REPORTE DE CASO

REVISTA VENEZOLANA de CIRUGÍA BUCO-MAXILOFACIAL

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# Neurilemmoma of the upper lip.

## REPORT OF TWO CASES

*Neurilemoma del labio superior. Reporte de dos casos*

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JORGE AUGUSTO GUZMAN-RUSSO [1]
WESLAY RODRIGUES DA SILVA [2,3]
NORIS GILSI HERNÁNDEZ-ARIAS [4]
OSCAR IVÁN MORCILLO-HERRERA [5]
MARGARITA OLIVER LLULL [5]
RONALDO DE CARVALHO RAIMUNDO [2]
MARIANA VILLARROEL-DORREGO [6]
ANA PAULA VERAS SOBRAL [2,3]

1. Departament of Stomatology at the "Dr. Jacinto Convit" Biomedical Institute - Vargas Hospital. Central University of Venezuela, Caracas, Venezuela.
2. Department of Oral and Maxillofacial Pathology, School of Dentistry, Postgraduation Program in Dentistry, Universidade de Pernambuco, Recife, Brazil
3. Oswaldo Cruz University Hospital (OCUH), Integrated Anatomic Pathology Center, Recife, Brazil
4. Faculty of Dentistry. Central University of Venezuela. Caracas, Venezuela
5. Derpartament of Dermatology at th "Dr. Jacinto Convit" Biomedical Institute - Vargas Hospital. Central University of Venezuela. Caracas, Venezuela
6. Department of Oral Medicine, School of Dentistry, Universidad Central de Venezuela, Caracas, Venezuela

Jorge Augusto Guzman-Russo orcid.org/0000-0003-3981-7395
Weslay Rodrigues da Silva orcid.org/0000-0002-0430-4656
Noris Gilsi Hernández-Arias orcid.org/0009-0004-4502-8063
Oscar Iván Morcillo-Herrera orcid.org/0009-0000-2443-8961
Margarita Oliver Llull orcid.org/0000-0001-7874-8703
Ronaldo de Carvalho Raimundo orcid.org/0000-0003-3847-0609
Mariana Villarroel-Dorrego orcid.org/0000-0002-0596-1527
Ana Paula Veras Sobral orcid.org/0000-0002-0801-9385

**Corresponding author:** Weslay Rodrigues da Silva. E-mail: weslay.rodriguess@upe.br

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## ABSTRACT

A neurilemmoma, also known as a schwannoma, is a benign neoplasm arising from the perineural Schwann cells, which originate during the fourth week of embryonic development. Although its etiology remains unclear, it has been associated with potential triggering factors. According to the World Health Organization, neurilemmomas are classified as peripheral nerve sheath tumors. These lesions may occur in various anatomical sites, including the tongue, floor of the mouth, palate, lower lip, parotid gland, and, more rarely, the upper lip. Clinically, they are typically asymptomatic and can affect individuals of both sexes, with a slight predilection for males. This article presents two cases of neurilemmoma located in the upper lip of patients without clinical evidence of neurofibromatosis.

**KEYS WORDS:** Neurilemoma; Schwannoma; neurinoma.

## RESUMEN

El neurilemmoma, también conocido como schwannoma, es una neoplasia benigna que surge de las células perineurales de Schwann, que se originan durante la cuarta semana del desarrollo embrionario. Aunque su etiología sigue siendo incierta, se ha asociado con posibles factores desencadenantes. Según la Organización Mundial de la Salud, las neurilemmomas se clasifican como tumores de la vaina nerviosa periférica. Estas lesiones pueden ocurrir en varios sitios anatómicos, incluyendo la lengua, el piso de la boca, el paladar, el labio inferior, la glándula parótida y, más raramente, el labio superior. Clínicamente, son típicamente asintomáticos y pueden afectar a individuos de ambos sexos, con una ligera predilección por los varones. Este artículo presenta dos casos de neurilemmoma localizados en el labio superior de pacientes sin evidencia clínica de neurofibromatosis.

