Hesham Ali

Awais Ali and Ovais Malik

Fibrous Dysplasia: Dental and Orthodontic Implications

Abstract: Fibrous dysplasia is a benign condition characterized by replacement of bone by a fibro-osseous tissue. This article describes the aetiology, diagnosis and classification of the condition. We discuss the clinical presentation of fibrous dysplasia along with its craniofacial effects. The presentation of fibrous dysplasia in the dental setting is described, along with specific implications for dental and orthodontic management of these patients.

CPD/Clinical Relevance: Given the wide array of conditions that can present to GDPs, it is important to be aware of fibrous dysplasia as a possible cause of some signs and symptoms. The presentation, diagnosis and dental management of this group of patients is presented from a clinical perspective.

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What is fibrous dysplasia?

Fibrous dysplasia (FD) is a progressive, benign fibro-osseous condition characterized by replacement of normal bone by fibrous tissue and irregular bony trabeculae.[1,2] Although the World Health Organization categorizes FD within various groups of diseases, the most descriptive of these is as an osteochondrodysplasia arising from a chromosomal abnormality.[3]

The actual incidence and prevalence are difficult to estimate as mild cases and asymptomatic lesions may go undiagnosed, but are reported to represent 1% of primary bone tumours, and approximately 5–7% of benign bone tumours.[1,2,4] The majority of lesions are detected by the age of 30 years, with no gender predilection.

Hesham Ali, BDS, MDPH, MSc (Orthodontics), MFDS RCSEd, MOrth RCSEng, FDS (Orth) RCSEd, Consultant in Orthodontics, Royal Bolton Hospital, Bolton. **Awais Ali**, BDS, MJDF (Eng), Clinical Dental Officer, Integrated Care Centre, Dental Department. **Ovais Malik**, BDS, MSc (Orth), MFDS RCSEd, MOrth RCSEng, MOrth RCSEd, FDS (Orth) RCSEng, Consultant in Orthodontics, Salford Royal NHS Foundation Trust, Manchester.
email: hesham.ali@nhs.net

Aetiology of FD

The aetiology of FD is linked to a mutation in the GNAS1 gene located at chromosome 20q13.2-13.3. The mutation develops sporadically during early pregnancy, and therefore, while FD is a genetic condition, it is not inherited, or passed on to offspring of affected individuals. The gene mutation leads to abnormal differentiation of osteoblasts, which are thought to contribute to the development of lesions through the formation of fibro-osseous tissue. Common presenting features are fractures, deformity and pain.

FD is categorized as either monostotic fibrous dysplasia (MFD) or polyostotic fibrous dysplasia (PFD), depending on the number of sites involved (Table 1). MFD accounts for 75–80% of cases.[5] FD may occur in isolation, or in conjunction with a syndrome, most notably McCune–Albright syndrome (MAS), a sporadic disorder characterized by polyostotic FD, light brown skin pigmentation with irregular borders (café-au-lait spots), and one of several endocrinopathies.[6] Indeed, the GNAS1 mutation was first identified in patients with MAS, and the various extra-skeletal manifestations of FD generally affect this group of patients. Their clinical presentation is often a function of the various endocrinopathies. Notably, precocious puberty affects 50% of females, although it is rare in males.[7]

Clinical presentation of FD

The clinical presentation of FD and its impact on health depends on the location and number of the affected sites. Any part of the skeleton can be involved, and lesions may be randomly distributed, although long bones of the arms and legs, craniofacial bones, and the ribs are most often affected.[8] Severity is highly variable between individuals. Clinically significant lesions often manifest in early childhood and may become less active in adulthood. Progression of lesions tends to be limited by general growth and appears to diminish as skeletal maturity is achieved, although

	Lesions and signs	Estimates of craniofacial involvement (%)
MFD	Single bone only	10–25
PFD	Multiple bones	50–90
MAS	PFM Café-au-lait spots Endocrinopathies: ■ Growth hormone excess ■ Hypophosphataemia ■ Hyperthyroidism ■ Precocious puberty Uncommon signs: ■ Gastrointestinal reflux and polyps ■ Pancreatitis ■ Platelet dysfunction	90

Table 1. Classification of fibrous dysplasia.

