ORIGINAL ARTICLE

Jawbone fibrous dysplasia: retrospective evaluation in a cases series surgically treated and short review of the literature

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Abstract. *Background and aim of the work.* Fibrous dysplasia is a fibro-osseous osteopathy in which the normal bone architecture is replaced by fibrous tissue and non-functional trabeculae-like osseous structures. In head and neck area monostotic or polyostotic lesions cause a progressively expanding destructive bone swelling producing cosmetic deformities and functional impairments. The aim of this article is to present a retrospective review of a clinical case series with pathologically confirmed jawbone fibrous dysplasia for over an 8-year-period. *Material and Methods.* Clinical presentation and radiographic features of fibrous dysplasia affecting the jawbone skeletal area, surgical procedures performed including the reconstructive methods employed and clinical outcomes were analysed for each patient. *Results.* Seven cases were classified as having monostotic fibrous dysplasia while the others four cases were classified as having polyostotic form. The mandible was most commonly involved. The most common presenting features included marked facial deformity, intraoral bulging, malocclusion and dental alterations. Aesthetic and/or functional impairments were the major indications for surgical treatment in all the patients of this series. Six patients underwent bone remodelling while in the remaining cases subtotal or total resection was performed. Bone reconstruction by means of autologous free bone grafts or revascularized free bone flaps was made in three cases. *Conclusion.* The choice of the tailored therapeutic approach should be evaluated according the patient's age, rate of growth, anatomic location, type of involvement and the presence or not of functional disturbances and cosmetic alterations. Surgery remains the best therapeutic option.

Keywords: Fibrous dysplasia, jawbone, bone remodelling, craniofacial dysmorphisms

Introduction

Fibrous dysplasia (FD) is an uncommon fibro-osseous lesion that tends to grow throughout the skeletal developmental process replacing the normal internal trabecular pattern of bone and altering its size and shape (1,2). FD begins as a fibrous replacement of the medullary component of the bone, which in turn is replaced by a metaplastic woven bone that eventually matures into dense lamellar bone (3,4).

Although its actual incidence is not clearly established, FD comprises approximately 2.5% of all bone tumours and nearly 7.5% of benign bone pathology (1,4). The spectrum of skeletal involvement varies from asymptomatic monostotic lesions to polyostotic involvement resulting in progressive functional alterations and/or aesthetics dysmorphisms. There seems to be no transition from one form to the other (2).

The monostotic form accounts approximately 70-80% of cases and involves most frequently the rib, femur, jawbones, tibia, humerus in decreasing order of frequency; while the polyostotic variant occurs in 20-30% of cases and more frequently involves the lower half of the skeletal area. It has been estimated that approximately in 50 to 100% of patients with polyostotic form and in 20 to 30 % with monostotic variant neuro-splanchnocranial location is present (3,4).

The most commonly involved bones of the craniofacial skeleton are the frontal, sphenoid, ethmoid and maxillary bones. Furthermore, the involvement of the pathology is not necessarily monostotic, especially in cases of jawbone disease. In this case the other adjacent bones separated by sutures (zygoma, sphenoid, frontal bone, nasal bone) are often involved. The designation of craniofacial Fibrous dysplasia seems to be more appropriate for these lesions (1,4).

Polyostotic FD may occur as part of McCune-Albright syndrome, a condition that also includes skin pigmentations and endocrinopathies (5-7). When polyostotic form occurs in absence of endocrine disturbances it has been clustered as Jaffe-Lichtenstein Syndrome (6).

The association of soft tissue intramuscular myxomas adjacent to lesion of FD has been described in Mazabraund syndrome, in which, while fibrous dysplasia begins during the growth period and may be asymptomatic or present with pain, deformity or skeletal fractures, the associated intramuscular myxoma is usually multifocal and typically develops adjacent to skeletal lesions (8,9). There are some reports that describe FD in association with aneurismal bone cyst and dentin dysplasia (10).

FD affecting the facial skeleton seems to be a pathological condition commonly found in juvenile and young adult but also an adult-onset form is occasionally encountered (1,4). It is common belief that the active phase of FD usually starts in early childhood and gradually becomes quiescent and finally, with the termination of skeletal growth, the process becomes inactive and then ceases to growth in the late teens or early twenties. An uncommon form clustered as aggressive juvenile FD grows at an even faster rate producing major often-grotesque deformity that result in loose of function of the affected bone (3,4).

