

Frontal bone fibrous dysplasia in a 6-months-old boy: A distinctive entity

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Abstract

Fibrous Dysplasia (FD) is a non-malignant condition caused by post-zygotic, activating mutations of the *GNAS* gene that results in inhibition of the differentiation and proliferation of bone-forming stromal cells and leads to the replacement of normal bone and marrow by fibrous tissue and woven bone. The clinical behavior and progression of FD is variable. The management of this condition is difficult and in every case is strictly individualized. We report a case of frontal fibrous dysplasia in a 6-month-old boy who underwent a successfully resection of the lesion with an excellent cosmetic effect.

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Key words: Fibrous dysplasia; *GNAS* mutation; 6-months-old boy.

Conflict of interest: The authors declare no conflict of interest.

Availability of data and materials: All data underlying the findings are fully available.

Ethics approval and consent to participate: No ethical committee approval was required for this case report by the Department, because this article does not contain any studies with human participants or animals. Informed consent was obtained from the patient included in this study.

Consent for publication: The patient's guardians gave their written consent to use the patient's personal data for the publication of this case report and any accompanying images.

Received for publication: 5 December 2019.
Accepted for publication: 2 March 2021.

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La Pediatria Medica e Chirurgica 2021; 43:225
doi:10.4081/pmc.2021.225

Introduction

Fibrous Dysplasia (FD) is a developmental disorder of one or more bones, characterized by replacement of normal bone by fibroosseous tissues.¹ This kind of bone dysplasia caused by post-zygotic mutation of *GNAS* gene that leads to the replacement of normal bone and marrow by fibrous tissue and woven bone.² It represents approximately 2.5% of all bone lesions and about 7% of all benign bone tumors.³ Is a non-familial disease with onset occurring by 10 years of age. Fibrous dysplasia has variable forms with involvement of one bone (monostotic form – MFD) 70% of cases, multiple bones (polyostotic form – PFD) 30% of cases, or McCune-Albright Syndrome (MAS), contained the triad of PFD, *café-au-lait* skin maculae's and precocious puberty.⁴ Craniofacial involvement occurs in 50% of patients with PFD and 30% with MFD.⁵ The most common presenting symptom in fibrous dysplasia is a gradual, painless enlargement of the involved bone or bones in the craniofacial region, clinically seen as facial asymmetry. In addition to clinical findings, diagnosis is based on results of the radiographic examination and histopathological findings. We present a case report of 6-months-old boy with fibrous dysplasia of the frontal bone, who underwent a successfully operative excision of the lesion.

Case Report

A 6-months-old boy, with no previous history of illness, was admitted on the Pediatric Surgery Department with a gradual swelling of the frontal bone during the last four months, localized in the midline area. Physical examination of the child revealed a painless in palpation mass. Associative symptoms such as visual loss or optic nerve decompression, facial asymmetry and headache were not found.

The imaging findings with contrast enhanced axial computed tomography showed a ground glass appearance of the diploe of the frontal bone. The lesion localized at the right side of the middle line with diameter 15,6x6,7 mm (Figure 1A). The imaging investigation continued with Magnetic Resonance Imaging (MRI), which revealed a process into the diploe of the frontal bone expanding as in front of the outer horseshoe of the diploe such as behind the inner one to the dura matter (Figure 1B,C). The dimensions of the lesion were 16,7x8mm and the differential diagnosis included Langerhans-cell histiocytosis, neuroblastoma with secondary localization and dermoid cyst.

According to the above imaging findings and paying attention to the progressive swelling of the frontal bone during the last four months of life, the child underwent an operative excision of the

lesion located into the diploe of the frontal bone and being in slight contact with the dura matter. After the removal of the pathological tissue a synthetic graft of dura matter was placed. There was no need for reconstruction of the anterior wall of the skull. A drain, penrose type was placed and the wound closed without tension. The child had a smooth postoperative period. The drainage was removed on the 4th postoperative day and the antibiotic treatment that was included and ceftriaxone was completed on the 7th postoperative day. The child was discharged on the 8th postoperative day.