Dental anomalies associated with FD
Rotation
Oligodontia
Displacement
Enamel hypoplasia
Enamel hypomineralization
Taurodontism
Retained deciduous tooth
Attrition

Table 2. Dental anomalies associated with FD.[17]

continued disease activity has occasionally been observed in adults.

Identification of lesions is often by chance, following a radiographic investigation for a different health concern, such as a fracture. The radiographic appearance is characteristically 'ground glass' and of variable radiolucency. Definitive diagnosis is based on an accurate clinical history, plain film radiographs, and CT and MRI scans (Figures 1 and 2). Technetium-99 bone scans can also be used to identify lesions in other parts of the body. In some instances, a biopsy may be required if a diagnosis cannot be established following radiographic examination, or if a lesion exhibits aggressive behaviour.

Lesions in leg bones can cause fractures owing to a reduced ability to bear weight, and the legs can eventually become bowed resulting in difficulty performing essential functions such as walking. Affected bones can become deformed, often seen with asymptomatic swelling of a rib, or scoliosis in the case of spinal involvement. The craniofacial effects are discussed later.

Rapid enlargement of lesions is usually related to secondary pathologies, such as aneurysmal bone cysts, or malignant change, although this is very rare (less than 1%). Typically, the malignancy is osteosarcoma, but others have been reported.[9,10] Osteomyelitis can also occur as a secondary complication, but is challenging to diagnose.

Craniofacial effects of FD

The involvement of the craniofacial bones is estimated to be between 10% and 25% in MFD, 50% and 90% in PFD,[11,12] and 90% of MAS patients.[12] Owing to the various pitfalls in diagnosing FD, there is a large variation in the reported frequency of involvement of the individual bones. Commonly affected bones are the ethmoid, sphenoid, frontal, maxilla and temporal bones, with some reports of occipital and mandibular lesions. The anterior cranial fossa is involved in 95% of patient with PFD or MAS. Lesions do not all behave in the same manner, and the following has been used to describe their variable presentation.[13]

- Quiescent: stable with no growth;
- Non-aggressive: slow growing;
- Aggressive: rapid growth with possible pain, paraesthesia, pathological fracture, malignant transformation, or association with a secondary lesion.

The first identifiable sign that may present to the dental team is an otherwise unexplained swelling that behaves most commonly as a slowly growing mass (Figure 3). Extra-orally, the degree of facial deformity varies greatly between individuals.[13,14] Bilateral lesions may easily be missed if they are mild, while larger lesions may give rise to noticeable deformity and associated cosmetic concern, mainly if they are unilateral and causing facial asymmetry. Lesions are not restricted by sutures and will often affect adjacent bones. Other extra-oral signs and symptoms depend on the location of the lesion and include frontal bossing, proptosis, vertical dystopia, pain and nasal congestion (Figure 1). FD affecting the orbits may cause constriction of the optic canal, although visual disturbances are rarely reported.

The location of the lesions also determines intra-oral findings. FD of the jaw may present with an associated buccal or palatal expansion, while the alveolar process tends to largely retain its original arch shape. Unilateral lesions may cause secondary occlusal problems due to asymmetric vertical, transverse and sagittal growth of the jaw. Teeth may be displaced, although this is not always a feature, and roots rarely exhibit resorption.[15] The most reported dental anomaly in FD patients is malocclusion. Weak associations with other anomalies have also been reported in the literature (Table 2).[16,17] The dental health experience of this group of patients tends to be worse than the general population, possibly owing to enamel hypoplasia or difficulties in accessing care. Radiographically, the inferior alveolar canal can be displaced by the lesion, and the periodontal ligament may be difficult to distinguish due to ill-defined lamina dura.[18]

General management of FD

There is no definitive medical or surgical treatment for FD, and spontaneous resolution does not occur.[19] A team approach should be used to address patients' needs, with management depending on:

- Patient's age and skeletal maturity;
- Site, severity and behaviour of lesions;
- Signs, symptoms and any secondary complications.

