



Original Article ●●●

Surgical approach to the treatment of craniofacial fibrous dysplasia – A 14 – year experienced dysplasia – 14 years experience

Abordagem cirúrgica no tratamento da displasia fibrosa craniofacial – experiência de 14 anos

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■ ABSTRACT

Introduction: Fibrous dysplasia is benign tumor of the craniofacial skeleton that primarily affects young patients. It is characterized by the progressive growth of benign fibrous tumors with resulting functional and aesthetic deformities. This study assesses the clinical and prognostic features in patients with fibrous dysplasia who underwent surgical treatment at our institution. **Methods:** Retrospective analysis of 19 patients with craniofacial fibrous dysplasia, treated between January 1997 and December 2011 with bone remodeling and surgical resection. We also review the literature regarding fibrous dysplasia. **Results:** Patients ranged between 8–65 years old, with a mean age of 21.75 years. Ten patients (52.7%) were women. The polyostotic form was predominant and present in 15 cases (78.9%). The sphenoid, ethmoid, and frontal bones were most commonly involved in the polyostotic form and the mandibular and zygomatic bones were most commonly involved in the monostotic form. The main complaint was asymmetry of the face. One patient developed decreased visual acuity. Treatment was based on surgical resection and graft reconstruction in the localized form of the disease, and bone abrasion and remodeling in the polyostotic form. Intracranial access was necessary in only one case (5.2%) where the optic nerve was compressed. Repeat surgical treatment due to recurrent tumor growth was necessary in three patients. The only complication occurred in a patient who developed lagophthalmos and epicanthus postoperatively after undergoing surgery using infraorbital access. No other complications occurred during short- and long-term follow-up. Functional preservation and facial contour recovery outcomes were satisfactory. **Conclusion:** Our experience, along with that of other investigators, demonstrates that surgery is effective in treating selected cases of craniofacial fibrous dysplasia.

Keywords: Fibrous Dysplasia; Craniofacial; Treatment; Surgery; Reconstruction.

■ RESUMO

Introdução: Dentre os tumores benignos do esqueleto craniofacial, a displasia fibrosa caracteriza-se pelo crescimento progressivo e acometimento de jovens, acarretando deformidade funcional e estética. Esse trabalho analisa aspectos clínicos e prognósticos de pacientes com essa pa-

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tologia, submetidos a tratamento cirúrgico. **Métodos:** Análise retrospectiva de 19 pacientes com displasia fibrosa craniofacial, acompanhados de janeiro de 1997 a dezembro de 2011, tratados com remodelamento ósseo e ressecção cirúrgica. Revisão da literatura sobre. **Resultados:** A distribuição etária variou de 8 a 65 anos, com média de 21,75 anos. Dez pacientes (52,7%) eram do sexo feminino. A forma poliostótica predominou, com 15 casos (78,9%). Entre os ossos acometidos destacaram-se esfenoide, etmóide e frontal, nas formas poliostóticas; e maxila e zígoma, nas monostóticas. A principal queixa foi de assimetria da face. Um paciente evoluiu com diminuição de acuidade visual. O tratamento baseou-se na ressecção cirúrgica e reconstrução com enxerto, quando doença localizada, e no desgaste e remodelamento ósseo, em formas poliostóticas. Em apenas um caso (5,2%), com compressão de nervo óptico, foi necessário acesso intracraniano. Reabordagem cirúrgica, por crescimento tumoral, foi necessária em três pacientes. Como complicações, tivemos um caso de lagoftalmo e epicanto no pós-operatório de paciente tratado por cirurgia com acesso infraorbitário. Ausência de outras intercorrências no seguimento a curto e longo prazo. Os resultados de preservação de função e recuperação de contorno facial foram satisfatórios. **Conclusão:** Essa experiência, em concordância com a literatura, permite concluir que a cirurgia é eficaz na abordagem de casos selecionados de displasia fibrosa craniofacial.

Descritores: Displasia Fibrosa; Craniofacial; Tratamento; Cirurgia; Reconstrução.

INTRODUCTION

Fibrous dysplasia is a benign bone disease first described by Lincheinstein in 1938¹. It is characterized by the replacement of normal bone with fibrous tissue and is due to a developmental anomaly of the mesenchymal tissue. It initially occurs during childhood and continues to progress through adolescence and puberty, until its progression finally halts after puberty.

