Arch Argent Pediatr 2023;121(3):e202202782

Pediatric neurofibromatosis of the larynx: report of atypical location

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ABSTRACT

Laryngeal neurofibromas (LNFs) are rare benign tumors mainly located in the supraglottis. LNFs occur with airway obstruction symptoms. The treatment is complete resection via an endoscopic technique; the open approach is reserved for large tumors.

Here we describe the case of a pediatric patient with LNF of atypical location associated with neurofibromatosis type 1 (NF-1). The tumor was resected with an endoscopic technique, and the pathological study reported a plexiform neurofibroma. It is important to suspect this condition in any child with atypical, progressive inspiratory stridor. Long-term follow-up is recommended due to the high rate of recurrence.

Key words: *laryngeal neoplasms; neurofibromatosis; plexiform neurofibroma; pediatrics; natural orifice endoscopic surgery.*

doi: http://dx.doi.org/10.5546/aap.2022-02782.eng

To cite: Varela-Goodall, Acosta MB, Scatolini ML, Cocciaglia A. Pediatric neurofibromatosis of the larynx: report of atypical location. *Arch Argent Pediatr* 2023;121(3):e202202782.

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Funding*: None.*

Conflict of interest*: None.*

Received*: 7-19-2022*
Accepted*: 9-6-2022*

INTRODUCTION

Laryngeal neurofibromas (LNFs) account for an extremely rare cause of upper airway obstruction in the pediatric population. Their location in the larynx is very rare[1] and mainly affects the supraglottis, most frequently the aryepiglottic folds and/or arytenoid cartilage.[2] In most cases, LNFs are found in association with neurofibromatosis type 1 or 2 (less frequently with the latter), but may also occur in isolation.[3]

Neurofibromatosis type 1 (NF-1) is an autosomal dominant, neurocutaneous, systemic disease.[3] It is characterized by the presence of *café-au-lait* skin spots, cutaneous neurofibromas, and Lisch nodules of the iris.[4] Histologically, neurofibromas are classified into plexiform and non-plexiform.[3] Plexiform neurofibromas (PNFs) are pathognomonic of NF-1. Laryngeal involvement is rare and most often manifests with airway obstruction symptoms.[5] The treatment of choice is tumor resection. Currently, minimally invasive endoscopic techniques are preferred; the open approach is reserved for large tumors.[6]

The objective of this study is to present a clinical case of laryngeal plexiform neurofibroma of atypical location.

CASE REPORT

This was a 3-month-old boy with a medical history of prematurity and gastroesophageal reflux assessed for continuous inspiratory stridor since 1 month of life that exacerbated after crying, with increasing respiratory distress. On physical examination, the patient had sternal and subcostal retraction, more than 6 *café-au-lait* skin spots with a diameter greater than 0.5 cm on the right knee, anterior face of both thighs, chest, right shoulder, left arm, left buttock, and with a diameter greater than 3.5 cm on the pelvis (*Figure 1*). He did not have cutaneous neurofibromas and no family history of neurofibromatosis type 1 or 2.

An X-ray of the neck showed a radiopaque structure in the retrocricoid region (*Figure 2 A*). A computed tomography showed a postcricoid isodense formation measuring 6.4 × 7.7 × 9.7 mm (*Figure 2 B-C*). A nasofibrolaryngoscopy showed a formation bulging the retrocricoid space, with preserved mucous membranes and good vocal cord motility.

The cardiac, musculoskeletal, and ophthalmological assessments were normal. A magnetic resonance imaging of the brain showed no lesions in the central nervous system.

Figure 1. *Café-au-lait* skin spot > 3.5 cm on the pelvis

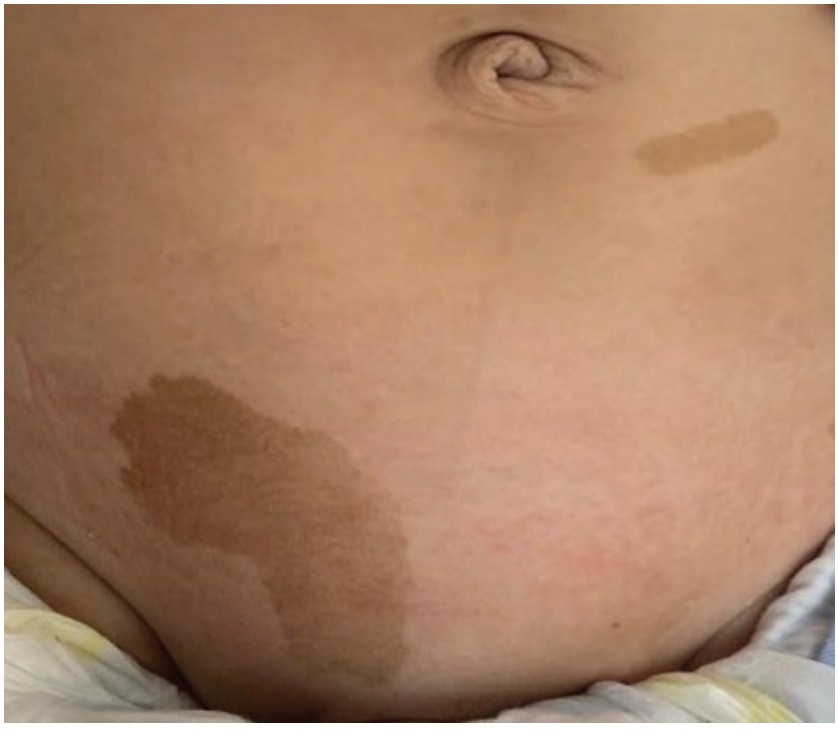
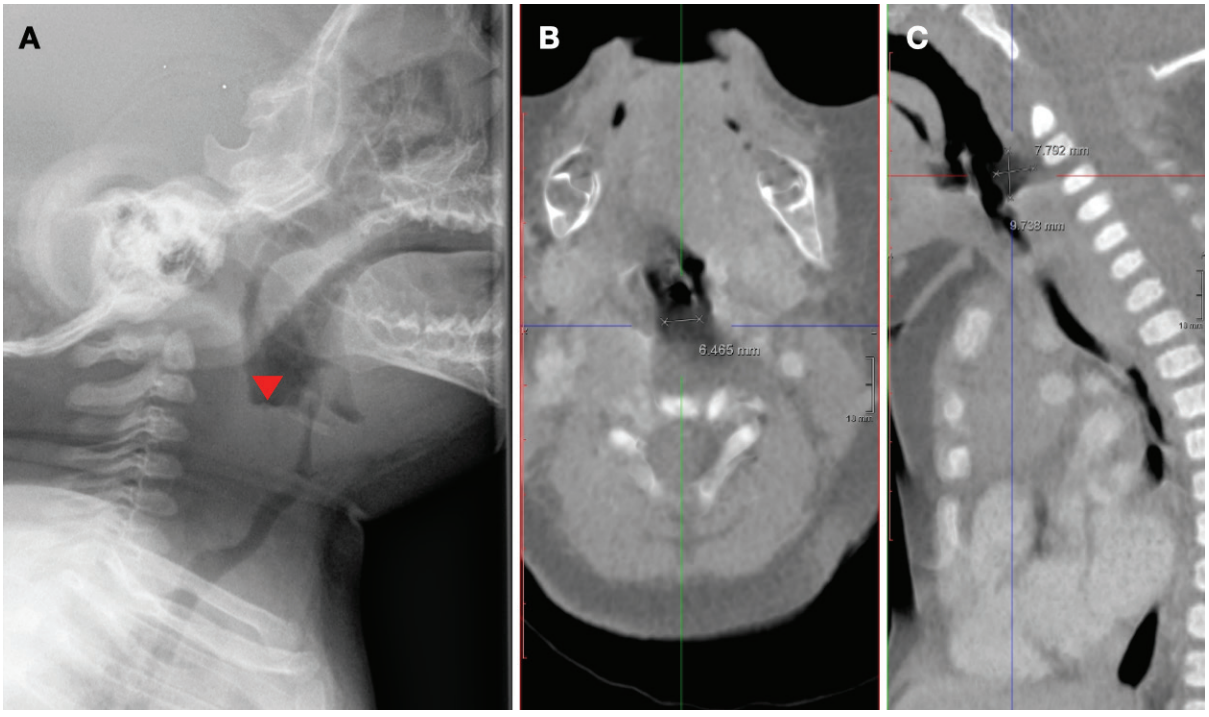