Most lesions do not progress after skeletal maturity has been achieved, and therefore

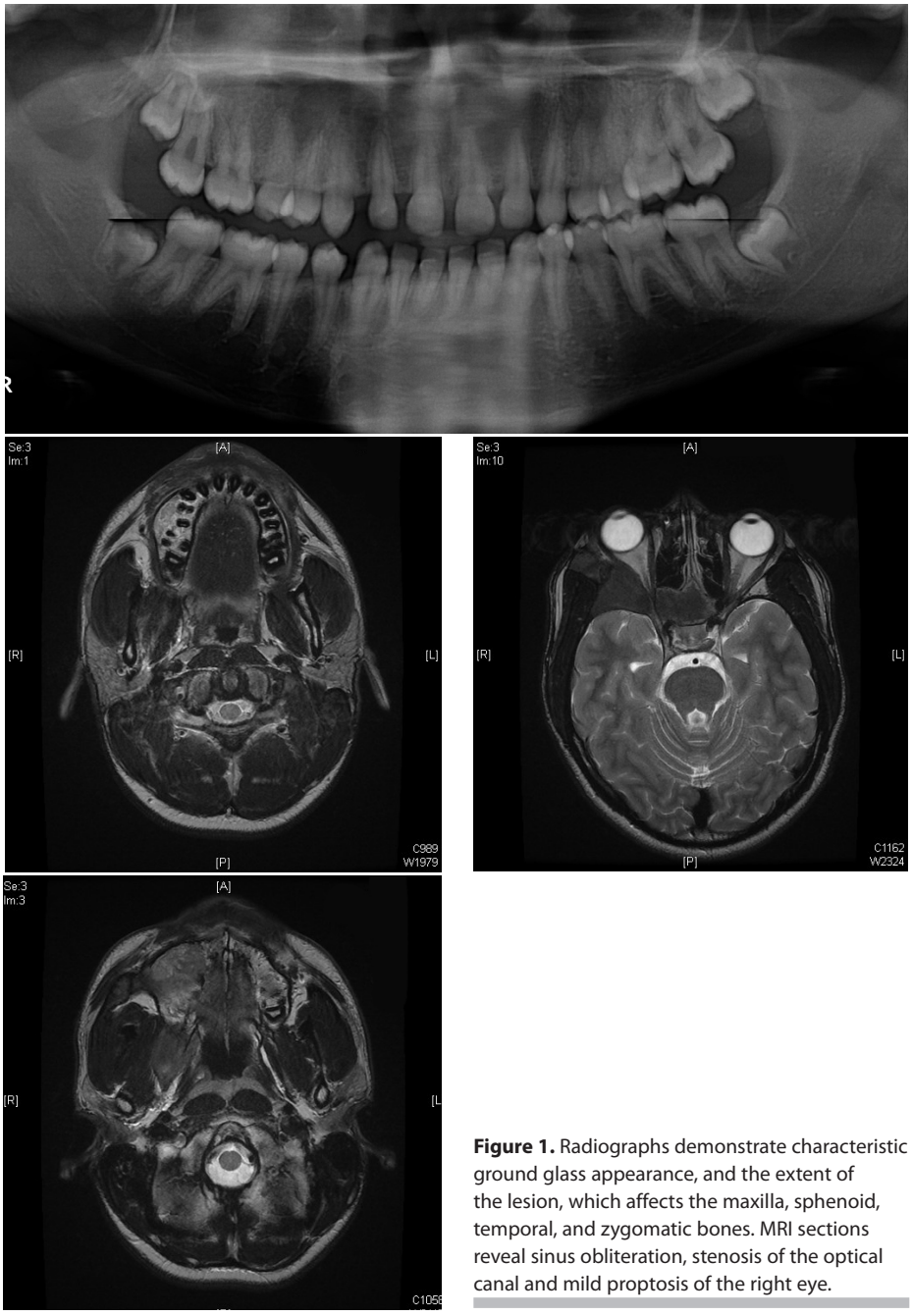

Figure 1. Radiographs demonstrate characteristic ground glass appearance, and the extent of the lesion, which affects the maxilla, sphenoid, temporal, and zygomatic bones. MRI sections reveal sinus obliteration, stenosis of the optical canal and mild proptosis of the right eye.

