International Journal of Pediatric Otorhinolaryngology Extra 9 (2014) 15–17

Contents lists available at ScienceDirect

International Journal of Pediatric Otorhinolaryngology Extra

journal homepage: www.elsevier.com/locate/ijporl

Case Report

Solitary plexiform neurofibroma of the forehead: A rare and unusual presentation

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ARTICLE INFO

Article history:
Received 12 September 2013
Received in revised form 5 November 2013
Accepted 9 November 2013

Keywords:
Solitary plexiform neurofibroma
Neurofibromatosis
Forehead mass
Supraorbital nerve

ABSTRACT

Plexiform neurofibromas are benign tumors of the peripheral nerves and are usually considered pathognomonic of neurofibromatosis type 1. We discuss the case of a child who presented with a forehead mass. Pathologic examination revealed a plexiform neurofibroma of the supraorbital nerve. No other signs or symptoms of neurofibromatosis were identified. Although rare, plexiform neurofibromas may rarely occur as solitary lesions not associated with the neurofibromatosis spectrum. It can be seen in unusual anatomic location such as the supraorbital or forehead region and should be considered in the diagnosis of soft tissue facial tumors.

1. Introduction

Neurofibromatosis type I (NF-1) is a disease that results from spontaneous mutations or familial transmitted mutations in the NF-1 gene located on chromosome 17q11.2. These mutations cause a loss-of-function in the protein neurofibromin, which typically functions as a tumor suppressor [1]. The criteria for diagnosis of NF-1 was established by the NIH in 1988 and is listed in Table 1 [2]. According to some authors, the triad of multiple neurofibromas, café-au-lait macules, and especially of Lisch nodules, is so reliable that their absence essentially excludes the diagnosis of NF-1 [3,4].

Neurofibromas are benign peripheral nerve sheath tumors that present as focal cutaneous/subcutaneous or nodular/diffuse plexiform lesions. Though we typically associate the more visible cutaneous neurofibromas with NF-1 (around 99% incidence), plexiform neurofibromas are also seen in up to 50% of NF-1 patients [1].

In this report, we discuss a case of a solitary plexiform neurofibroma of the supraorbital nerve.

2. Case presentation

A six-year-old Caucasian female presented with a slowly growing, irregularly shaped left sided forehead mass present since nine months of age. The patient's parents considered the mass to have occurred after a history of mild trauma to the forehead. A biopsy in 2008 was noted to be a benign fibroadipose tissue nodule. Ultrasound imaging described the nodule as having a bilobed hypoechoic consistency. There was no history of other lesions or masses and no family history of similar lesions.

General physical examination including the ophthalmologic and dermatologic exams of the patient was normal. Facial movement and sensation were symmetric bilaterally. Palpation of the left supraorbital foramen region revealed a firm, mobile left forehead lesion, extending from the left lateral brow medially to midline and measured 4.0 × 2.5 cm. Fixation to bone was not noted.

The patient was taken for surgery to remove the lesion. A minimal incision was designed within the relaxed skin tension lines of the forehead. Dissection through the galea aponeurosis exposed a flesh-colored, tubular mass that appeared to have fibroadipose appendages. The mass was seen to have small finger-like extensions, which were traced until their termination. The mass was removed off the periosteum and noted inferiorly to be contiguous with the supraorbital nerve (Fig. 1). The tumor extent was dissected under loupe magnification until the stalk of the tumor was noted just outside the supraorbital notch. Considerations for further dissection into the foramen might have included

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1871-4048
http://dx.doi.org/10.1016/j.pedex.2013.11.002

Table 1
NIH consensus guidelines: diagnostic criteria for neurofibromatosis I [2] Two or more of the following.