The histopathological result revealed lesion composed of trabeculae of woven bone surrounded by moderately cellular fibroblastic proliferation. The tumor issue index for cell proliferation Ki-67 had a low score between 2-3%. Immunocytochemistry showed positive staining of some tumor cells for smooth muscle actin and negative for S-100 (Figure 2).

The wound had an excellent healing with the help of silicone ointment and the follow up 6 months after the excision is without recurrence (Figure 1D). The parents are certainly aware of the continuation of the monitoring till the end of cranio-facial growth.

Discussion

Fibrous Dysplasia has been regarded as a disease of childhood with symptoms occur within the first two decades of life.⁶ The disease occurs equally in male and female patients. However, some

authors have noted the slight female predilection.⁷ Our patient is the first described in the current literature case of craniofacial FD under five years of age.⁸ The underlying molecular abnormality seems to be a somatic mutation of the *GNAS* gene coding for the α subunit of protein G, resulting in osteoblast differentiation deficit, fibrous medullary proliferation and osteoclast hyperactivity partly due to overexpression of IL-6 within mutated cells. The mutation can also affects other cell types and the disease may be associated with cutaneous (*café-au-lait* maculae's) and endocrine effects (early puberty, hyperthyroidism, acromegaly, Cushing's syndrome) in a McCune-Albright syndrome, phosphate diabetes by overexpression of phosphaturia-inducing FGF-23 (Fibroblast Growth Factor 23), or myxomas in Mazabraud's syndrome.⁹

The most common locations of FD are the craniofacial bones, proximal femur and rib. The monostotic form is predominant, at 80%, as in the present series, mainly involving the ethmoid (71%), sphenoid (43%), frontal bone (33%) or maxilla (29%), and less frequently the temporal (24%), parietal (14%) or occipital bone (5%).¹⁰ In the present series, the most frequent location was sphenoid, and secondly frontal.

As far as concerned the clinical behavior of CFD, depends on the expansion and compression of pathological bone against adjacent structures. Large reported series found that CFD was without symptomatology. Further studies revealed that painless bony enlargement resulting in skeletal deformity was the major symptom. In our case the child suffered from a progressive swelling of the frontal bone. Because of the little age of the child we can't