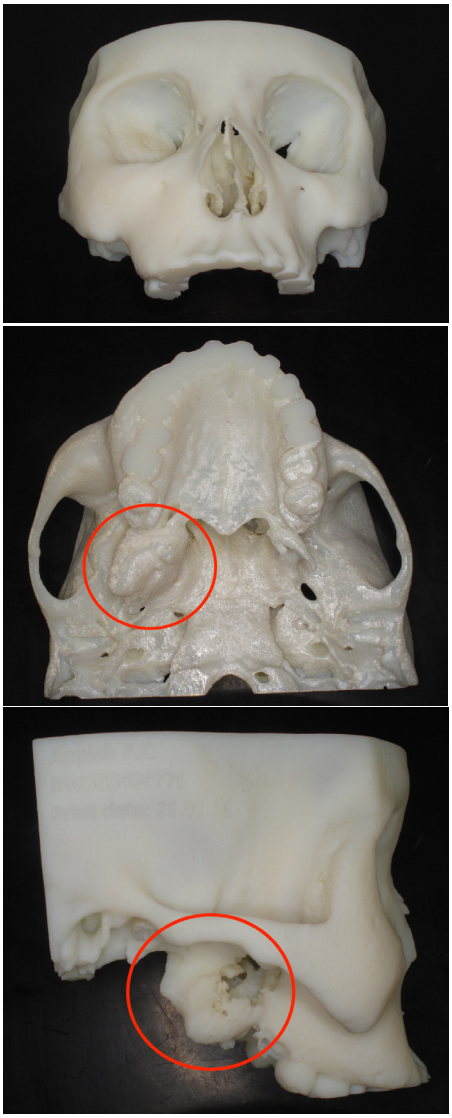

Figure 2. A 3D printed stereolithographic model of the patient's skull was produced from the MRI. This will assist in any planning being under taken by the maxillo-facial and neurosurgical teams. Noticeable growth affecting the right pterygoid plates and maxilla, with narrowing of the optic canal.

intervention is best delayed until this time. Any extra-skeletal lesions or problems should be addressed, along with treatment for bony lesions, as the various issues tend to be inter-linked, and failure to address the former will often lead to a relapse of the latter. The various strategies are listed in Table 3.

Any orthopaedic treatment aims are to maximize function while minimizing morbidity associated with treatment, in particular, pain, fractures and deformity. Conservative measures are normally used for paediatric patients, with emphasis placed on physical therapy to maintain strength and mobility of the affected areas. Bisphosphonates have been used to treat FD by pharmaceutically reducing the rate of bone turnover, and have been suggested to reduce the fracture rate and pain associated with lesions.[20]

Management of craniofacial FD

The aims of treatment for craniofacial lesions remain the same, but with additional consideration for aesthetics given the visibility of lesions affecting this area (Figure 4).

Approximately 40% of patients with craniofacial FD complain of pain.[21] This can be managed with NSAIDs, or with bisphosphonates, which may also help to