**PALABRAS CLAVE:** Neurilemoma; Schwannoma; neurinoma.

## › INTRODUCTION

Neurilemmoma, also referred to as schwannoma, neurinoma, or perineural fibroblastoma, is a benign, slow-growing neoplasm that originates from perineural Schwann cells. These glial cells envelop neuronal axons, forming the myelin sheath, which plays a crucial role in nerve conduction as well as in the growth and structural support of the axon[1,2]. The first description of this group of neurogenic tumors was provided by Verocay in 1910, who named them "neurinomas." However, in 1935, it was established that these tumors arise from the nerve sheath, and the term "neurilemmoma" was subsequently adopted[1,2].

Neurilemmomas may arise from the neural sheath of peripheral motor, sensory, sympathetic, and cranial nerves, with the exception of the first and second cranial nerves (olfactory and optic), which lack Schwann cell sheaths[1]. Although the exact etiology remains unknown, several factors have been implicated in their development, including chronic trauma, sustained irritation, and exposure to radiation[1,2].

In the most recent publication of the classification of Bone and Soft Tissue Tumors, the fifth edition of the World Health Organization (WHO) 2020, is positioned in the session of peripheral nerve sheath tumors[3]. These tumors have been reported in the head and neck region, accounting for approximately 20% to 40% of all soft tissue tumors, although only 1% to 12% occur intraorally. Within the oral cavity, the tongue is the most frequently affected site[4–7]. The aim of this study is to report two cases of neurilemmoma presenting in the upper lip, an uncommon location for this neoplasm.

## › CASE REPORT

### Case 1

A 44-year-old female patient presented to the oral medicine service with a complaint of a persistent upper lip swelling that had been present for approximately 20 years, reportedly arising after facial trauma. Her medical history was unremarkable. Intraoral examination revealed a well-circumscribed, firm, mobile, yellowish-white nodule with telangiectatic surface vessels, measuring approximately 2 cm in diameter, located on the right side of the upper lip **(Figure 1)**. Ultrasonographic evaluation demonstrated an oval, hypoechoic, and vascularized lesion. Based on these clinical and imaging features, a provisional diagnosis of a minor salivary gland cyst was proposed. An excisional biopsy was performed, and the specimen was submitted for histopathological analysis.

Microscopic examination revealed a well-circumscribed and encapsulated benign neoplasm composed of interlacing bundles of spindle-shaped cells exhibiting nuclear palisading (Antoni A pattern) and Verocay bodies, alternating with less organized, myxoid regions (Antoni B pattern) with a central myxoid area **(Figure 2)**. These findings were consistent with a diagnosis of neurilemmoma. The possibility of neurofibromatosis was investigated and subsequently ruled out. The patient has been under clinical follow-up for 18 months, with no evidence of recurrence to date.

### Case 2

A 56-year-old male patient presented to the oral diagnostic service with a lesion on the upper lip of unknown duration. Intraoral examination revealed a localized swelling on the upper lip **(Figure 3)**, displaying a normal mucosal color, rounded shape, well-defined borders, fibrous consistency, and mobility on palpation. Based on the clinical presentation, a provisional diagnosis of fibrous hyperplasia was established. An excisional biopsy was performed, and the specimen was submitted for histopathological evaluation.