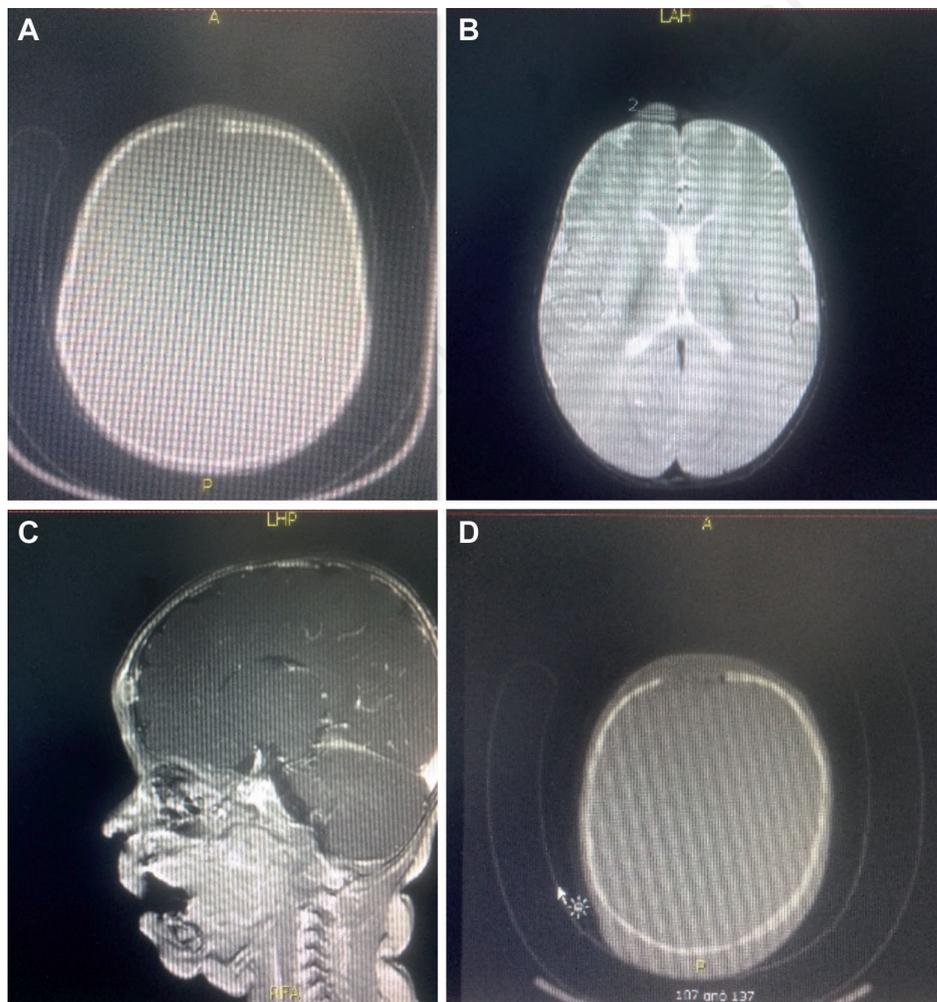


Figure 1. A and B) Contrast enhanced axial computed tomography showed a ground glass appearance of the diploe of the frontal bone. The lesion localized at the right side of the middle line with diameter 15,6x6,7 mm; C) Magnetic Resonance Imaging revealed a process into the diploe of the frontal bone expanding as an inner horseshoe shape behind the inner one to the dura matter; D) Contrast enhanced axial computed tomography 6 months after surgery.

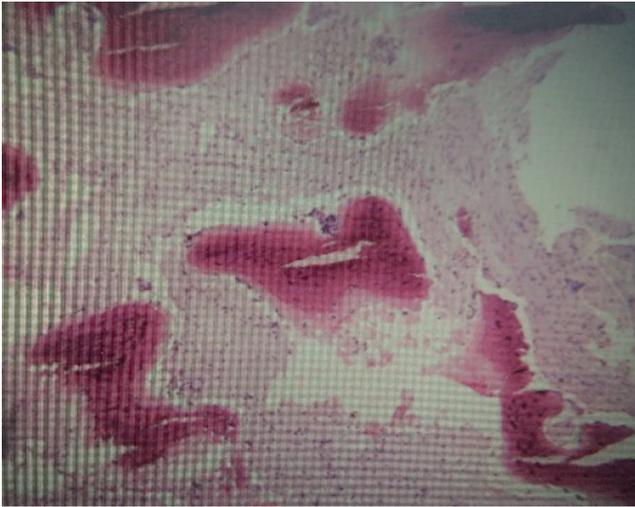


Figure 2. Lesion composed of trabeculae of woven bone surrounded by moderately cellular fibroplastic proliferation. Immunohistochemistry showed positive staining of some tumor cells for smooth muscle actin and negative for S-100.

make a conclusion about the degree in the pain scale of the patient. Nonetheless, during physical examination the swelling seemed to be painless.

Associative symptoms such as visual loss or optic nerve decompression, facial asymmetry and headache were not found.

Malignant transformation is rare, occurring in 0.4% to 4% of cases, depending on the series, and in either form (polyostotic or monostotic). Osteosarcoma is the most frequent malignancy, although fibrosarcoma and chondrosarcoma have also been reported.¹¹

Physical examination, CT and MRI imaging are recommended to define the anatomy and the extent of the lesion. The definite conformation of the FD can be done only by a bone biopsy. The ground glass appearance with thin cortex and without distinct borders is the most specific characteristic of the disease.¹²