The biological behaviour of this uncommon bone disease seems to indicate that it does not represent a neoplastic disease (11). Malignant degeneration however has been reported in conjunction with FD and may include most commonly osteosarcoma as well fibrosarcoma, chondrosarcoma and malignant fibro histiocytoma (11-13).

FD is diagnosed on the basis of a series of data afforded by the clinical, instrumental and histopathological study. In this context the histology exhibits different patterns according the evolutive stage of disease (2-3,14). The stromal component of the lesion is fibrous, though the cellularity and amount of collagen may vary. The osseous structure is seen to be replaced by irregularly shaped trabeculae of immature bone. The bone trabeculaes are not connected to each other and often exhibits a disperse arrangement in the form of Chinese script writing and are not surrounded by plump appositional osteoblastic cellular pattern. Thin calcified spherules may be seen rarely. The lesioned bone fuses directly to normal bone at the periphery of the lesion so that no capsule or line of demarcation is encountered. Although FD of the long bones does not undergo involvement jawbones and skull lesions tend to be more ossified than their counterparts in the rest of skeleton and this is mainly observed in older patients (2,4).

The functional impairments and cosmetic deformities represent the main surgical concerns. In an effort to gain an improved appreciation for the clinical spectrum of this disorder, in this article we present the results of a retrospective analysis of ten surgically treated cases of FD affecting the maxillary skeletal area. The clinical presentations, instrumental imaging evaluative features and the therapeutic procedures performed with the long-term outcomes are analysed. The literature will be reviewed in the process.

Material and Methods

We retrospectively reviewed ten cases of histologically proven FD, treated in the Oral and Maxillo-Facial Department of Verona University Hospital from January 2000 to December 2008. The following records were subjected to a detailed analysis: medical history and clinical features, imaging studies (simple radiographs, CT scans), surgical procedures performed including reconstructive methods used, histopathological observations and outpatient clinical follow-up recordings. The clinic-radiological and therapeutic findings with the follow-up results are summarized in table I.

In the present series all patients were Caucasians and there was a female predominance with a female/male ratio of 6:4. At the moment of diagnosis their ages ranged from 14 to 53 years with an average age of 28,9 years while the age distribution based on the referred time of onset disease ranged from 10 to 48 with an average of 26,3 years. In particular, 40% of patients were in the second decade of life, 30% in the third decade, 30% in the fifth decade. Seven patients were classified as having monostotic FD based on involvement of only a single jawbone: in six cases the mandible on one side (case n° 1,4,5,6,8,10), and in the remaining case the maxillary bone was involved (case n° 2). The remaining three cases were classified as having polyostotic FD because of involvement of multiple bones throughout the facial skeleton: in one case (case n° 3) FD involved the left maxillary bone, showing a upward spreading with partial obliteration of the maxillary sinus and distortion of the nasal fossa, and affecting the homolateral zygomatic bone; in two other cases (case n° 7, 9) the involvement of the maxillo-malar bone occurred, whereas only in one case bilateral mandibular FD was observed.

Results

In all the patients of our series progressive localized or diffused swelling causing a facial deformity was one of the main presenting complaints (Fig.1). Intraorally, bone deformation and malocclusion were observed in the majority of the cases during the clinical exploration and the main dental alterations were variably consistent with preternatural mobility, maligned dentition, premature loss or impingement of tooth (Fig.2,3). Sinusitis and nasal obstruction were observed in one patient (case n° 3) (Fig.4). Mild orbital dystopia associated with homolateral proptosis, diplopia without visual impairments and evidence of infraorbital nerve dysfunction was noted in one patient (case n° 7) (Fig.5). Facial numbness in correspondence of the area of distribution of the infraorbital nerve was also observed in a case with maxillo-malar lesion (case n° 9). Spontaneous pain involving the alveolar crest and the lateral margin of the mandible with evidence of nervous dysfunction in the area innervated by the left mental nerve was observed in an adulthood patient with unifocal mandibular lesions (case n° 6). Total anaesthesia of the chin on the same side of the lesion and negative responsivity to the vitality tooth tests was assessed in an adulthood patient with previous history of repeated remodelling procedures of the mandibular lesion performed in a different institution (case n° 5).