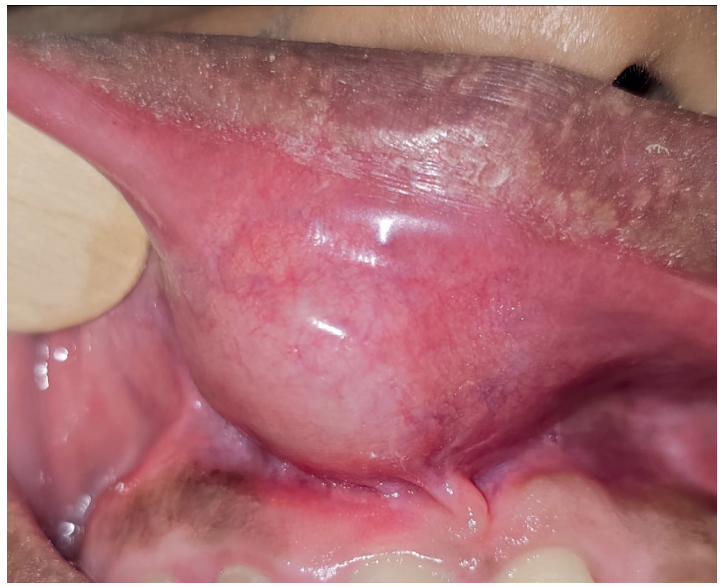

**FIG. 1.** Clinical presentation showing a well-defined nodular lesion on the upper lip.

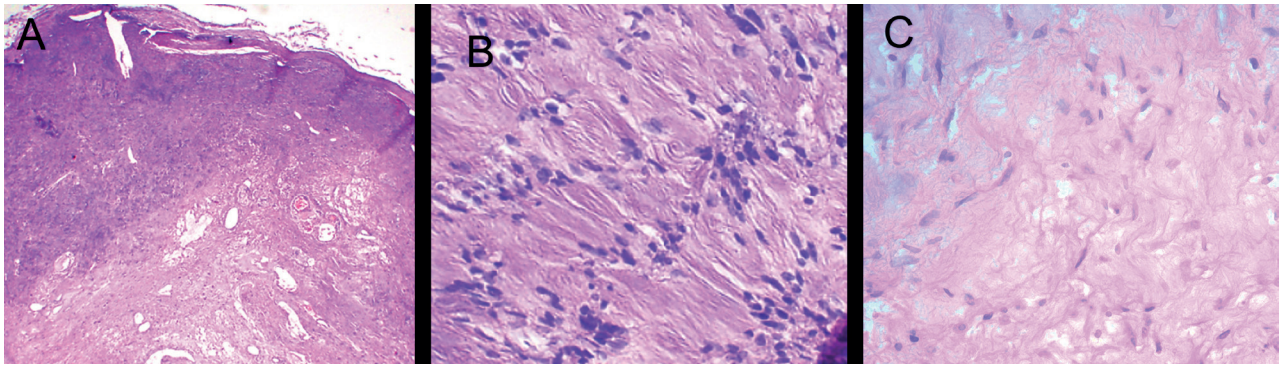


**FIG. 2.** Histopathological features of neurilemmoma. (A) Encapsulated, well-circumscribed nodule observed at low magnification (hematoxylin and eosin stain). (B) Fascicles of spindle-shaped cells demonstrating the Antoni A pattern, with palisading nuclei and Verocay bodies, alternating with loosely organized areas consistent with the Antoni B pattern (low magnification, hematoxylin and eosin stain). (C) Area of myxoid degeneration observed at high magnification (hematoxylin and eosin stain).

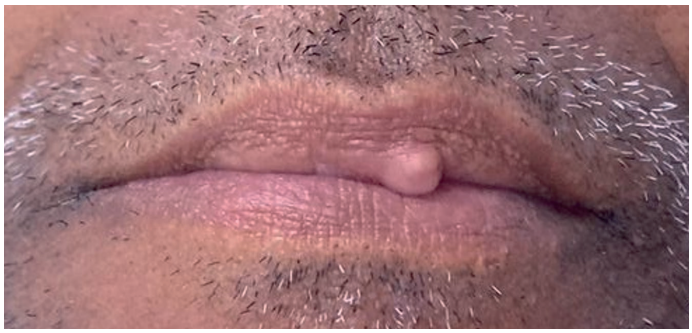

**FIG. 3.** Clinical presentation of neurilemmoma demonstrating increased volume in the upper lip.

Microscopic analysis revealed a well-circumscribed, non-encapsulated lesion characterized by the proliferation of spindle-shaped cells arranged in varying proportions of Antoni A and Antoni B patterns **(Figure 4 A–C)**. Immunohistochemical staining demonstrated strong positivity for S-100 and SOX-10 proteins **(Figure 4 D–F)**, confirming the diagnosis of neurilemmoma. In light of this diagnosis, the possibility of neurofibromatosis was investigated and excluded. The patient has been under clinical follow-up for 12 months, with no evidence of recurrence.

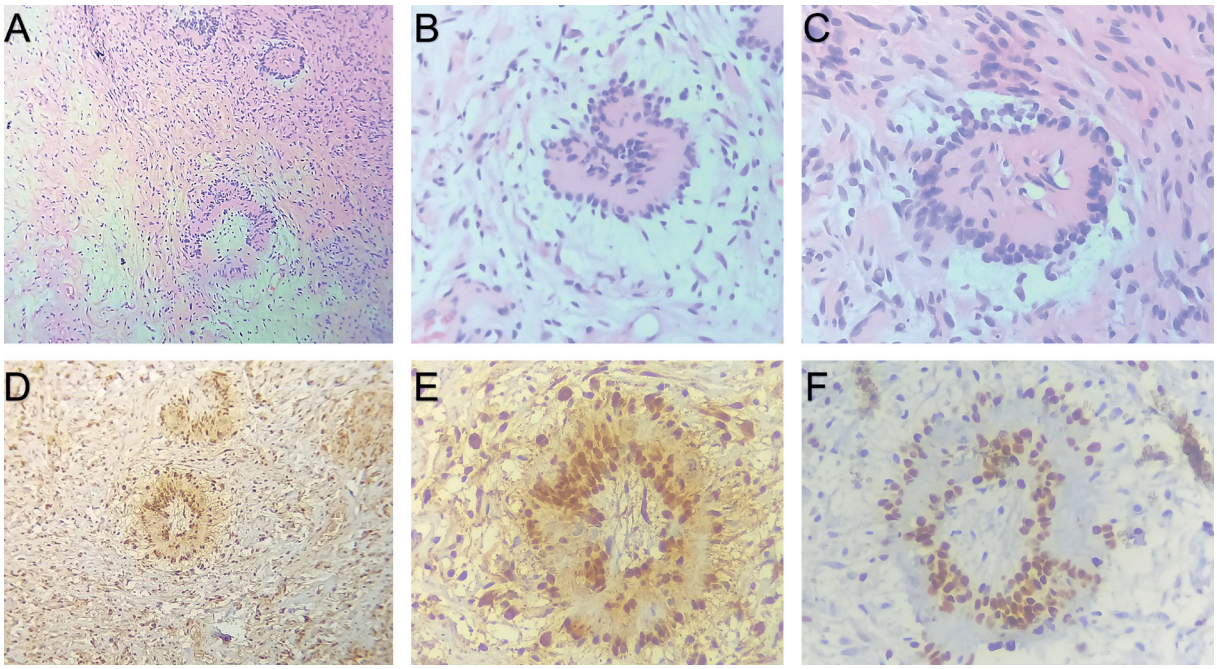


**FIG. 4.** Histopathological and immunohistochemical findings of neurilemmoma. (A) Photomicrograph at medium magnification showing alternating Antoni A and Antoni B areas (hematoxylin and eosin stain). (B–C) Antoni A areas showing palisading nuclei and Verocay bodies (medium magnification, hematoxylin and eosin stain). (D–E) Immunohistochemical staining for S-100 showing strong, diffuse positivity at medium and high magnifications, respectively. (F) Immunohistochemical staining for Sox-10 showing positive nuclear expression at medium magnification.

## › DISCUSSION

Neurilemmomas are benign, slow-growing, and well-encapsulated neoplasms that account for approximately 1% of all tumors in the oral cavity[5]. Although the precise etiology remains unknown, several factors have been proposed, including genetic predisposition, spontaneous proliferation, exposure to radiation, and local trauma. The latter, particularly relevant in the context of the rich innervation of the upper lip by the infraorbital nerve, may explain the development of the lesion following facial trauma, as observed in the present case.

