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McCune–Albright syndrome with craniofacial dysplasia: Clinical review and surgical management

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Abstract

Background: Fibrous dysplasia (FD) is a benign fibro-osseous lesion related to an abnormal bone development and replacement by fibrous tissue. FD has three clinical patterns namely monostotic, polyostotic, and the McCune–Albright syndrome (MAS). MAS is a rare genetic disorder (about 3% of all FD's) that comprises a triad of polyostotic FD, café-au-lait skin macules, and precocious puberty. MAS can involve the orbit region and cause stenosis in the optic canal, leading the patient to a progressive visual loss.

Methods: We reported a case of craniofacial FD in MAS in a 9-year-old male with progressive visual loss, submitted to optic nerve decompression by fronto-orbito-zygomatic approach, with total recovery. A research was made at Bireme, PubMed, Cochrane, LILACS, and MEDLINE with the keywords: FD/craniofacial/McCune–Albright/Optic compression for the clinical review.

Results: A clinical review of the disease was made, the multiple, clinical, and surgical management options were presented, and the case report was reported.

Conclusion: MAS is a rare disease with a progressive polyostotic FD. Whenever it affects the orbit region, the optic canal, and it is associated with a progressive visual loss, the urgent optic nerve decompression is mandatory, either manually or with a rapid drill. It is known that aggressive approach is associated with less recurrence; it is also associated with worsening of the visual loss in optic nerve decompression. In MAS cases, multiple and less aggressive surgeries seem to be more suitable.

Key Words: Craniofacial dysplasia, fibrous dysplasia, McCune–Albright syndrome, orbit fibrous dysplasia, visual loss

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INTRODUCTION

Fibrous dysplasia (FD) is a benign intramedullary fibro-osseous lesion related to an abnormal bone development and replacement of bone and marrow bone by fibrous tissue. FD has three clinical patterns namely monostotic, polyostotic, and the McCune–Albright Syndrome (MAS). MAS is a rare sporadic genetic disorder (about 3% of all FD's) that comprises a triad

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of polyostotic FD, café-au-lait skin macules, precocious puberty, and it is a subtype of the general FD.

CASE REPORT

Male, 9 years old, had a femur bone fracture while running; an orthopedic surgery was performed and referred to the Endocrinology Department [Figure 1]. After 6 months of fracture, the patient started to present a progressive holocranial headache. After 1 month, he started to have a progressive temporal visual loss and proptosis on the right side [Figure 2]. During the clinical investigation, the patient had café-au-lait spots [Figure 3] and precocious puberty, with an increase of the testosterone levels and somatomedin. Moreover, the computed tomography (CT) and magnetic resonance imaging (MRI) scans showed that the lateral/roof of the orbital cavity was increased with optic nerve compression [Figures 4 and 5]. The patient was diagnosed with MAS, FD of the orbit bone, and optic nerve compression. Decompression surgery was performed with a fronto-orbito-zygomatic approach using a small sphenoid drill and optic canal decompression with manual instruments. The reconstruction of the lateral orbit was performed; the patient had a good recovery of the visual capacity after surgery and did not have new symptoms after 1 year of follow-up. The pathology confirmed the fibrous osseous tissue and FD [Figure 6].

DISCUSSION

FD is a benign lesion wherein normal bone is replaced by fibrous tissue and immature bone due to a defect on osteoblastic differentiation and maturation.