Depending on the degree of bone involvement, this disease is classified as monostotic or polyostotic, based on whether one or more bones are affected, respectively. When fibrous dysplasia is combined with endocrine disorders it is known as the McCune-Albright syndrome, manifest by areas of skin hyperpigmentation (café au lait spots) and precocious puberty.

The disease is due to an anomaly in the differentiation of the mesenchymal cells that originate in bone. The Gsa gene, located on chromosome 20q13.2-13.3, is responsible for regulating a protein whose alteration results in the hyperactivity of osteoprogenitor cells^{2,3}. This mutation was first identified in patients with the McCune-Albright syndrome and is present in both the monostotic and polyostotic forms of fibrous dysplasia.

Clinical presentation depends on the site, duration, extension, and nature of the lesion. In the craniofacial area, symptoms range from mild edema and localized asymmetry to proptosis and auditory and visual sensory loss due to cranial nerve compression. There is skull involvement in 27% of monostotic patients and up to 50% of polyostotic patients^{4,5}. The jaw is the most commonly affected bone in single face disorder^{6,7}. The base of the skull, especially the sphenoid bone, is also commonly involved.

Fibrous dysplasia demonstrates a chronic and benign

progression, and many patients remain asymptomatic. Malignant transformation is rare, but sarcoma is the most common histological type when this occurs^{8,9}.

Clinical suspicion requires investigation with radiological examinations. A computerized tomography scan (CT) may suggest the diagnosis without biopsy. The CT may show three different types of lesions:

- Sclerotic (compact) lesions: the most common finding (50%); typical sign: frosted glass between the diploe.
- Lytic lesions: radio-transparent.
- Pseudo pagetoid lesions: a mix of the two forms.

Magnetic resonance imaging (MRI) is used to confirm neural involvement and to provide further information about the lesion. Histological examination confirms the diagnosis.

The treatment of fibrous dysplasia is not definitive. Although the disease is localized, it is progressive and invasive. Clinically, alendronate can be used to control symptoms and provide radiologic improvement in some cases¹⁰. However, surgical intervention, including bone resection and abrasion, is often necessary to correct or improve functional problems and to achieve facial symmetry.

We will discuss the therapeutic approach to patients with craniofacial fibrous dysplasia, and review the epidemiological and progress data.

METHODS

A retrospective analysis of patients with fibrous dysplasia with involvement of the craniofacial area was performed. Patients were treated between January 1997 and December 2011. Nineteen patients were assessed clinically and radiologically. Of these, 18 patients underwent surgical treat-

ment. The outcome of the intervention and the progress of the disease were assessed.

RESULTS

Of the 19 patients affected with fibrous dysplasia there were 9 men and 10 women (52%). Patients ranged from 8–65 years old at the time of first presentation with a mean age of 21.75 years and a median age of 19.5 years.

In general, patients presenting at an earlier age showed more diffuse involvement and more apparent symptoms. The most prevalent clinical sign was progressive deformity of the facial contour. Fronto-orbital region involvement, leading to asymmetry and proptosis, was present in 10 cases. Nasal obstruction was reported by 3 patients. In 2 patients, the entire face was involved. Maxillo-mandibular disproportion and disocclusion were observed in a patient awaiting orthognathic surgery. One patient developed changes in visual acuity during follow-up secondary to compression of the optic nerve caused by the bone disease. Regarding comorbidities, one patient was diagnosed with factor VII deficiency, a relevant factor when planning surgery. The same patient presented with a midline fissure with agenesis of the nasal bones and duplication of the septum, demonstrated with a CT scan of the face.

All patients underwent CT scanning of the skull and face. The diagnosis was based on the characteristic frosted glass tomographic appearance of the lesions and was confirmed with pathological examination in those patients undergoing surgical intervention.

On the basis of the radiographic studies, 15 patients (79%) presented with the polyostotic form with involvement of multiple bones of the craniofacial region. Only 4 (21%) patients showed involvement localized to one bone, the characteristic finding of monostotic dysplasia. In the polyostotic form, the sphenoid bone was involved in 13 patients (68%), the ethmoid bone in 12 patients (63%), and the frontal bone in 11 patients (57%). The parietal bone, at the base of the skull, the mandible, and the zygomatic bone were involved in 8 patients (42%), the temporal bone was involved in 7 patients (36%), and the occipital bone and mandible were involved in 4 patients (21%). In the monostotic form, the mandible and the zygomatic bone were affected in 3 and 2 patients, respectively.