Figure 2. A) Lateral X-ray of the neck showing a retrocricoid mass. B and C) Computed tomography of the neck (axial and sagittal sections). Hypodense postcricoid formation



A direct laryngoscopy was performed under general anesthesia, which found a mobile, soft, rounded mass in the retrocricoid area protruding into the esophagus that measured 0.5 × 1 cm in diameter (*Figure 3*). After securing the airway by orotracheal intubation, the mass was completely resected with cold instruments.

During the post-operative period, the patient developed respiratory distress after extubation and a tracheostomy was performed. The pathological study reported a plexiform neurofibroma positive for S-100.

At 12 months of follow-up, the child is still tracheostomized with good secretion management, uses a voice prosthesis and is doing swallowing rehabilitation as part of a decannulation plan. The patient follow-up includes periodic controls, with no evidence of tumor recurrence.

DISCUSSION

Neurofibromas are benign tumors originating in the peripheral nerve sheath that are usually associated with neurofibromatosis type 1 and 2 or occur in isolation.[7] NF-1 was first described by von Recklinghausen in 1882.[6] It is an autosomal, dominant disease with neurocutaneous manifestation. Almost all patients have typical *café-au-lait* skin spots that are usually diagnosed in the first months of life. The cutaneous manifestations may also include lentigines (freckles) in the groin, armpits, and neck. The diagnosis of NF-1 is based on the presence of 2 or more criteria[8,9] (*Table 1*), and the presence of a single plexiform neurofibroma is a diagnostic criterion, which in this clinical case confirmed it.

PNF location in the larynx is rare, even more so in the pediatric population. LNF associated with neurofibromatosis was first described in 1930 by Colledge et al.,[10] while Hoover described the first case of LNF in a pediatric patient in 1940.[11] To date, 3 bibliographic reviews have been published;[6,10,12] the most recent one was conducted by Chinn et al.,[6] in 2014 and included 62 cases of pediatric neurofibromatosis of the larynx. Until this date, 72 cases of neurofibromatosis of the larynx have been reported in pediatrics, with a similar distribution between both sexes. It is believed that they originate from the internal branch of the superior laryngeal nerve,[1] which explains their occurrence mainly in the supraglottic region (arytenoid cartilage and aryepiglottic fold). In this