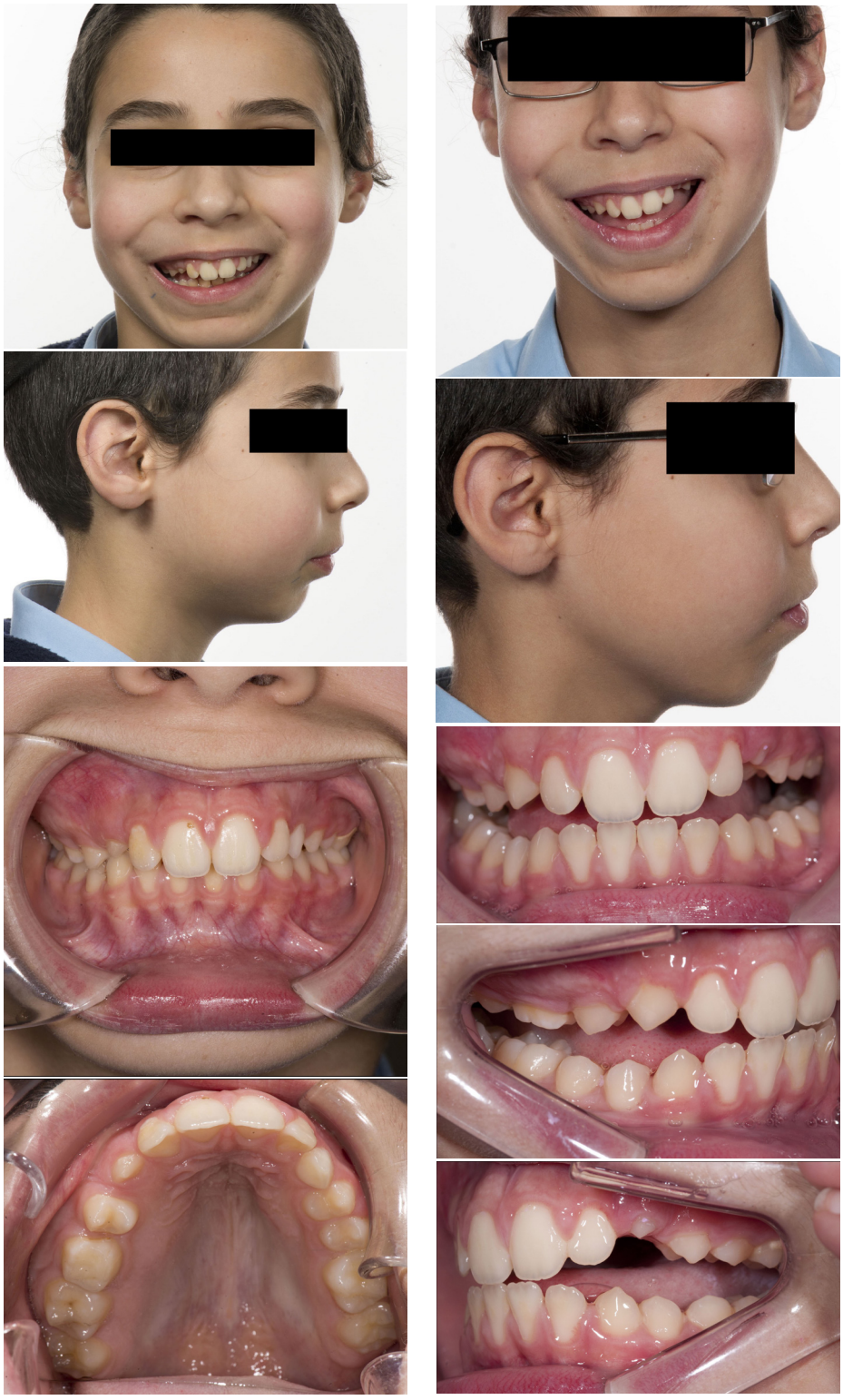

Figure 3. Photographs and radiographs of a patient affected by craniofacial MFD. Note the right side facial swelling and prominent occlusal cant. There is a Class II malocclusion, with noticeable buccal and palatal expansion in the upper right quadrant. Vertical overgrowth of the maxilla has caused compensatory changes in the mandible. A modified twin block appliance was used to attempt growth modification, with one larger block to compensate for asymmetric growth. The asymmetry has persisted.

reduce the growth rate of lesions, although changes in radiographic appearance are highly variable.

While mild or quiescent lesions may only be monitored, surgery remains the mainstay of treatment for lesions causing deformity or functional impairment. The following approaches may be taken:

- Debulking and recontouring procedures are often undertaken to reduce the size of deformity and improve facial appearance. There is a tendency for recurrence due to post-operative growth, although the exact mechanism is not understood. This approach is, therefore, best undertaken once growth is complete. However, patients with gross deformity may be treated earlier to improve function and appearance but should be advised of the potential need for repeat procedures.
- Resection and reconstruction can also be a treatment option, but is generally limited to patients with MFD. This has a lower recurrence rate (45%) than debulking (82%),[22] but patients experience greater morbidity. The involvement of multiple bones where the disease is extensive, as in PFD and MAS, usually precludes the use of surgical resection.