Imaging studies (plain radiographs and CT scans) showed variably localized ground glass, woolly or sclerotic changes in most of the monostotic lesions (case n° 2, 4, 5,6). Multilocular radiolucency with characteristic
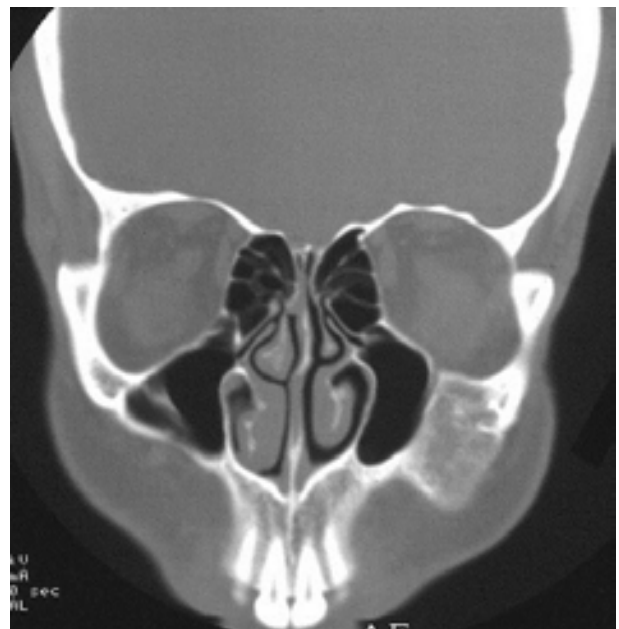
Figure 1. Coronal computed tomography (CT) scan shows a pagetoid-like lesion of the left maxillo-malar bone
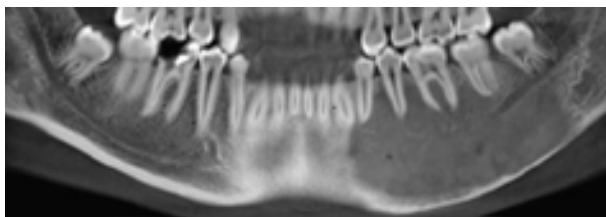
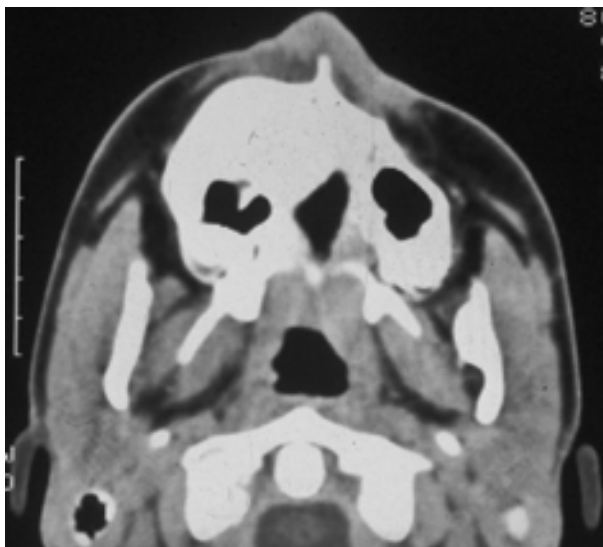**Figure 2.** Coronal tomography dental scan scan showing a left mandibular bone lesion with cotton-wool appearence

Figure 3. Three-Dimensional computed tomography scan of the mandible. The exam shows a lesion enlarging the left mandibular body

Figure 4. Axial Computed Tomography (CT) scan showing an extensive hyperostosing of sclerotic type of the right facial bones

Figure 4. Antero-posterior Radiograph showing a ground-glass opacification of the left maxillary bone

soap-bubble appearance were found in a case with mandibular involvement (case n°1). Jawbones polyostotic disease (case n° 3, 7) showed mainly pagetoid-like features, pathology that presents an alteration in the cycle of resorption and neoformation of the bones, of greater dimensions but nevertheless more fragile.

Surgical treatment guided by clinical presentation was performed in all of ten cases.

Bone remodelling procedures were performed in six patients (four with lower jaw lesions and two with upper jaw involvement). Two of these patients required bone reshaping associated with nervous decompression (case n°6,9) in order to improve the local neurological symptomatology. In the young patient with extensive maxillary-nose-ethmoidal involvement (case n°3) conservative bone contouring was attempted in association with a trans-antral partial excision.