Figura 3. Direct laryngoscopy. Submucosal retrocricoid mass

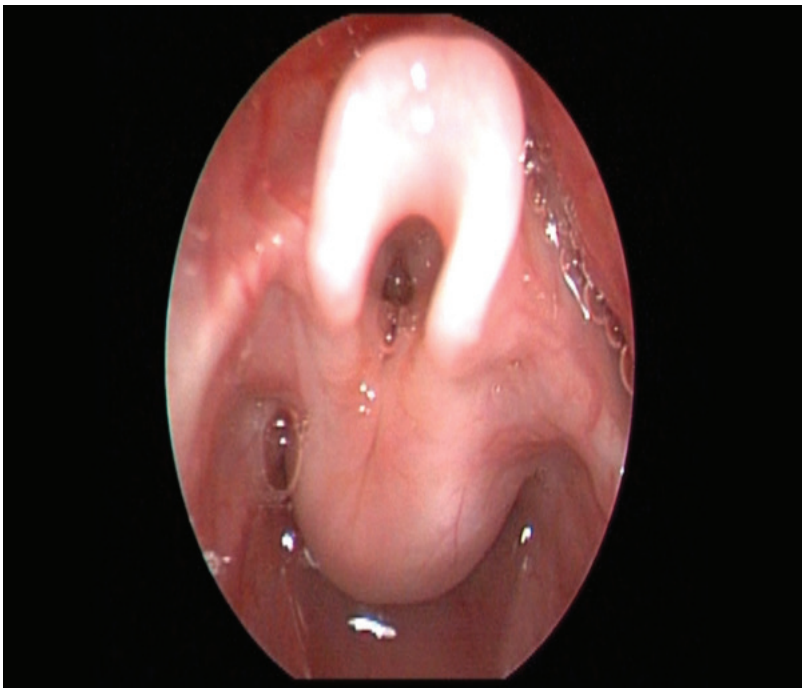


Table 1. Diagnostic criteria for neurofibromatosis type 1

- Six or more *café-au-lait* spots bigger than 1.5 cm in diameter in postpubertal children and bigger than 0.5 cm in prepubertal children.
- Two or more neurofibromas of any kind, or one or more plexiform neurofibromas.
- Freckling in the armpits and/or groin.
- Optic nerve glioma(s).
- Two or more Lisch nodules (benign iris hamartomas).
- Distinctive bone lesion (sphenoid bone dysplasia or dysplasia or thinning of long bone cortex, with or without pseudarthrosis).
- First-degree relative with neurofibromatosis type 1.

case report, we describe a patient with a PNF in the retrocricoid region; when analyzing all reported cases, this case accounts for the second most uncommon site (8.3%).

The most frequent symptom is stridor (59.7%), followed by dyspnea (25%), which is consistent with the presentation of our clinical case and previously published reports.[6,10,12] An asymptomatic presentation is exceptional, whose finding is incidental (4.1%).[1,13,14]

The preliminary assessment includes performing a flexible fibrolaryngoscopy and/or airway endoscopy, which shows a submucosal mass with smooth surface,[6] mostly located in the supraglottis.

A computed tomography and a magnetic resonance imaging are useful to assess the extent of the tumor and to plan the surgical approach.[4] The definitive diagnosis is confirmed by biopsy and the presence of a plexiform neurofibroma. PNFs are made up of spindle cells with elongated nuclei immersed in a myxoid stroma; a positive S-100 pattern is characteristically observed in immunohistochemistry techniques,[4] as in this case.

The treatment of choice is surgical resection. The surgical approach will depend on the size and extent of the tumor; an endoscopic approach is preferred for small tumors, whereas an open surgery is used for larger tumors.[2] Of the 72 cases

of LNFs, 30.5% were resected via endoscopic surgery, including our patient. It is worth noting that until 1990, when the first endoscopic resection was performed, the approach of choice was external, either by thyrotomy or lateral pharyngotomy.[2,6] Currently, the endoscopic technique is preferred because it is less invasive and in an attempt to preserve laryngeal functions. Since LNFs are non-encapsulated tumors with an infiltrative growth pattern, it is difficult to achieve complete resection of the lesion, which increases the possibility of recurrence.[3,4] The recurrence rate reaches 9.7%, with the need for multiple surgeries, always prioritizing the endoscopic technique over the open approach, due to its lower morbidity and lower rate of recurrence (approximately 27%); however, this information is limited by the lack of reporting and/or a short follow-up provided to many patients.

As a novelty in the treatment of LNFs, in 2018, Arnold et al.,[15] described the first case managed with transoral robotic surgery in a pediatric patient; to date, it has been the only case reported, with excellent functional outcomes and no recurrence at 5 months of follow-up.

The complications may include bleeding, airway obstruction, vocal cord palsy, and post-obstructive pulmonary edema.[1,2,4] In some cases, a tracheostomy is necessary, which is required in approximately 40% of cases, including our patient.

Long-term follow-up is of utmost importance because of the high rate of recurrence or residual disease and the risk of malignancy (2–5%).[4] There is no consensus on follow-up frequency, but it should be performed by direct laryngoscopy to detect recurrences.

Given that few studies have been carried out and that all are based on case reports and retrospective reviews, there is no absolute evidence about the diagnostic algorithm or gold standard treatment. Prospective studies are limited due to the rarity of LNFs.

CONCLUSIONS

The retrocricoid location of LNF is very rare. It would be important to suspect this condition in the presence of stridor, dysphonia, dysphagia and/or airway obstruction symptoms in patients with diagnosed or suspected NF-1 and in the absence of indicators of other more common differential diagnoses, especially in the presence of skin lesions suggestive of LNF. A thorough assessment, including direct laryngoscopy under general anesthesia, should always be performed to obtain a biopsy specimen and confirm the diagnosis. If possible, the treatment of choice will be minimally invasive endoscopic resection to reduce complications and follow-up should be performed periodically due to the high probability of recurrence. ■

REFERENCES

1. Kasapoglu F, Özdemircan T, Erisen L. Laryngeal plexiform neurofibroma in a child. *Ear Nose Throat J.* 2013; 92(6):E31.
2. Chen YC, Lee KS, Yang CC, Chang KC. Laryngeal neurofibroma: Case report of a child. *Int J Pediatr Otorhinolaryngol.* 2002; 65(2):167-70.
3. Rahbar R, Litrovnik BG, Vargas SO, Robson CD, et al. The biology and management of laryngeal neurofibroma. *Arch Otolaryngol Head Neck Surg.* 2004; 130(12):1400-6.
4. Rodriguez H, Cuestas G, Cocciaglia A, García de Dávila M. Neurofibromatosis tipo 1 con compromiso laríngeo en un lactante. *Acta Otorrinolaringologica Española.* 2015; 66(5):299-301.
5. Mahdoufi R, Barhmi I, Tazi N, Sami R, et al. Plexiform Neurofibroma of the Larynx in Children: About an Unusual Case Report. *Arch Otolaryngol Rhinol.* 2016; 2(1):35-7.
6. Chinn SB, Collar RM, McHugh JB, Hogikyan ND, Thorne MC. Pediatric laryngeal neurofibroma: Case report and review of the literature. *Int J Pediatr Otorhinolaryngol.* 2014; 78(1):142-7.
7. White AK, Smith RJ, Bigler CR, Brooke WF, Schauer PR. Head and neck manifestations of neurofibromatosis. *Laryngoscope*. 1986; 96(7):732-7.
8. Fernández N, Casuriaga AL, Giachetto G. Neurofibroma cervicodorsal en una niña con Neurofibromatosis Tipo 1. *An Fa Med*. 2018; 5(1):64-9.
9. Neurofibromatosis. Conference statement. National Institutes of Health Consensus Development Conference. *Arch Neurol*. 1988; 45(5):575-8.
10. Chang-LoM. Laryngeal involvement in von Recklinghausen's disease: a case report and review of the literature. *Laryngoscope*. 1977; 87(3):435-42.
11. Hoover WB. Benign tumors of the larynx, their diagnosis and treatment. *Surg Clin North Am*. 1940; 20:697-719.
12. Masip MJ, Esteban E, Alberto C, Menor F, Cortina H. Laryngeal involvement in pediatric neurofibromatosis: a case report and review of the literature. *Pediatr Radiol.* 1996; 26(7):488-92.
13. Martin DS, Stith J, Awwad EE, Handler S. MR in neurofibromatosis of the larynx. *AJNR Am J Neuroradiol*. 1995; 16(3):503-6.
14. Greinwald J, Derkay CS, Schechter GL. Management of massive head and neck neurofibromas in children. *Am J Otolaryngol*. 1996; 17(2):136-42.
15. Arnold MA, Mortelliti AJ, Marzouk MF. Transoral resection of extensive pediatric supraglottic neurofibroma. *Laryngoscope*. 2018; 128(11):2525-8.