" and may exhibit nuclear atypia, often leading to misdiagnosis as malignant lesions. Mast cells are rare components of schwannomas but are commonly found in neurofibromas and Malignant Peripheral Nerve Sheath Tumours (MPNSTs). Schwannomas may also exhibit areas with an epithelioid morphology [13]. The histological variants of neurilemmoma include conventional, cellular, plexiform, and melanotic variants. The most common variant is the conventional schwannoma, while large, old tumours exhibiting nuclear atypia are classified as ancient schwannomas, which is a subvariant of conventional schwannoma [13].

While the conventional H&E stain is considered the gold standard for pathology diagnosis, IHC plays a crucial role in surgical pathology. IHC is a more precise method that can further distinguish between morphologically similar findings on H&E stain by utilising specific markers. This not only aids in the interpretation of a precise diagnosis based on the cell of origin but also helps in selecting appropriate therapy for each individual case. Therefore, IHC has become an integral part of the diagnostic armamentarium in neuropathology. [Table/Fig-3] presents the IHC markers that have been studied thus far to differentiate between different variants of schwannoma, such as cellular, plexiform, and melanotic types [2,3,13-16]. [Table/Fig-4] provides insights into the IHC markers relevant to the differential diagnosis of schwannomas from other neural origin lesions, neurofibromas, perineuromas, and MPNSTs [14-26]. Finally, [Table/Fig-5] summarises previously reported cases of neurilemmomas since the year 2000 [4-10].

IHC marker	Cellular schwannoma	Plexiform schwannoma	Melanotic schwannoma
GFAP [14]	Variable expression	Strongly positive	Negative
S100 [15],[16]	Strongly positive with uniform and diffuse staining	Strongly positive with uniform staining	Positive
PRKAR1a [16]	Negative	Negative	Positive
Melan-A [16]	Negative	Negative	Positive
HMB-45 [16]	Negative	Negative	Positive
Type IV collagen [2]	Negative	Negative	Positive
Laminin [2]	Negative	Negative	Positive
CDH4 [13]	Positive	-	-

[Table/Fig-3]: IHC markers which distinguish between different variants of schwannoma [2,3,13-16].
IHC: Immunohistochemistry; GFAP: Glial fibrillary acidic protein; PRKAR1a: Protein kinase a; HMB-45: Human melanoma black-45; CDH4: Cadherin-4

IHC marker	Schwannoma	Neurofibromas	Perineuriomas	Malignant peripheral nerve sheath tumors
S-100 [14,15,17-19]	Strong and diffuse nuclear and cytoplasmic	Moderately positive	Negative	Mild or moderate only in epithiloid varient
Leu-7 antigen [16]	Mild or negative	Mild or negative	-	-
SOX10 [17, 18]	Extensive nuclear staining, strongly positive	Strongly positive	-	Mild to moderate staining
Calretinin [19]	Strongly positive	Mild	-	-
Ki 67 [19, 20,26]	Mild to moderate staining	-	Positively stained	Moderate to strong staining
Nestin [14], 21]	Moderate to negative staining	Moderately staining	-	Moderately staining
TLE1 [19,21]	Strongly positive	Mild to moderate staining	-	Mild to moderate staining
EMA [17,19, 22,23]	Negative	Negative	Positively stained	Positively stained
CD34 [21,23,24]	Strongly positive	Strongly positive	Positive	Mild to moderate staining
Podoplanin [24]	Moderately staining	Negative	-	Mild to moderate staining
CD56/PGP9.5 [14,25]	Moderately staining	Moderately staining	-	Moderately staining

[Table/Fig-4]: IHC markers pertaining to differential diagnosis of schwannomas , neurofibroma, perineuromas and malignant peripheral nerve sheath tumor [14-26].
Blank space, no information obtained by this marker; SOX10: Sry-related HMg-Box gene 10; CD34: Cluster of differentiation 34; TLE1: Transducin-like enhancer of split 1; PGP: Protein gene product; EMA: Epithelial membrane antigen; GFAP: Glial fibrillary acidic protein; IHC: NSE: Neuron-specific enolase; MPNST: Malignant peripheral nerve sheath tumour

Author	Age/sex	Location	Differential diagnosis
Yang SW et al., [4]	22 years/female	Upper lip	NA
Krishnan B et al., [5]	28 years/female	Upper lip	Adenoma
Hajong R et al., [6]	14 years/female	Upper lip	Lipoma
Haigh T et al., [7]	23 years/female	Upper lip	Mucocele
Desai J [8]	14 years/male	Upper lip	Fibroma/labial minor salivary gland tumour, or swelling secondary to trauma
Miyasaka C et al., [9]	14 years/male	Upper lip	Neurofibroma
Humber CC et al., [10]	82 years/female	Upper lip	Mesenchymal tumours

[Table/Fig-5]: Reported cases of benign schwannomas of the upper lip since 2000 [4-10].
NA, data not available

CONCLUSION(S)

Benign schwannomas are a pathology that is often overlooked in clinical practice. Differential diagnosis must be considered in conjunction with numerous benign neoplasms originating from epithelial and connective tissues, as well as malignant tumours. Immunohistochemical characteristics can be helpful in determining neural differentiation, and the intensity of staining can serve as an essential diagnostic tool.

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