Resective surgery was attempted in the remaining four cases of the present series (two cases with mandibular lesions and the other two with maxillary lesions). In a patient with massive involvement of the left mandibular body and ascending ramus (case n°5) hemi mandibulectomy without condylar disarticulation and immediate reconstruction with a revascularized free fibular flap was undertaken. Other two patients respectively with orbito-maxillary complex (case n° 7) and mandibular involvement (case n° 8) required a radical excision and the residual bone defects were reconstructed primarily with autologous bone grafts.

One patient with wide monostotic maxillary FD (case n° 2) was undertaken to radical excision without surgical reconstruction because it was refused so the defect was closed with local soft tissue flaps.

The histological findings of all surgical specimens were similar showing mainly dysplastic bone with irregular trabeculae of woven bone surrounded by a variable number of fibroblasts, osteoblastic giant cells, lymphocytes and hemosiderin filled macrophages.

Post-operative course was uneventful, and all ten patients had substantial improvement of their facial cosmetic appearance and functional impairments. The two cases with preoperative neurodysfunction findings (case n° 6,9) showed a significant relief following bone remodelling combined with nervous decompressive procedure. The patient with maxillary-nose-ethmoid lesion showed a partial reduction in nasal symptoms. Patients that underwent radical resection and immediate reconstruction with autologous bone grafts (case n° 7,8) and free revascularized fibular flap (case n° 5) had not gait deficit or pain associated with the harvest site.

There was no surgical morbidity in this series. Subsequently six patients of this series went to had a prosthetic rehabilitation in order to restore the mastication: in two patients (case n° 2, 6) it was performed a removable prosthesis while in the remaining four patients (case 5,7,8,10) it was done an implant-supported prosthesis. These patients were followed-up by clinical instrumental examination from 12 months to 5 years. In all the cases there was not evidence of recurrences of disease at clinic and instrumental examinations, using TC study, with the exception of one patient with mandibular lesion (case n° 4) previously treated with bone reshaping. This patient presented a slight regrowth in the lingual cortical aspect of the hemimandible 1 years after surgery that was managed with a further bone reshaping. The youngest patient of this series treated with bone remodelling and limited trans-antral resection of the maxillary-nose-ethmoidal lesion (case n° 3) showed no regrowth at the time of his last examination and actually in adult-age he is being considered to orthodontics and orthognathic surgery in order to correct a oral-facial deformity including malocclusion and a maxillary shift with an elongated maxilla.

Regarding follow-up on reconstruction, of the 2 patients who had free bone grafts, both have showed complete integration of these grafts while in the patient with osseous free flap reconstruction, the neomandible is still stable and is functioning normally.

Discussion

Fibrous Dysplasia involves the replacement of normal bone by growing fibrous tissue that posteriorly tends to undergo to bony metaplasia. The precise ethiology is still unknown although various theories have been reported (1-2,4).

FD appears to arise from a perturbation in the mesenchymal precursor of bone, producing a defect in osteoblastic differentiation and subsequent maturation of bone structure. There is clinical evidence that local infection or traumatic event may precipitate the disease under yet unrecognised condition (3,4).

Recently molecular biological investigations have indicated that FD may be caused by a mutation of the GNAS-1 (guanine nucleotide-binding protein, alpha- stimulating activity polypeptide 1) gene which give rise to an anomaly of the intracellular signalling (c-AMP) that produces increased cell proliferation and inappropriate cell differentiation, resulting in a disorganized fibrotic bone matrix (1,15-22). Additionally, increased synthesis of Interleukin-6, a cytokine involved in recruitment of osteoclastic cells, may play a role in the development of FD (18).

The clinical phenotype of this disease could to depend on the stage of development and location at which the mutation occurs. FD is thought to be a congenital disorder and some authors have suggested that this condition can be inherited by autosomal dominant inheritance (23-25).

Onset of FD is typically in adolescence or late childhood and most lesions are believed to be self-limiting after puberty when the patient's growth is complete (2,25-26). However, in literature several reports have disagreed this self-limiting growth proving this to be untrue (22). Rarely, the lesion is not evident until later in life, possibly reflecting the insidious asymptomatic nature of this process therefore lesions may also occur spontaneously in adult patients resembling

those of the mature juvenile FD. In our series there were three patients in whom the initial presentation and progression of this disease occurred in adulthood which does support the aforementioned contention of an adult-onset disease.