All patients were followed up by the craniomaxillofacial surgery team and, depending on the degree of involvement and symptoms, other medical specialties, such as endocrinology, neurosurgery, otorhinolaryngology, ophthalmology, and head and neck surgery.

Eighteen of the 19 cases underwent a surgical procedure. One young female patient, with progressive disease but without significant functional involvement did not undergo surgery and remains in outpatient follow-up. The surgical approach in most cases consisted of bone abrasion, with remodeling of the affected region in an effort to restore symmetry. In 3 patients with the monostotic form, involving the mandibular or zygomatic bone, osteotomy was performed with resection of the tumor from the affected bone, followed by bone graft reconstruction. Endonasal intervention was performed in 3 cases, with widening of the nasal cavity through reduction of

fibrous dysplasia involving the nasal turbinates and septum. Craniotomy was required to access and decompress the optic nerve in one patient. All other procedures were extracranial. Of the 19 cases, 3 (15%) patients required more than one surgical intervention for the treatment of bone dysplasia. All of these patients had polyostotic involvement.

With regard to postop complications, one patient developed lagophthalmos and epicanthus following sub tarsal access for biopsy of a jaw lesion, a procedure performed by a different team. A second patient complained of a depression over the temporal region as a result of localized muscle atrophy.

Two patients (10%) also received bisphosphonates for treatment of their fibrous dysplasia. The bisphosphonate pamidronate was administered intravenous every 6 months in a hospital setting, and was combined with daily calcium carbonate and vitamin D replacement therapy orally. No change in disease progression was observed in these patients and the treatment had no effect on symptoms or the eventual need for surgical intervention.

DISCUSSION

Fibrous dysplasia is a progressive, though self-limited, disease. Described by Licheinstein, it consists of the replacement of bone with fibrous tissue^{1,11,12}, leading to thickening of the involved tissues and to the associated signs and symptoms.

Its etiology is related to a mutation of the Gsa gene on chromosome 20q13.2–13.3, present in patients with the McCune-Albright syndrome and in the monostotic and polyostotic forms of fibrous dysplasia^{13,14}. The disease affects individuals in their childhood and teenage years, and tends to remain stable in adulthood, though some adults may continue to experience bone growth. Wei et al. showed that 61.73% of cases noted their first symptoms before they reached the age of 20 years,¹⁵ whereas Kransdorf et al¹⁶, reported that 75% of patients with fibrous dysplasia were younger than 30 years of age. The presence of the disease in childhood is rare, but there are some reports claiming that 34% of patient involvement occurs below the age of 6.¹⁷ In our study, the mean age of the affected individuals, at the time of initial presentation, was 21.75 years. There was no gender difference in our study, although some studies have shown a tendency for the disease to be more predominant among women¹⁵.

The monostotic form of fibrous dysplasia is considered to be most common, with an incidence of 70%¹⁵, in contrast to our findings. However, a meta-analysis has shown that the polyostotic form was predominant in 50% of patients¹⁸. It is worth noting that, in general, craniofacial fibrous dysplasia is diffuse and that no case of McCune-Albright syndrome was included in our study.

Regarding the affected sites, the predominant areas of involvement include the orbital region and the skull base. According to Maher et al¹⁹, the frontal, sphenoid, and ethmoid bones are most frequently affected. Yetiser et al²⁰, reported that the frontal, parietal, sphenoid, and occipital bones were most commonly affected. The results of our study are in line with the literature.

In the craniofacial region involvement leads to contour deformities, reduction of the orbital and nasal cavities, maxillo-mandibular disproportion, and, occasionally, compression of cranial nerves. The main complaint in our patients was facial asymmetry, particularly in the fronto-orbital region, with proptosis. Twenty-one percent of our patients complained of nasal obstruction.

Proptosis is a common finding (30%) in previous reports, and a reduction in the optic canal diameter may occur with sphenoid bone involvement. However, its relationship with visual impairment is not proportional²¹. Chen et al. showed that a third of patients will have visual deficits and two thirds of patients will present with some degree of visual impairment if the optic nerve is shown to be involved on imaging scans²². Lee et al²³, in contrast, reported that the vast majority of cases remain asymptomatic, even if there is radiological evidence of optic nerve compression. We had a 5% incidence of visual deficits in our patients, consistent with narrowing of the optic canal observed in CT scans of the face and skull. There is no consensus in the literature regarding the need for optic nerve decompression in fibrous dysplasia. The recommendation is for regular ophthalmologic follow-up in cases where optic canal stenosis is present and for surgical decompression when functional deterioration occurs. Prophylactic decompression does not appear to be beneficial and is not recommended²⁴, since it does not affect prognosis.