The presence of the lesion in the craniofacial region is unique in that the presence of important structures in the vicinity can hamper complete removal of the pathology. Treatment for CFD aims at achieving cosmetic or functional goals. While several surgical options are available to treat facial fibrous dysplasia, child's treatment will depend on the location of the bones affected and the severity of the condition. Surgical resection is indicated only when the disease is symptomatic, and especially in case of accompanied-sensorineural disorders, or for cosmetic purposes. If the affected areas of the face are small and easily accessible, treatment usually involves complete surgical removal (resection) of the area and reconstruction using a combination of bone grafts and materials such as titanium plates and screws. If the area affected is too large or too important to be removed, the size of the bone may be reduced to normal using a high-speed burr. In some patients, a combination of bone reduction with a burr and bone grafting may be utilized. In our case the operative management included the removal of the

pathological bone tissue and reconstruction of the dura mater with synthetic graft. Gross total resection is indicated in cases of fibrous dysplasia of the skull in childhood where the risk of neurologic morbidity is low and cosmetic results will be acceptable.

The follow up includes a physical exam, X-rays or CT scan of the affected area until the child reaches skeletal maturity.

Conclusions

The fibrous dysplasia affecting the craniofacial region is a distinctive entity, with symptoms occurring within the first two decades of life. Although in the majority of cases the clinical picture is asymptomatic, in patients with symptomatic disease or cosmetic defects the surgical resection and reconstruction is the proposed treatment. Close monitoring of the patient until the age of skeletal maturity is required.

References

1. Assaf AT, Benecke AW, Riecke B, et al. Craniofacial fibrous dysplasia (CFD) of the maxilla in an 11-year old boy: A case report. *J Craniomaxillofac Surg* 2012;40:788–92.
2. Demirdöver C, Sahin B, Ozkan HS, et al. Isolated fibrous dysplasia of the zygomatic bone. *J Craniofac Surg* 2010;21:1583–4.
3. Ricalde P, Horswell BB. Craniofacial fibrous dysplasia of the fronto-orbital region: A case series and literature review. *J Oral Maxillofac Surg* 2001;59:157–67.
4. Keskin M, Karabekmez FE, Ozkan BT, et al. Simultaneous occurrence of facial fibrous dysplasia and ameloblastoma. *J Craniomaxillofac Surg* 2009;37:102–5.
5. Ben HadjHamida F, Jlaiel R, Ben Rayana N, et al. Craniofacial fibrous dysplasia: A case report. *J Fr Ophtalmol* 2005;28:e6.
6. Kruse A, Pieles U, Riener MO, et al. Craniomaxillofacial fibrous dysplasia: A 10 year database 1996-2006. *Br J Oral Maxillofac Surg* 2009;47:302–5.
7. Rahman AM, Madge SN, Billing K, et al. Craniofacial fibrous dysplasia: Clinical characteristics and long-term outcomes. *Eye (Lond)* 2009;23:2175–81.
8. Chourmouzi D, Psoma E, Drevelegas A. Ground-glass pattern fibrous dysplasia of frontal sinus. *JBR-BTR* 2013;96:378-80.
9. Bousson V, Rey-Jouvin C, Laredo JD, et al. Fibrous dysplasia and McCune-Albright syndrome: imaging for positive and differential diagnoses, prognosis, and follow-up guidelines. *Eur J Radiol* 2014;83:1828-42.
10. Lustig LR, Holliday MJ, McCarthy EF, Nager GT. Fibrous dysplasia involving the skull base and temporal bone. *Arch Otolaryngol Head Neck Surg* 2001;127:1239-47.
11. Ruggieri P, Sim FH, Bond JR, Unni KK. Malignancies in fibrous dysplasia. *Cancer* 1994;73:1411-24.
12. Tabareau Delalande F, Collin C, GomezBrouchet A, et al. Diagnostic value of investigating GNAS mutations in fibro-osseous lesions: a retrospective study of 91 cases of fibrous dysplasia and 40 other fibro-osseous lesions. *Mod Pathol Off J U S Can Acad Pathol Inc* 2013;26:911-21.