An Unusual Presentation of Craniofacial Fibrous Dysplasia: A Case Report, Review and Update on Management


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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 phenotype is variable and may be isolated to a single skeletal site or multiple sites and sometimes is associated with extra skeletal manifestations in the skin and/or endocrine organs (McCune-Albright syndrome). The clinical behavior and progression of FD may also vary, thereby making the management of this condition difficult with few established clinical guidelines. This case report provides a clinically-focused comprehensive description of craniofacial FD, its natural progression, the components of the diagnostic evaluation and the multi-disciplinary management.

Keywords: Monostotic Fibrous Dysplasia; