

CASE REPORT

An unusual presentation of plexiform neurofibroma in the oropharynx of a young woman with NF1: a case report

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Summary

Introduction: Neurofibromatosis type 1 (NF1) is a hereditary disorder that most commonly presents with cutaneous manifestations and peripheral neurofibromas. Although head and neck involvement occur in up to 10% of cases, oropharyngeal neurofibroma is extremely rare. This case report presents an unusual localization of a plexiform neurofibroma in the oropharyngeal region of a young adult.

Patient Review: A 30-year-old female with a previously established diagnosis of NF1 presented with progressive dysphagia lasting approximately one year. ENT examination revealed a submucosal mass on the posterior wall of the oropharynx extending toward the hypopharynx. MRI of the head and neck demonstrated a well-defined lesion located in the retropharyngeal space, measuring 30×15×38 mm. The tumor was surgically excised via a transoral approach under general anesthesia. Histopathological analysis confirmed the diagnosis of plexiform neurofibroma. The patient has been under regular follow-up and remains asymptomatic, with no signs of recurrence 18 months postoperatively.

Conclusion: This case highlights the importance of including plexiform neurofibroma in the differential diagnosis of submucosal oropharyngeal lesions, particularly in patients with known NF1. Early recognition and complete surgical excision can result in favorable outcomes with a low recurrence rate.

Keywords: neurofibromatosis type 1, plexiform neurofibroma, oropharyngeal lesion, surgical treatment, case report

INTRODUCTION

Neurofibromatosis type 1 (NF1) is a common autosomal dominant hereditary disorder. Clinical manifestations typically begin in early childhood and progress with age, reflecting the disease's multisystem nature. Cutaneous signs, particularly café-au-lait macules and axillary or inguinal freckling are often the earliest features, followed by the development of multiple neurofibromas arising from peripheral nerves. (1) NF1 can affect multiple organ systems, including the skin, nervous system, skeletal system, and soft tissues, necessitating a multidisciplinary approach to diagnosis, treatment, and long-term surveillance. Although involvement of the head and neck region occurs in up to 10% of patients with NF1, lesions most commonly affect the skin, orbit, or cervical region. At the same time, intraoral and oropharyngeal localizations are extremely rare (2,3). Oropharyngeal neurofibromas

are typically submucosal and may remain asymptomatic for long periods, becoming clinically evident only when symptoms such as dysphagia or foreign body sensation develop (3). Due to their rarity and nonspecific clinical and radiological features, neurofibromas of the oropharynx may mimic other benign or malignant lesions, making preoperative diagnosis challenging. Imaging, particularly magnetic resonance imaging, is essential for assessing tumor extent and its relationship to surrounding structures, while definitive diagnosis relies on histopathological and immunohistochemical examination (3). We present this case to highlight an unusual presentation of a plexiform neurofibroma located in the oropharynx of a young woman with known NF1, emphasizing the diagnostic and therapeutic challenges associated with this rare anatomical localization.