There are three subtypes of FD: (1) Monostotic, with one bone involvement and the most common subtype. (2) Polyostotic, with multiple bones involvement. (3) MAS which combines polyostotic FD, endocrinopathy, and café-au-lait spots.[3] The clinical diagnosis of this uncommon syndrome can be made with two of these criteria. It occurs in children and adults, in both sex,[22] but the precocious puberty is more common in females (85%) and less common in males (10–15%).[16]

The genetic mutation is located in the chromosome 20q13 in the GNAS locus. The substitution of arginine for cysteine or histidine leads to a hyperactivation of the GSα–cyclic AMP. The overproduction and increased concentration of cAMP in bones over activate the proliferation and abnormal differentiation.[11,20] The elevated cAMP levels lead to an inflammatory cytokines response, in special the interleukin-6, and lead to this osteoclast differentiation.[25] This mutation can be also seen in hypersecretive thyroid tumors, Leydig cell tumors, and more than 40% of the secreting pituitary adenomas. The GNAS locus is a complex imprinted gene that generates multiple products, and the GSα is encoded by multiple exons (1–13) of the GNAS locus, most of them biallelic.[23] However, heterozygous mutations in maternal allele can lead to MAS with resistance for parathyroid hormone, thyroid-stimulating hormone, and gonadotropin, whereas mutation in paternal allele leads to MAS alone.[14] Genetic studies are important due to the differential diagnosis of the FD and other FD-like diseases, such as low-grade central osteosarcoma, which presents a low-incidence of GNAS mutation.[14,18,23]

The macroscopic white and brown aspect is typical, and microscopically there is a replace of marrow space by soft fibrous tissue composed of bland spindle cells and abnormal osseous component with irregular trabeculae.

Radiological findings are typical but not pathognomonic and can be divided into three groups:

- Pagetoid pattern: The rate of bone-fibrous matrix is equal
- Sclerotic pattern: The bone structure is in foreground
- Radiolucent pattern: Fibrous matrix in the