The occurrence of multiple neurilemmomas is referred to as schwannomatosis, which is frequently associated with neurofibromatosis type II. The etiopathogenesis of this syndrome involves the loss of function of the Merlin protein, encoded by the NF2 gene located on chromosome 22, which plays a key role in regulating mitotic signaling pathways[4].

Neurilemmomas occur in the head and neck region in approximately 20% to 40% of cases, with intraoral involvement reported in about 1% to 12%. The prevalence appears to be equally distributed between sexes. The most frequent intraoral site is the tongue, followed by the floor of the mouth, buccal mucosa, soft palate, and, more rarely, the lips[5]. Consistent with our cases, the upper lip represents an uncommon anatomical location for this neoplasm. Clinically, these lesions are typically described as asymptomatic nodular or tumoral masses, well circumscribed, with a smooth surface, and may be either firm or fluctuant in consistency. They tend to exhibit a gradual increase in size, potentially resulting in aesthetic concerns and facial asymmetry[6].

Various imaging modalities can aid in the diagnostic evaluation of these lesions, including computed tomography, magnetic resonance imaging, and soft tissue ultrasound. Among these, ultrasound is particularly advantageous due to its low cost and wide accessibility[7]. Differential diagnoses should be considered based on the lesion's anatomical location, encompassing all entities that present clinically as well-encapsulated soft tissue nodules or tumors. However, given the heterogeneous clinical presentation and the rarity of such lesions, histopathological examination remains the gold standard for definitive diagnosis[8].

Histopathologically, neurilemmomas typically exhibit alternating architectural patterns, as observed in our case. These include well-differentiated Antoni A areas, characterized by compactly arranged, elongated spindle cells organized in palisading patterns around acellular eosinophilic zones known as Verocay bodies, which are composed of delicate cytoplasmic processes. In contrast, Antoni B areas are less cellular, consisting of loosely arranged spindle cells within a myxoid stroma[9]. The histopathological differential diagnosis of neurilemmoma includes other peripheral nerve sheath tumors, such as neurofibroma, palisaded encapsulated neuroma, and traumatic neuroma[10]. Neurofibromas are composed of interlacing bundles of spindle cells with wavy nuclei and a variably myxoid background. Importantly, they lack the alternating Antoni A and B patterns that are characteristic of neurilemmomas.

Immunohistochemical analysis demonstrates a stronger and more uniform reactivity for S-100 protein in neurilemmomas compared to neurofibromas. This difference in S-100 expression is attributed to the relatively homogeneous cellular composition of neurilemmomas, which are predominantly derived from Schwann cells. In contrast, neurofibromas exhibit a more heterogeneous cellular makeup, including Schwann cells, fibroblasts and perineurial-like cells[10]. Additionally, neurilemmomas also show positive immunoreactivity for Sox-10, further supporting their Schwann cell origin[11,12]. In the present report, Case 1 was diagnosed based solely on morphological criteria, whereas Case 2 included immunohistochemical analysis for diagnostic confirmation.

The treatment of choice for neurilemmomas is complete surgical excision of the lesion[13]. In our cases, curative management was successfully achieved through total excision, with no postoperative complications. Surgical removal using a $CO_2$ laser has also been reported as an effective therapeutic alternative, offering satisfactory clinical outcomes[13]. The recurrence rate is generally low, with up to 8% of cases recurring, typically associated with incomplete excision of the lesion[10]. Although malignant transformation of neurilemmomas is considered rare, the incidences ranging from 8% to 13.9%[14].

## › CONCLUSION

In summary, neurilemmomas are rare benign tumors that should be included in the differential diagnosis of head and neck neoplasms. Their occurrence in the upper lip is uncommon. Imaging modalities, particularly soft tissue ultrasound, can serve as valuable tools in preoperative planning, especially for well-encapsulated lesions. Nevertheless, histopathological examination remains the gold standard for definitive diagnosis, as the clinical presentation of neurilemmomas may mimic other lesions affecting the lips and oral cavity.

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