Dental implications

General dental practitioners play an essential role in the care of these patients, particularly those affected by MFD. Often, the presenting sign or symptom may be an unexplained intra- or extra-oral swelling, which may easily be disregarded as a variation of normal anatomy. Jaw pain and problems eating may also suggest a diagnosis of FD. With the possibility of significant deleterious effects, GDPs should be aware of the possible presenting features of FD, be able to recognize the characteristic ground glass radiographic appearance and understand when a referral to secondary care centres is appropriate. This would typically be the local maxillo-facial or orthodontic department, where a multidisciplinary team can plan long-term care.

Given the vast array of potential health concerns affecting this group of patients, their dental health may be neglected.

Figure 4. Photographs of a patient affected by craniofacial PFD**.** Note the mild swelling overlying the right maxilla. There is a Class I malocclusion, with noticeable buccal expansion of the right maxillary alveolar process. The LL4 and LL5 have also been displaced into a lingual crossbite.

Lesions affecting the jaws may cause the development of malocclusion that hinders effective oral hygiene measures. The caries history of FD patients is worse than the general population,[17] and as such, it would be prudent to increase the frequency of recall visits and provide intensive preventive therapy, including the use of topical fluoride application and fissure sealants. Preventive dentistry is fundamental in protecting their long-term dental health and minimizing the need for complicated treatment, for example endodontic treatment for taurodonts, or extraction of unrestorable teeth that risks the development of osteonecrosis of the jaw in patients receiving bisphosphonate therapy. Once caries extends to the pulp chamber in a tooth with a taurodontic pulp, root canal therapy might be challenging. This is an indication for early referral to an endodontic specialist for treatment. Severe malocclusion may also require orthodontic intervention. When orthodontic treatment is clinically indicated, the timing should be carefully coordinated between the general dental practitioner and the orthodontist.

The other factors contributing to a high caries rate include inadequate access to care, particularly given the lack of information available to dentists in treating patients with FD, along with enamel hypoplasia and hypomineralization. The need for preventive measures is underlined here again. Should teeth be lost, replacement may take the form of dentures or bridgework, although the provision of effective removable prostheses may be limited by unfavourable bone contours, which may be dynamic in the non-aggressive and aggressive forms of FD. Implants have also been successfully used to replace missing teeth, although the numbers reported are small and with a variable period of follow up.[23] While bony healing and osseo-integration do occur, the process may be slower and with a lesser quality of bone compared to a healthy population. Placement of implants should be delayed until lesions demonstrate quiescence.

Orthodontic implications

The sparse literature on the orthodontic management of FD patients is limited mainly to case reports and observational studies. Therefore, the knowledge base around this topic is a construct of theory and reports of experience. Patients should be appropriately informed about the potential risks of treatment during the consent process. The following considerations should be made when making decisions about orthodontic care:

- Variable tooth movement: although there is a suggestion of slower tooth movement, some authors have reported reduced treatment time in patients with FD.[24] The basal rate of tooth movement may also be modified by bisphosphonate therapy. The use of this group of drugs does not contraindicate orthodontic treatment, but has the possible effect of reducing the rate of tooth movement and the risk of relapse as a result of decreased bone turnover.
- General health: affected patients may be experiencing non-orthodontic problems of higher priority; therefore, the treatment strategy should be adjusted to address the needs of individual patients. This may take the form of limiting the aims of treatment, altering extraction patterns, or indeed, avoiding extractions entirely.
- Customized mechanics: orthodontic mechanics should be tailored to address particular occlusal traits. For example, the use of an asymmetric twin block appliance may be helpful in managing patients with a vertical or transverse discrepancy arising from a unilateral lesion (Figure 3), or the use

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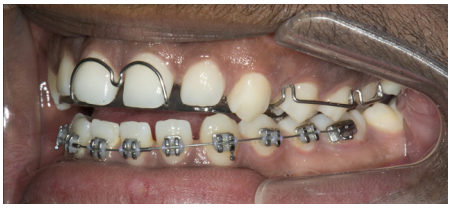

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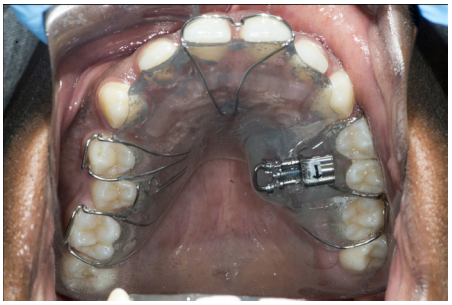

Figure 5. (a, b) A lower fixed appliance with an expanded nickel–titanium archwire combined with a URA to constrict the UL45 is being used to correct the transverse occlusal traits.

of a removable appliance to contract the upper arch when teeth have been displaced buccally (Figure 5).