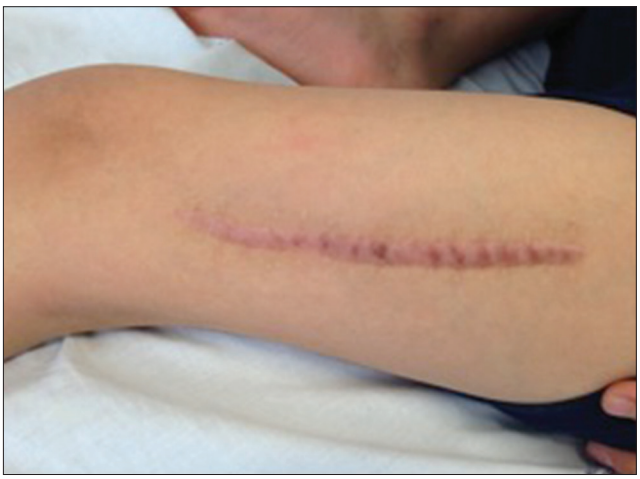

Figure 1: Scar from the surgical approach of the femur fracture

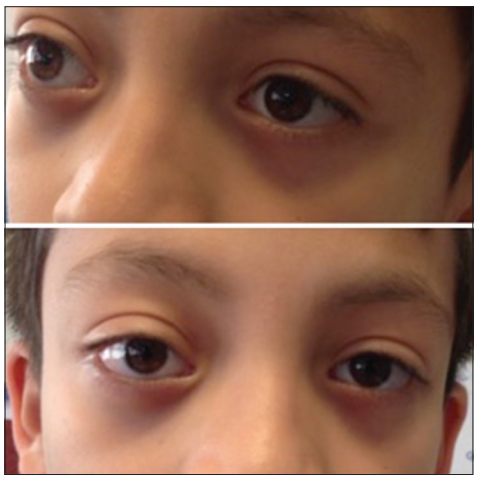

Figure 2: Proptosis of the right eye

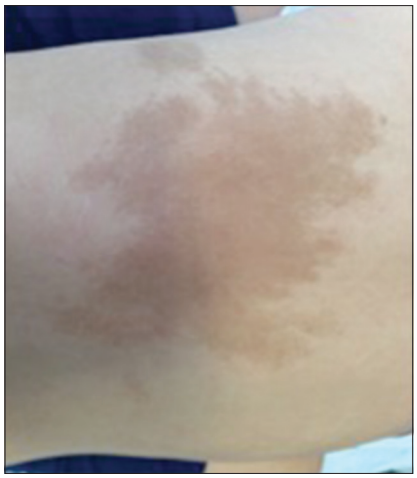

Figure 3: Café-au-lait macule

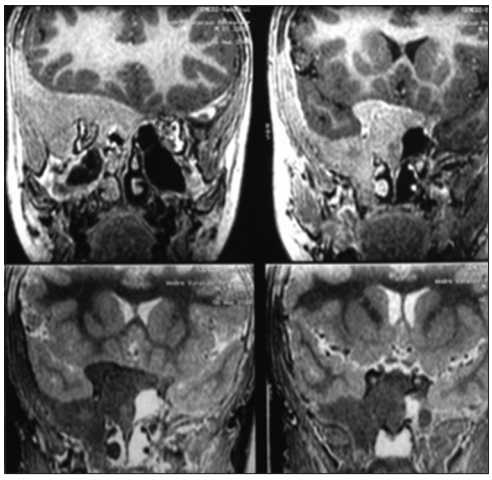

Figure 5: Magnetic resonance imaging: High sign at T1 and low sign at T2 sequences show the fibrous dysplastic pattern

foreground, with cystic degeneration (simple or aneurysmal).[4,12]

During investigation, three differential diagnosis can be considered in skull lesions: Osteosarcoma, en plaque meningioma, and osteitis.[4]

When limited to the craniofacial region, it is considered to be the monostotic form, even if more than one bone is affected, because it is one focus of the disease.[19] The facial FD occurs more frequently in the unilateral form than the bilateral form, in both gender and equal side percentage.[24] Chen and Noordhoff[7] proposed a surgical classification by zones of the deformity, and indication of intervention based on functional or reconstructive criteria.[6,7] The most common symptoms are facial asymmetry (85%), orbital/facial mass (60%), blurred vision (24%), and eyelid position disturbance (10%).[15] Pain complaint is less frequent in children and more in adults, and female patients experience an increased pain level during pregnancy and during the menstrual cycle because of the estrogen receptors found in FD.[10,15] The pain

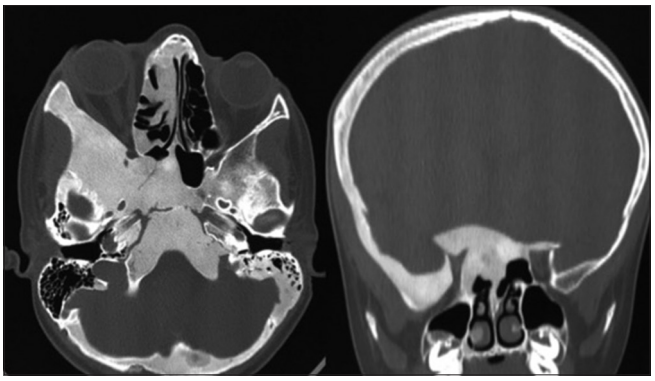

Figure 4: Computed tomography scan shows fibrous dysplasia of the skull base and orbit with narrowing of the optic canal

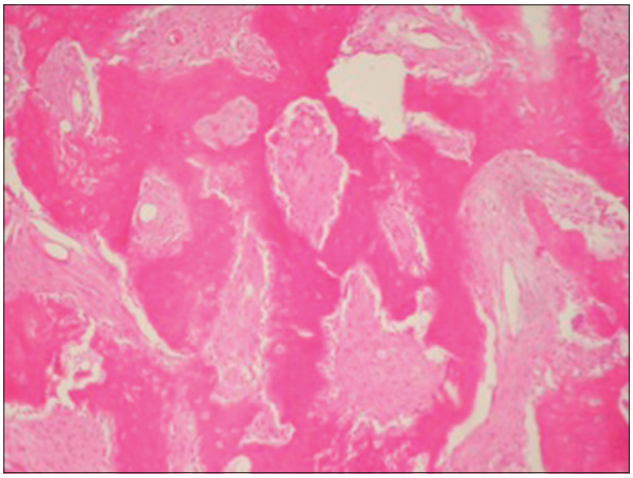

Figure 6: Substitution of the bone marrow by a soft fibroblastic tissue with irregular trabeculae

management can be clinical for the persistent, severe pain; endovenous treatment with bisphosphonates is indicated. Oral bisphosphonates and alendronate have been shown to be ineffective for treatment of bone pain.[5]