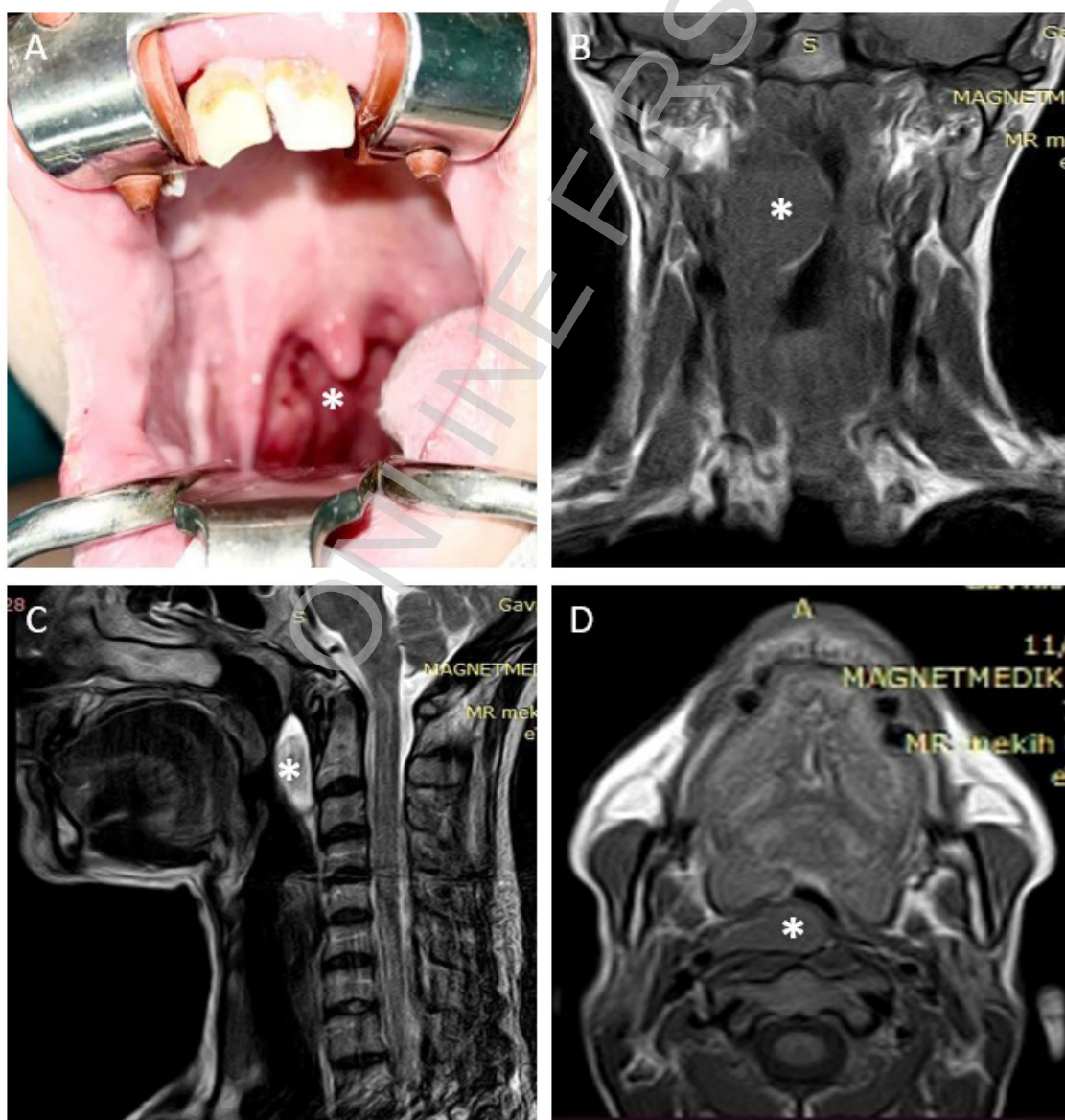


Figure 1. Clinical and radiological findings of a retropharyngeal neurofibroma. A) Intraoral view shows a submucosal tumor on the right side of the posterior wall of the oropharynx (asterisk). B, C, D) T1 and T2 weighted MRI of head and neck showing a well-defined lesion (30×15×38 mm) within the retropharyngeal space (asterisk - coronal, sagittal, and axial view)