Radiological investigation, with CT scans of the face and skull, was helpful in the diagnosis and treatment of our patients. The frosted glass appearance of lesions on CT scan, a typical sign, provided confirmation of our clinical suspicion, allowed the detailed assessment of bone involvement, and served as a guide for planning our surgical approach. According to Maskiel et al²⁵, tomography is the first-line exam in the investigation of patients with a clinical suspicion of fibrous dysplasia.

Fibrous dysplasia is a disease with functional as well as aesthetic implications. In spite of its slow progression, with rare malignant transformation, we believe that this progressive, deforming disease that affects a younger population demands intervention.

It appears that cases with an early onset and polyostotic involvement have a worse prognosis. There is no effective therapy to slow disease progression and there appears to be no reliable data on which to base a patient's prognosis for further progression. Therapeutic options are limited, and since the disease is the result of a mutation in osteoblastic cells, the available interventions do not alter the progression of the disease, but only address the consequences of the disease.

Since the 1990s, bisphosphonates, potent inhibitors of osteoclast-mediated bone resorption, have been used in an attempt to reduce turnover in bones affected with fibrous dysplasia. Long-term intravenous therapy with pamidronate has been shown to be safe and efficacious in reducing pain and promoting radiological improvements in 50% of patients. In a study of 58 patients, most with long bone and pelvic involvement, treatment with pamidronate over 50 months resulted in a reduction in the intensity of pain in 41% of patients after the first cycle and in 69% of patients with subsequent administra-

tions²⁶. However, pamidronate did not change the course of the disease.

In another study, oral alendronate therapy reduced painful symptoms and tumor growth during the 6 months of treatment in only 3 patients. However, the treatment period was considered too short for a thorough assessment of the drug's efficacy²⁷.

The indications for the use of bisphosphonate therapy in patients without pain remain undefined. However, adult patients with significant osteolytic lesions seem to benefit from such therapy when at high risk for disease-related fracture. However, the need for surgical intervention is not reduced²⁶. In the 2 patients that received intravenous pamidronate therapy in our study, there was no change in symptoms, the progression of dysplasia, or the indications for surgery.

The main treatment for fibrous dysplasia, especially of the craniofacial region, remains surgical. The main goal of surgery is the restoration of functionality, along with of the relief of pain and sensory impairment. The aesthetic concerns of the patient are also important. Since the disease demonstrates a limited progression, clinicians often wait for clinical stability before proceeding with surgical intervention. However, in the presence of a functional impairment such as visual alterations due to nerve compression, nasal obstruction, and limitation in mouth opening, surgical intervention should not be delayed. Surgery is generally more effective after puberty, due to lower risks and a more predictable clinical course, allowing certain predictability in outcome. Regardless of the timing of surgical intervention, the possibility of a recurrence must always be considered²⁸.

The ideal therapeutic modality would be total resection of the area of fibrous dysplasia with immediate reconstruction using an autologous graft. However, due to the diffuse involvement, complex anatomy, limited surgical access, and the low rate of malignant transformation, the removal of the affected bone in its entirety is often not possible^{28,29}. Therefore, bone remodeling surgery with the goal of airway opening, nerve decompression, occlusal adjustment, and asymmetry and positioning correction is the treatment of choice in many cases of craniofacial fibrous dysplasia.

Surgical intervention requires a multidisciplinary team, based on the affected site and the disease manifestations. The indications for surgery are based on the clinical progression and symptoms of the disease, and it is preferably performed after puberty in light of the clinical course and pathophysiology of fibrous dysplasia.

CONCLUSION

Fibrous dysplasia, when involving the craniofacial region, has functional and aesthetic repercussions. Surgical intervention remains the most effective treatment for the control of symptoms and correction of deformity. Resection and reconstruction of the affected bone is the treatment of choice. Abrasion and remodeling become necessary in the polyostotic forms, aiming to restore facial symmetry and to improve function. The indications for surgery are based on the patient's complaints and degree of impairment, and surgery is more predictably performed after disease progression stabilizes.

Surgery may be performed more urgently when cranial nerves or other vital structures are affected.

In the future, intervention in the pathophysiology of the disease and the regulation of osteoclastic activity in fibrous dysplasia may offer a more promising and definitive therapy.

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