Patient age at presentation is highly variable. In Weeraprandist's series the mean age reported was 22 years with a range of 6-52 years (27). In turn other authors have reported a mean age of 25 years with a range of 5-55 years (28-29). In our series, the mean age at onset disease of 26,3 years with a range of 10-45 years and the M:F ratio of 4:6 is consistent with those reported in the literature.

Concerning the jawbones anatomical location, in literature it is reported that the maxilla is affected more often than the mandible, (1,3-4) however in our series the mandible was the anatomic site more involved with the posterior aspect more commonly affected.

According to the data of literature, in our series monostotic FD was the more prevalent form of bone disease affecting the middle and lower facial skeleton.

Clinically facial deformity is the most common presenting feature and sometime initially may be so mild as to be considered within normal range. In early-stage lesions involving the facial bones may go unnoticed because asymptomatic being often diagnosed incidentally after radiographic evaluation for other reasons like traumas to the facial massif or infectious pathologies. Teeth are often displaced, rotated, maligned producing a severe malocclusion as observed in the majority of our cases. The aggressive form of juvenile FD becomes symptomatic if the lesion is traumatized and ulcerated because of impingement by teeth during mastication and this was also observed in two of our cases. Pain may be present as consequence of the gradual expansion of the bone or less commonly by pressing on an adjacent nerve. Nasal obstruction and sinusitis have been related for lesion involving the maxillary bone and producing sinusal dislocation and nasal fossae distortion. Variable degree of orbital dystopia with proptosis and diplopia with or without visual impairments are consequence of orbital involvement (18).

While cosmetic deformities generally occur before functional problems, the combination of both occurs in severe cases as observed in our study.

The conventional x-ray presentation of Fibrous dysplasia is variable and depends on the stage of maturity of the lesion (1,2,30,31). In early-stage lesions may be radiolucent becoming more radiopaque as more bone is formed. A mature lesion retains none of the normal architecture of trabecular bone having replaced it with abnormal bone that produces a ground glass or orange-peel radiological pattern. There is no line of demarcation because the lesion blends with the surrounding bone. Expansion of the cortical plates, rarefaction of the lamina dura and displacement of tooth is common. Involvement of the mandible often results not only in expansion of the lingual and buccal plates but also bulging of the lower border (30-33). Displacement of the mandibular channel is not uncommon as showed in our series. In upper jaw involvement the lesioned tissue tends to displace the sinus floor superiorly and commonly obliterates the maxillary sinus as well as the nasal fossae (3,34).

Expansion and replacement of the bone as well as compromise of the anatomic structures are more precisely visualized on the CT scans. The CT investigation demonstrates the nature of lesion better by characterizing the matrix of the lesion. Cross-sectional imaging clearly defines cystic, sclerotic and mixed changes and bone window settings commonly show multiloculated lesions separate by bone trabeculaes (31,35). Areas of low attenuation (lytic) intermingled with areas of hyperattenuating (sclerotic) expansion give these lesions a pagetoid-like appearance. Three-dimensional CT scanning also is extremely useful in delineating the lesion and guiding the surgeon when intervention is being planned.

Bone scintigraphy shows an abnormal uptake in dysplastic bone lesions and may be performed in order to examine the systemic skeletal system of patients with Fibrous Dysplasia (36).

Laboratory studies in patients with Fibrous Dysplasia are characteristically within normal limits. However slight elevation of serum alkaline phosphatase and calcium may be observed and this probably because of high focal activity (3-4). In our cases, laboratory blood chemistry results were normal.

The differential diagnosis of jawbone FD varies according on the location, extent of involvement and the appearance of the lesion. Based on clinical and

instrumental imaging evaluations, in the differential diagnosis of FD must be contemplated some bone diseases that may be neoplastic, dysplastic or reactive in nature. In the differential diagnosis of monostotic FD solitary unicameral cyst, non-osteogenic fibroma, giant cell tumour of bone, aneurismal bone cyst, ameloblastomas, eosinophilic granuloma, plasma cell myeloma, other fibro-osseous lesions and sarcomatous neoplasms must be considered. The differential diagnosis of the polyostotic variant of FD should include hyperparathyroidism, polyostotic osteitis deformants, enchondromatosis, neurofibromatosis and cherubism (6).

It must be emphasized that precise diagnosis requires accurate clinical, radiologic and histologic assessment because the histological findings alone sometime may be similar for other fibro-osseous lesions with different behaviour and prognosis (37).