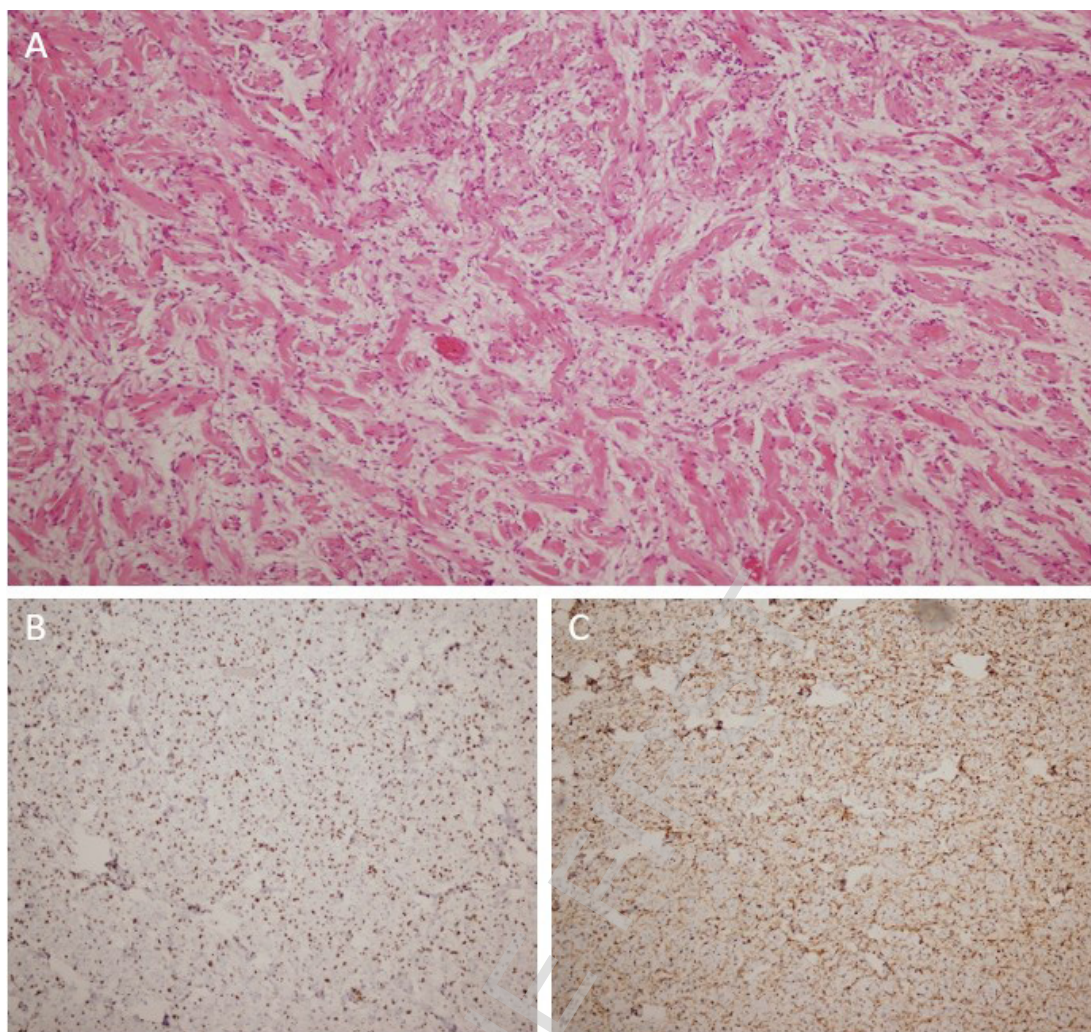


Figure 2. Histopathological and immunohistochemical features of a neurofibroma. A) Hematoxylin and eosin (H&E) stained section of a neurofibroma at $\times 100$ magnification. The image shows a non-encapsulated lesion composed of elongated, spindle-shaped cells with wavy nuclei embedded in a collagenous stroma. Scattered mast cells and areas of myxoid change are visible. B) Immunohistochemical staining for S100 protein in a neurofibroma at $\times 100$ magnification. The majority of spindle cells show diffuse and strong nuclear and cytoplasmic positivity for S100, consistent with Schwann cell differentiation. C) Immunohistochemical staining for SOX10 in a neurofibroma at $\times 100$ magnification. Strong and diffuse nuclear staining is observed in the spindle cells, further supporting Schwannian lineage and confirming the neural crest origin of the tumor.

Case report

A 30-year-old female patient with a known diagnosis of neurofibromatosis type 1 presented to our clinic with a one-year history of progressive dysphagia. Written informed consent was obtained from the patient for publication of this case report and accompanying images. ENT examination revealed a submucosal tumor on the posterior wall of the oropharynx, predominantly on the right side, extending toward the hypopharynx (**Figure 1A**). The tongue mobility was preserved, with normal soft palate elevation and no signs of vocal fold dysfunction. There was no evidence of cervical lymphadenopathy on palpation. Magnetic resonance imaging (MRI) of the head and neck demonstrated a well-demarcated lesion within the retropharyngeal space, measuring $30 \times 15 \times 38$ mm (**Figures 1B-D**). The lesion displayed imaging characteristics suggestive of a neoplastic process. Considering the submucosal localization, well-circumscribed appearance

on MRI, and absence of suspicious features suggestive of malignancy, a decision was made to proceed directly to complete surgical excision without preoperative biopsy. Surgical management involved transoral excision of the lesion under general anesthesia. Direct laryngoscopy under general anesthesia was performed before excision to assess the exact extent of the lesion and its relation to surrounding structures. Based on endoscopic findings and MRI characteristics, a transoral surgical approach was considered feasible and safe. The wound was closed using resorbable sutures. The postoperative course was uneventful. The patient resumed oral intake on the second postoperative day, initially with a soft diet, which was gradually advanced to a regular diet over the following days, without the need for a nasogastric feeding tube. On gross examination, the excised mass measured $34 \times 22 \times 9$ mm and appeared as a well-defined, firm, greyish nodule. Histopathological analysis confirmed the diagnosis of plexiform neurofibroma (**Figures 2A-C**). The patient



Figure 3. Physical examination after 18-month follow-up shows no signs of recurrence or new lesions.

has been followed regularly postoperatively. At the 18-month follow-up, she remains asymptomatic, with no clinical or radiological evidence of recurrence (**Figure 3**).