Malignant transformation in FD is very rare (about 0.4–4%) and more common in the polyostotic disease and the histological types such as osteosarcoma, fibrosarcoma, and chondrosarcoma.[13]

Recent studies show that the narrowing of the optic canal is not directly correlated to visual loss,[14,19] even if the optic nerve is 100% evolved by fibrous bone.[21] Rahman *et al.* showed that most of the patients with optic canal stenosis did not progress to optic neuropathy, and about 40% will have a chronic visual loss in a long-term follow-up; also, just a few of them will have optic neuropathy progression. This data show that patients with FD without signs of aneurysmal bone cyst or mucoceles have a stable progression. On the other hand, in patients with excessive hormone drive, it tends to be more aggressive and recurrent, such as in MAS and other growth hormone-producing tumors.

Visual loss tends to be chronic and acute visual loss is related to aneurysmal bone cysts and mucoceles. Despite the low plasticity of the nerve, urgent decompression of the optic nerve can reverse it.[21] The real mechanism of the lesion is unclear and multifactorial, related to neuronal changes and blood flow.[1,2] In addition, it is known that the initial compression of the optic nerve can lead to a partially reversible demyelination, however, it could also lead to an irreversible conduction blockage and a Wallerian degeneration due to direct compression or traction.[8,17] This theory is congruent to justify the postoperative surgical complication of visual loss worsening. This important surgical complication might be considered for the decision of surgery, specially with the patients that could undergo to a prophylactic measure.[9]

The operative management of craniofacial dysplasia in MAS is not well-established because it is a rare syndrome with few case reports in long-term follow-up, with variable outcomes and timing of intervention.[6,7,14,19]

Surgical technique of decompression can be divided into two subtypes: Conservative decompression and radical surgery. The conservative surgery consists in shaping the dysplastic bone, and it is often repeated over time with the objective of postponing the radical surgery, if needed. The radical approach consists in the radical removal of dysplastic bone and reconstruction with autologous bone graft.[19] Moreover, the prophylactic surgery for the optic nerve is reserved for the lesions that could lead to acute visual loss such as the ones related to aneurysmal bone cysts and mucoceles.[9]

Postoperative complications occur in 50% of patients and include infections, binocular diplopia, cranial nerve palsy, pain, epistaxis, and ectropion.[19] Prophylactic decompression is controversial, and the removal of the dysplastic bone increases the risk of surgical visual loss complication.

CONCLUSION

MAS is a rare subtype of FD with endocrinopathy. The FD of the orbital region can lead to optic nerve compression and possibly to visual loss. Nowadays, there are no evidences that support the benefits of prophylactic surgery in children with normal visual fields and optic canal narrowing, shown by the CT or MRI, and there is no method to predict which child will stabilize or deteriorate the visual loss. The cystic degenerations can lead to sudden visual loss and is the only possible indication for prophylactic surgery, but the risk of nerve damage should be considered and well-explained. In all other cases of normal visual fields and CT/MRI optic canal narrowing, prophylactic surgery is not indicated, and follow-up should be done. On the other hand, early decompression of symptomatic children is a great standard for a better chance of visual loss reverse.

The surgical technique is not well-established and depends on the case and surgeon expertise, but the conservative approach seems to be more adequate and multiple interventions might be required, especially in McCune–Albright and polyostotic lesions.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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