1.	Six or more café-au-lait macules that are (in greatest diameter) >5 mm in pre-pubertal individuals >15 mm in post-pubertal individuals
2.	Two or more neurofibromas of any type, or one plexiform neurofibroma
3.	Axillary/inguinal freckling
4.	Optic glioma
5.	Two or more Lisch nodules
6.	Distinctive osseous lesion (i.e. sphenoid dysplasia or thinning of long bone cortex with or without pseudoarthrosis)
7.	First degree relative with NF-1

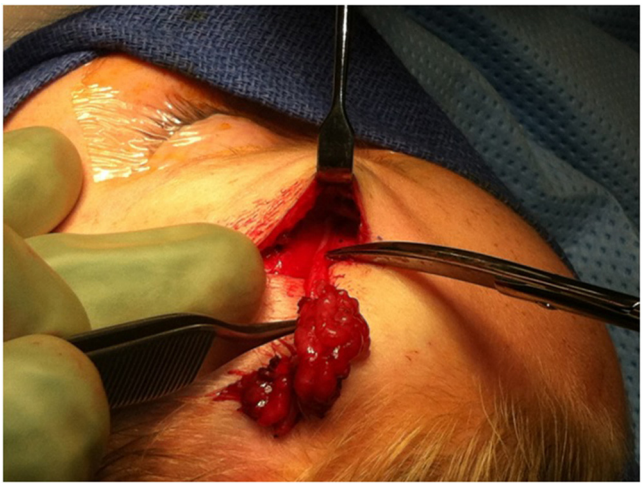

Fig. 1. View of forehead mass during surgical excision. Left eye at the top of the image, hairline at the bottom. At the tip of the scissors, small finger-like extensions can be seen extending into the supraorbital nerve.

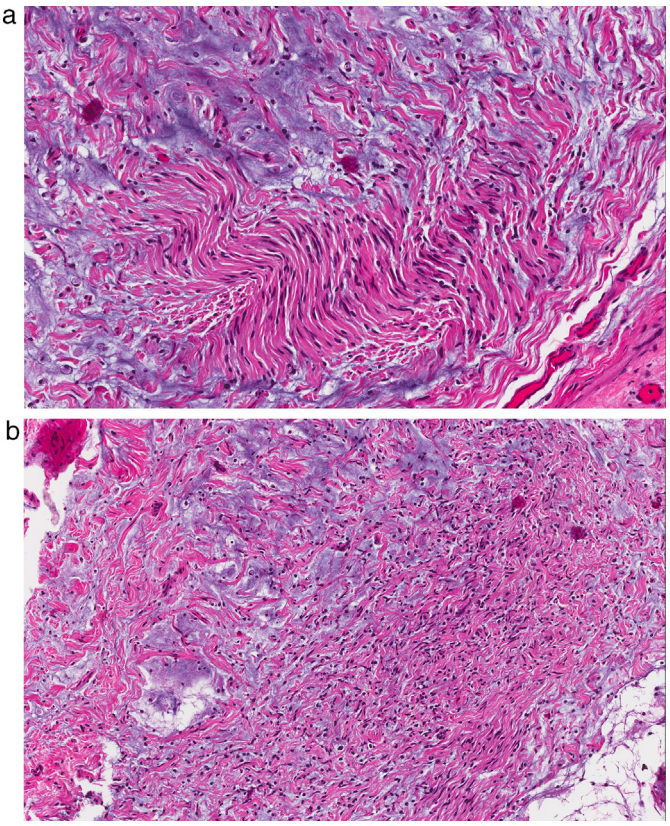

Fig. 2. (a) 10× H&E stain of left forehead mass showing wavy bundles of collagen with spindle-shaped neoplastic cells consistent with plexiform neurofibroma. (b) 20× H&E cross-section through the plexiform neurofibroma showing expanded nerve branches and increased endoneurial matrix material.

using a small osteotome to release the neurovascular bundle from the foramen (as is completed in coronal approaches to the frontal sinus). The initial pathologic frozen section suggested spindle cell lesion, benign in nature.

Under microscope, the lesion showed a mass composed of expanded nerve branches, with spindle-shaped neoplastic cells arrayed between wavy bundles of collagen or in pools of mucoid material, features diagnostic of neurofibroma (Fig. 2). No anaplastic features were present to indicate malignancy. The final pathological diagnosis was plexiform neurofibroma. Pediatric genetic consultation did not reveal additional findings of NF-1. She was found to lack the typical signs of NF-1 with absence of Lisch nodules, café-au-lait spots, optic gliomas, multiple other neurofibromas or axillary/inguinal freckling. With clinical exclusion of NF-1, she was determined to have a solitary, non-syndromic plexiform neurofibroma. The surveillance of the patient will include follow-up every 6 months for the first year, then annually for 5 years.

3. Discussion

When evaluating a forehead mass, the differential diagnosis can be quite broad, and includes hematoma, abscess, lipoma, arteriovenous malformation, pilomatrixoma, sebaceous cysts, and malignant entities. In the setting of a patient without obvious signs of NF-1, the diagnosis of a plexiform neurofibroma typically does not cross the mind of the clinician.

Diagnostic work-up in our patient included ultrasound imaging. Of note, imaging modalities such as CT/MRI should be considered if multiple head/neck lesions are suspected or for masses fixed to underlying bone. In our patient however, given the mobile nature of the mass and low clinical suspicion of additional lesions on physical examination, additional imaging was not pursued. MRI would have allowed evaluation of the extent of tumor into the foramen, but may have required an anesthetic for child's examination. In general, radiation exposure is minimized (CT scan). If the mass was fixated to the frontal bone, a CT may have been considered. The increasing evidence of risks of radiation exposure in pediatric patients, may limit the use of CT imaging in these cases [5].

Plexiform neurofibromas originate from a proliferation of nerve sheath cells, extending across the length of the nerve, often involving multiple nerve fascicles, and ultimately creating a mass of thickened nerve branches [6]. Under a microscope, these lesions are composed of a variety of elements including Schwann cells, collagen, fibroblasts, vascular cells and mast cell infiltrate as seen in Fig. 2.

Plexiform neurofibromas are a more aggressive subtype of neurofibroma, infiltrating through the soft tissue to grow along the length of the affected nerve. If the face is involved, significant disfigurement may be seen during the first three years of life [7]. These lesions can be seen throughout the body, including the head/neck region. The trigeminal nerve and its smaller branches are the most likely cranial nerves to be affected and involvement of the ophthalmic branch may cause proptosis or other disfiguring consequences as the tumor grows within the eyelid or orbit [6]. Occasionally, plexiform neurofibromas may develop into malignant peripheral nerve sheath tumors, which confers a poor prognosis to the patient [1].

Removal of the lesion is difficult due the significant infiltration of surrounding tissues and requires surgery for

definitive treatment. Tumor recurrence is high, and is two times more likely in cases presenting in the head/neck, two times more likely to recur if resected prior to 10 years old, and two times more likely to recur in a subtotal versus total resection [8]. However, new modalities of treatment including Imatinib mesylate have shown promise in reducing tumor volume and activity, providing not only symptomatic, but therapeutic relief to the patient [7].

Plexiform neurofibromas are described to be heavily linked to NF-1. According to previous literature, their presence in an individual was described to be ''pathognomonic'' for NF-1 [9]. However, more recent papers suggest that this linkage may not be as strong as once thought; similar case reports have described isolated plexiform neurofibromas of the oropharynx, tongue, orbit, tip of nose, and palm in the absence of signs of NF-1 [10–12].

Our case was unusual in that it presented without family history or further systemic symptoms as described above. To our knowledge, the location of the plexiform neurofibroma located on the supraorbital nerve has not been described in the literature. Although the tumor is rare, it should be considered in the differential diagnosis for a supraorbital subcutaneous mass.

Conflict of interest

The authors have no conflicts of interest.

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