DISCUSSION

Neurofibromatosis refers to a group of hereditary conditions characterized by the development of tumors in the nervous system and surrounding structures. From a clinical and genetic standpoint, it is broadly categorized into neurofibromatosis type 1 (NF1), also known as peripheral or von Recklinghausen neurofibromatosis, and neurofibromatosis type 2, which predominantly affects the central nervous system and is commonly associated with bilateral vestibular schwannomas (4,5). NF1 is the more frequently encountered entity and represents one of the most prevalent autosomal dominant disorders, with an estimated incidence ranging from 1 in 2,000 to 1 in 3,500 individuals (1). The condition was first described by German pathologist Friedrich Daniel von Recklinghausen in 1882. The condition is often referred to as von Recklinghausen disease (6). At the molecular level, NF1 results from pathogenic mutations of the NF1 tumor suppressor gene, leading to loss of neurofibromin function. Approximately half of affected patients inherit the mutation from an affected parent, whereas the remaining cases arise sporadically due to *de novo* genetic alterations (1). In 90% of cases, the most common signs are cutaneous findings, including multiple café-au-lait macules and numerous neurofibromas along peripheral nerves (1,7).

According to the diagnostic criteria established by the National Institutes of Health Consensus Development Conference, the diagnosis of neurofibromatosis type 1 requires at least two specific clinical features. These include the occurrence of six or more café-au-lait macules, the presence of two or more neurofibromas of any type or a single plexiform neurofibroma, axillary or inguinal freckling, optic pathway glioma, one or more iris hamartomas (Lisch nodules), characteristic skeletal abnormalities such as sphenoid wing dysplasia, or a confirmed diagnosis of neurofibromatosis type 1 in a first-degree relative (7).

Neurofibromas are typically identified through physical examination and imaging studies when needed. In our case, the oropharyngeal lesion was evident on physical examination; imaging was needed to assess its extent and evaluate the surrounding structures. Neurofibromas can occur along deeper peripheral nerves, involving organs such as the intestines, larynx, kidneys, and even the heart. In the head and neck region, the oral cavity and neck are the most commonly affected areas, resulting in symptoms such as difficulty swallowing or a sensation of something stuck in the throat. **Table 1** shows examples of neurofibromas localized in the oral cavity and oropharynx found in the literature, as well as the symptoms that patients experienced.

The differential diagnosis for a submucosal lesion in the oropharynx should include a variety of conditions, such as salivary gland tumors, fibromas, lipomas, and other benign tumors. Squamous cell carcinoma can sometimes present as a submucosal lesion. Osteofites on cervical vertebrae can cause submucosal bulges in oropharynx. Although biopsy is generally recommended to establish a definitive diagnosis of submucosal oropharyngeal lesions, in selected cases, complete surgical excision without prior biopsy may be justified. This is particularly applicable when imaging findings suggest a benign, well-circumscribed lesion and when complete resection can be safely achieved. In our case, the decision to proceed directly to surgery was based on clinical and radiological assessment.

Histologically, neurofibroma consists of a mixture of cell types, including Schwann cells, perineural cells, fibroblasts, mast cells, macrophages, and endothelial cells, with scattered, intermingled myelinated and unmyelinated axons, surrounded by a collagenous, sometimes mixoid, extracellular matrix (21). Immunohistochemical staining is used to detect neural involvement.

Treatment of NF1 is directed towards controlling symptoms and managing complications. The best treatment option for neurofibroma is complete surgical resection. The choice of surgical approach depends on tumor size, location, extent, and relationship to surrounding neurovascular structures. Transoral resection is minimally invasive and suitable for well-circumscribed, medially located lesions without major vascular involvement. However, alternative approaches for retropharyngeal and parapharyngeal lesions, such as transcervical or transmandibular routes, may be required for larger tumors, lesions with lateral extension, or when adequate exposure cannot be achieved transorally. These approaches provide better visualization and control of vital structures but are associated with increased morbidity. In the present case, the lesion was favorably positioned for transoral excision, which allowed complete removal with minimal invasiveness. Considering these tumors are not radio-sensitive, postoperative radiotherapy is avoided, knowing the risks of developing radiation-induced secondary

Table 1. Examples of neurofibromas localized in the oral cavity and oropharynx found in the literature