- Surgical correction: patients with skeletal discrepancies may require a combined orthodontic and orthognathic approach to correct their malocclusion, which may be caused by, or superimposed on, FD lesions. Orthognathic surgery should only be performed once lesions are quiescent, and should ideally coincide with any debulking, recontouring, or other surgery, for example correction of ear canal stenosis. Conventional rigid internal fixation has been reported with normal healing thereafter.[25] The surgical team should also continue to review the patient to monitor health and identify any recurrence.
- Multidisciplinary care: in light of the above, patients' overall management plans, and in particular craniofacial surgery, should be planned by a multidisciplinary team. Depending on the severity of disease, this will include oral and maxillofacial surgeons, plastic surgeons, neurosurgeons, paediatric dentists and orthodontists. This team-based approach will reduce the number of general anaesthetics, surgical time and morbidity for affected patients.

Conclusion

Fibrous dysplasia is a complex genetic condition, which may be subclinical or present as a wide range of signs and symptoms. Clinicians should be attentive to possible presentations and non-craniofacial effects of this disease and ensure appropriate and timely referral to relevant specialities. Affected patients have greater dental care needs compared to the general population, and therefore, general dental practitioners are encouraged to deliver more intensive preventive strategies to reduce the burden of care on patients in the long term. Review of the literature indicates that routine dental care can be safely and successfully carried out in FD patients with minimum complications.[13] Treatment for malocclusion should be provided in secondary care settings, and planned by a multidisciplinary team, particularly if any surgery is being considered. Awareness of different presentation, complications and treatment strategies is essential to making early diagnoses, formulating appropriate management plans, and optimizing outcomes for affected patients.

Sign/symptom	Aetiology/frequency	Other information	Management
Nasal congestion	Sinus obliteration	Sphenoid sinus most frequently affected Associated with GH excess Symptoms include headaches, facial pain, recurrent sinusitis and hyposmia	Nasal sprays (saline and steroid) Sinus surgery is uncommon
Visual disturbance	Narrowing of the optic canal leading to optic nerve compressions Rare	Associated with GH excess	Close monitoring by ophthalmologist Prophylactic decompression is not recommended
Auditory impairment	Temporal bone lesions leading to conductive and sensorineural hearing loss as a result of crowding of the ossicular chain[22] Stenosis of the external auditory meatus	Usually mild to moderate Stenosis is responsible for a minority of cases	Surgery for complications including cholesteatoma and neat total stenosis
Weakness of facial muscles	Compression of facial nerve Rare	Location of compression may be difficult to assess	High resolution CT to diagnose. Referral to surgical team

Table 3. Management strategies for the various signs and symptoms of craniofacial FD.

Compliance with Ethical Standards

Conflict of Interest: The authors declare that they have no conflict of interest.

Informed Consent: Informed consent was obtained from all individual participants included in the article.

