CASE STUDY

Neurofibromatosis Type 1 With Laryngeal Involvement in an Infant

Neurofibromatosis tipo 1 con compromiso laringeo en un lactante

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Clinical Case

A 10-month-old female patient presented at the respiratory endoscopy service with inspiratory stridor, which she had suffered from the age of one month, impaired swallowing and increasing difficulty in breathing.

A fibrolaryngoscopy was performed which showed a submucous mass which occupied the arytenoids and the left aryepiglottic fold and partially occluded the laryngeal lumen (Fig. 1A). Computerised tomography showed a 11.7 mm × 5.8 mm lesion which was limited to the supraglottis (Fig. 2A and B).

Physical examination revealed more than 6 “café au lait” spots on the skin, over 0.5 cm (Fig. 2C) in diameter. Neither cutaneous neurofibromas were present nor any family history of type 1 or 2 neurofibromatosis. Ophthalmology tested as normal, with no presence of Lisch nodules in the iris. A Brain MRI and neurological assessment also tested normal.

A direct laryngoscopy was performed under general anaesthesia and after ensuring the airway via orotracheal intubation, the lesion was partially resected with CO2 laser under microscopic control.

The patient was extubated after 48 h and received post-operative treatment with antibiotics and corticosteroids. After 72 h, the patient presented with stridor, supraclavicular and intercostal retractions and difficulty in feeding, and we therefore performed a tracheotomy.

Anatomical pathology revealed the presence of fusiform cells with elongated nuclei between wavy collagen fibres and myxoid stroma which adopted a multinodular pattern with no atypias, confirming the diagnosis of plexiform neurofibroma (Fig. 1B).

The patient continues to have the tracheotomy cannula after 4 months follow-up, and has no swallowing difficulties (Fig. 2D). A strategy of watchful waiting has been adopted due to the infiltrating nature and growth of residual tumour and the patient will be periodically reviewed in order to decide the most appropriate surgical procedure and be able to decannulate her.

Discussion

Laryngeal tumours represent 2% of laryngeal anomalies in paediatrics. 98% are benign with the most common symptoms being recurrent respiratory papillomatosis and angioma.1

Laryngeal neurofibroma is a very rare benign tumour. Incidence is higher in females (ratio 3:2).2 It is mainly

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Figure 1  Laryngeal neurofibroma. (A) Endoscopic imaging showing the submucous mass occupying the left arytenoid space. (B) Histopathology of the plexiform neurofibroma, comprising fusiform cells with elongated nuclei and myxoid stroma.

located in the supraglottis: arytenoids and/or aryepiglottic folds, which are rich in nerve fibres.\textsuperscript{3,4} It stems from the internal branch of the superior laryngeal nerve or from anastomosis between the upper laryngeal nerve and the recurrent laryngeal nerve.\textsuperscript{3}

It can present in isolation, although it is more commonly associated with type 1 neurofibromatosis (NF1).\textsuperscript{3} NF1 laryngeal involvement is rare and few cases have been reported.\textsuperscript{4,5}

NF1, also known as von Recklinghausen’s disease, is a genetic autosomal, dominant neurodermal disorder, although in between 30% and 50% of cases mutation is spontaneous.\textsuperscript{3} It affects one in every 2500 people, and is caused by mutation of the NF1 gene on chromosome 17q11.2, which encodes the protein neurofibromin that would play a role in tumour suppression.\textsuperscript{3,4} It is characterised by the presence of “café au lait” spots on the skin, Lisch nodules in the iris, and dermal neurofibromas. The neurofibromas may affect any nerve in the body, with presence in the larynx being extremely rare.\textsuperscript{7} Histologically, neurofibromas are classified as plexiform and non-plexiform.\textsuperscript{3}

Plexiform neurofibromas usually appear in early infancy,

Figure 2  (A) and (B) Computerised tomography showing the tumour delimited by the supraglottis (arrows). (A) Axial section. (B) Sagittal section. (C) "Café au lait" spots on the skin (arrow). (D) Post-operative image after 4 months showing the residual tumour in the left arytenoid, with greater permeability of the laryngeal inlet.
they are pathognomonic of NF1 and characterised by their involvement of a nerve trunk and peripheral branches.6

Diagnosis of NF1 is based on the presence of 2 or more of the following: 6 or more “café au lait” spots (at least 5 mm in diameter before puberty or 15 mm after it), 2 or more neurofibromas or one plexiform neurofibroma, freckles in the armpits or groin, 2 or more Lisch nodules, optic glioma, characteristic skeletal abnormality (sphenoid dysplasia, alteration of the bones of the orbit or long bones) or grade one NF1 in a family member.5,9

In our patient, NF1 diagnosis was based on the presence of dermal macules and laryngeal plexiform neurofibroma. Laryngeal neurofibroma usually manifests with obstruction of the airway.10 It may present with stridor, dysphonia, difficulty in feeding and/or progressive dyspnoea.

Computerised tomography or magnetic resonance is useful in determining the extent of the lesion. Diagnosis is confirmed via direct laryngoscopy and biopsy.

Different laryngeal diseases may cause stridor in the newborn and nursing infant, with laryngomalacia being the most common congenital anomaly of the larynx and the main cause of stridor in infants under 6 months. Differential diagnosis of laryngeal mass includes, among others, sacular cyst, laryngoceles, hemangioma, hamartoma and teratoma.11

Surgical treatment is indicated. Depending on the size and location of the tumour, the approach will be via endoscopy or open surgery (thyrotomy or lateral pharyngotomy).12 Temporary tracheotomy may be necessary on occasion to establish a secure airway.2,3

The treatment of choice is tumour removal with performance of an endoscopy, with preservation of the laryngeal functions.1 An external approach is reserved for cases where the lesion is extensive. As these are non-encapsulated tumours, and infiltrating, complete resection of the lesion is often difficult with recurrence being frequent, regardless of the chosen surgical approach.2

Post-operative complications include bleeding, compromise of the airway, laryngeal stenosis, ipsilateral caudal paralysis and post-obstructive pulmonary oedema.2,7

Long-term follow-up is important due to the high recurrence rate or rate of residual disease and the risk of malignant transformation (2%-5%).1,2 Malignant transformation to neurofibrosacoma and malignant schwannoma has been reported mainly in patients with NF1 and plexiform type neurofibroma.7 The grounds for suspicion of malignancy may be sudden increase in pre-existing tumour size or the onset of pain.2,8

We would emphasise the importance of considering evaluation via endoscopy of the airway of every child presenting with stridor which does not evolve as expected in order to determine the cause of the condition. Although laryngeal neurofibroma is rare, it must be considered in the differential diagnosis of stridor and progressive airway obstruction in nursing infants. This disease must be considered in every child presenting with a submucous laryngeal mass, even when there are no other clinical NF1 symptoms.

Conflict of Interests

The authors have no conflict of interests to declare.

References