Author	Publication year	Patient sex	Patient age at the time of diagnosis	Localisation of tumor	Symptoms
Sinha et al. (8)	2002	Female	50	Right side of soft palate	swallowing and speech difficulties
Surwald et al. (9)	2002	Male	28	Right tonsil	gagging sensation, painless fullness in his throat
Aliyu et al. (10)	2012	Male	40	Left side of soft palate	muffled voice, swallowing difficulties, pain
Madhumita et al. (11)	2007	Female	49	Palatine tonsil	pain in the throat
Sakata et al. (3)	2012	Male	52	Left tonsil	pain in the throat
Rezaee et al. (12)	2022	Male	27	Base of the tongue	mild swallowing difficulties
Guner et al. (13)	2006	Female	3	Left side of the tongue	disturbance of mastication and phonation
Sharma et al. (14)	2013	Female	11	Right side of the tongue	difficulty in swallowing, breathing, and clear speaking
Tanaka et al. (15)	2010	Male	59	Base of the tongue	swallowing difficulties
Lykke et al. (16)	2013	Female	62	Right side of the tongue	irritation on the right side of the tongue
Singh et al. (17)	2015	Male	14	Base of the tongue	swallowing difficulties
Roy et al. (18)	2014	Male	75	Base of the tongue	swallowing difficulties, pain
Narasimhan et al. (19)	2024	Female	63	Right side of the tongue	burning sensation, pain during chewing
Ballage et al. (20)	2019	Male	18	Right side of the tongue	asymptomatic mass

malignancies. The recurrence rate after surgical resection depends on several factors, including patient age at the time of surgery, tumor type, tumor location, and surgical margins. Patients younger than 10 years, with plexiform neurofibroma, with tumors located on the head and neck, or who had incomplete surgical resection, tend to have a higher recurrence rate after the surgery. Imaging studies (MRI) are a valuable method for the early detection of tumor recurrence (22).

Over the past few decades, molecularly targeted agents have shown promising results as a new approach in the treatment of neurofibromatosis type 1. These agents can reduce tumor size and relieve symptoms in some patients. Molecular analyses have shown that patients with neurofibromatosis type 1 have an overactive RAS-MAPK signaling pathway due to loss of NF1 gene function. MEK inhibitors, the most significant examples of molecularly targeted agents, work by inhibiting MEK, a protein in this pathway (23). Further research and clinical trials are expected to explore new treatment strategies for individuals with neurofibromatosis.

CONCLUSION

Neurofibromas are most frequently encountered as cutaneous or subcutaneous lesions, and their occurrence in the oropharynx is exceptionally rare. Because of this atypical localization, the diagnosis can be challenging

and is often not initially considered in the differential work-up of submucosal oropharyngeal masses. Clinical presentation may be subtle and nonspecific, and imaging findings can mimic those of other benign or malignant lesions. Therefore, definitive diagnosis relies on histopathological and immunohistochemical analyses. This case underscores the importance of maintaining a broad differential diagnosis when evaluating oropharyngeal masses, especially in patients with known neurofibromatosis type 1.

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Ethical approval: The study was approved by the Ethics Committee of the Clinical Center of Serbia under decision No. 635/40 dated June 25, 2026.

Informed consent: Written informed consent has been obtained from the patient for the publication of this paper.

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NEOBIČNA PREZENTACIJA PLEKSIFORMNOG NEUROFIBROMA U OROFARINKSU KOD MLADE ŽENE SA NF1: PRIKAZ SLUČAJA

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Sažetak

Uvod: Neurofibromatoza tip 1 (NF1) je nasledno oboljenje koje se najčešće prezentuje kožnim promenama i perifernim neurofibromima. Iako se lokalizacija u glavi i vratu javlja u do 10% slučajeva, neurofibrom orofarinksa je izuzetno redak. Cilj ovog rada je prikaz neuobičajenog slučaja plexiformnog neurofibroma smeštenog u orofaringealnoj regiji kod mlade odrasle osobe.

Prikaz bolesnika: Pacijentkinja stara 30 godina, sa ranije postavljenom dijagnozom NF1, javila se zbog disfagije koja je trajala oko godinu dana. Kliničkim ORL pregledom uočen je submukozni tumor na zadnjem zidu orofarinksa, koji se širio ka hipofarinksu. Magnetna rezonanca glave i vrata prikazala je jasno ograničenu leziju

u retrofaringealnom prostoru dimenzija 30×15×38 mm. Tumor je hirurški uklonjen transoralnim pristupom u opštoj anesteziji. Histopatološka analiza potvrdila je dijagnozu plexiformnog neurofibroma. Tokom praćenja od 18 meseci nakon operacije, pacijentkinja je bez tegoba i bez znakova recidiva.

Zaključak: Ovaj slučaj ukazuje na važnost razmatranja plexiformnog neurofibroma u diferencijalnoj dijagnozi submukoznih lezija orofarinksa, naročito kod pacijenata sa poznatom dijagnozom NF1. Rano prepoznavanje i hirurško lečenje mogu dovesti do uspešnog kliničkog ishoda bez recidiva.

Ključne reči: neurofibromatoza tip 1, plexiformni neurofibrom, orofaringealna lezija, hirurško lečenje, prikaz slučaja

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