Concerning the treatment planning, a strategy based on an expected spontaneous regression in disease activity after adolescence is no longer advocated. Young patient with smaller lesions may require only biopsy for histopathological diagnosis and routinary clinic-instrumental observation (32).

As pointed-out by several authors, surgical treatment should be pursued as soon as possible when perceived and unacceptable cosmetic deformity becomes substantial or significant acute or progressive functional impairments such as alteration of sight, breathing, mastication or speech is documented by means of serial examinations (38-43). In this sense the surgical management of FD is so aimed to correcting functional problems and achieving normal facial cosmesis.

Depending on patient's age, rate of growth, anatomic location and type of bone involvement, functional and/or cosmetic impairments, surgical procedures performable range from conservative remodelling bone to subtotal or total resective procedures (38).

Although conservative surgical procedures represent the most common treatments of FD sometime aggressive surgery seems to be necessary because can prevent recurrences, stop further deformity and functional disturbances as well as possibly avoid malignant degeneration (3,39-44).

Sometime the diffuse nature and large size of the lesion affecting young patients require usually surgical reduction of the lesions to an acceptable contour without attempts to remove entirely the lesion. In these cases, cosmetic result is usually good, but regrowth of the lesion may occur over the time as show in our case n° 4.

The effective prevalence of these phenomena is difficult to determine, and it has been estimated that between 25% and 50% of patients treated show regrowth after surgical reduction being observed mainly in younger patients (38,39).

Furtherly some clinicians (3-4) believe that constant surgical osteoplasty of a lesion may accelerate an indolent to an aggressive course resulting in greater distortion that might otherwise occur. However other authors don't corroborate this observation (38).

We have to keep in mind that most asymptomatic lesions of the juvenile FD do not require treatment until the patients has reached early adulthood. At this time the degree of cosmetic improvement that can be accomplished by surgery is assessed.

In the patients of our series, conservative surgical treatment was performed for wide lesions both in a still growing patient with symptomatic polyostotic disease and young-adult or adult patients with important location of the disease causing obvious facial deformity while radical surgery was undertaken in order to obtain the complete removal of the pathologic bone tissue mainly in adulthood patients.

Furthermore, the improvement of rebuilding techniques has allowed the immediate reconstruction with satisfactory morpho-functional results (45-49). In this sense bone reconstruction represents the first stage of one more complex functional rehabilitation being it crucial to achieve the correct functional and aesthetic balance.

In our own experience size and location of the bone defect resulting from extensive surgical approach are the main parameters that we have to consider for the choice of the reconstructive technique. Commonly we perform the surgical reconstruction with iliac crest or calvarial bone grafts in those cases that present a bone defect less than 5-6 cm with no osseous contour disruption while in more large bone defect with discontinuity we prefer to perform the bone reconstruction by means of revascularized free bone flaps. In this last case the vascular independence of the recipient site

and the osseous healing process of the vascularized free bone flap allow for a high success rate (46,47).

Moreover, the modern endoscopic surgery is gaining space in other chronic pathologies of the facial massif, representing a possible therapeutic option in the different craniofacial dysmorphisms (47).

Sometime dentofacial deformities arising as a result of the progressive distortion of the mid and lower facial skeleton caused by the dysplastic bone may require obviously orthognathic surgery to correct both dental and skeletal relationships. In these cases, early excision of bone disease with primary reconstruction provides the fundamental architecture on which to base the planning of subsequent orthognathic surgical procedure (50).

Radiotherapy is not indicated because it carries the risk for development of post-irradiation bone sarcomatous malignancies (3-4,51). Medical management of Fibrous Dysplasia remains still poorly characterized, presenting a minor role only in the management of symptoms disease related (52,53). Some studies, have shown that in selected patients with FD may have considerable benefit from the intravenous infusion of bisphosphonates, calcitonin and mithramycin, targeted at reducing bone resorption based on the acknowledge that increased osteoclastic activity is seen with FD, though it is not specifically approved for the treatment of this disease (51-56).

Conclusion

The therapeutic guidelines for Fibrous Dysplasia of jawbones must be tailored to the individual patient and must be founded on clinical, radiological and patho-anatomical data: patient's age, anatomic location, type of involvement and the presence or not of functional limitation and/or cosmetic deformity should influence the choice of a specific and adequate treatment planning, always respecting what therapeutical innovations and recently health guidelines established (57).

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