References

1. Coley BL. *Neoplasms of Bone and Related Conditions; Aetiology, Pathogenesis, Diagnosis, and Treatment.* 2nd edn. New York: Hoeber, 1960.
2. Campanacci M. *Bone and Soft Tissue Tumors: Clinical Features, Imaging, Pathology and Treatment*. 2nd edn. New York: Springer, 1999.
3. World Health Organization. International Classification of Diseases 11. 2018. Available at: https://icd.who.int/en (accessed March 2021).
4. Parekh SG, Rao DR, Ricchetti E, Lackman RD. Fibrous dysplasia. *J Am Acad Orthop Surg* 2004; **12**: 305–313.
5. Grabias S L, Campbell C J. Fibrous dysplasia. *Orthop Clin North Am* 1997; **8**: 771–783.
6. Weinstein LS, Shenker A, Gejman PV et al. Activating mutations of the stimulating G protein in the McCune-Albright syndrome. *N Engl J Med* 1991; **325**: 1688–1695.
7. Collins MT, Singer FR, Eugster E. McCune-Albright syndrome and the extraskeletal manifestations of fibrous dysplasia. *Orphanet J Rare Dis* 2012; **7 (Suppl 1)**: S4.
8. Ippolito E, Bray E W, Corsi A et al. Natural history and treatment of fibrous dysplasia of bone: a multicenter clinicopathologic study promoted by the European Pediatric Orthopaedic Society. *J Pediatr Orthop B* 2003; **12**: 155–177.
9. Sadeghi S M, Hosseini SN. Spontaneous conversion of fibrous dysplasia into osteosarcoma. *J Craniofac Surg* 2011; **22**: 959–961.
10. Varghese AI, Harrop CW, Smith WP. Malignant transformation of fibrous dysplasia of the maxilla. *Int J Clin Pract* 2010; **64**: 121–122.
11. Neville BW, Damm DD, Allen CM, Bouquot JE. Bone pathology. In Neville BW, Damm DD, Allen CM, Bouquot JE (eds). *Oral and Maxillofacial Pathology*. 3rd edn. Philadelphia, PA: WB Saunders, 2002; 553–557.
12. Ricalde P, Magliocca KR, Lee JS. Craniofacial fibrous dysplasia. *Oral Maxillofac Surg Clin North Am* 2012; **24**: 427–441.
13. Lee JS, FitzGibbon EJ, Chen YR et al. Clinical guidelines for the management of craniofacial fibrous dysplasia. *Orphanet J Rare Dis* 2012; **7 (Suppl 1)**: S2.
14. DiCaprio MR, Enneking WF. Fibrous dysplasia: pathophysiology, evaluation, and treatment. *J Bone Joint Surg Am* 2005; **87**: 1848–1864.
15. MacDonald DS. Maxillofacial fibro-osseous lesions. *Clin Radiol* 2015; **70**: 25–36.
16. Akintoye SO, Otis LL, Atkinson JC et al. Analyses of variable panoramic radiographic characteristics of maxillo-mandibular fibrous dysplasia in McCune-Albright syndrome. *Oral Dis* 2004; **10**: 36–43.
17. Akintoye SO, Lee JS, Feimster T et al. Dental characteristics of fibrous dysplasia and McCune-Albright syndrome. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2003; **96**: 275–282.
18. Neville BW. Oral and Maxillofacial Pathology. 3rd edn. St Louis, Mo: Saunders, 2009.
19. Charpurlat RD, Meunier PJ. Fibrous dysplasia of bone. *Bailliere's Clin Best Pract Res Clin Rheumatol* 2000; **14**: 385–398.
20. Lane JM, Khan SN, O'Connor WJ et al. Bisphosphonate therapy in fibrous dysplasia. *Clin Orthop Relat Res* 2001; **382**: 6–12.
21. Kelly MH, Brillante B, Collins MT. Pain in fibrous dysplasia of bone: age-related changes and the anatomical distribution of skeletal lesions. *Osteoporos Int* 2008; **19**: 57–63.
22. Boyce AM, Burke A, Cutler Peck C et al. Surgical management of polyostotic craniofacial fibrous dysplasia: long-term outcomes and predictors for postoperative regrowth. *Plast Reconstr Surg* 2016; **137**: 1833–1839.
23. Bajwa MS, Ethunandan M, Flood TR. Oral rehabilitation with endosseous implants in a patient with fibrous dysplasia (McCune-Albright syndrome): a case report. *J Oral Maxillofac Surg* 2008; **66**: 2605–2608.
24. Burke A, Collins MT, Boyce AM. Fibrous dysplasia of bone: craniofacial and dental implications. *Oral Dis* 2017; **23**: 697–708.
25. Yeow VK, Chen YR. Orthognathic surgery in craniomaxillofacial fibrous dysplasia. *J Craniofac Surg* 1999; **10**: 155–159.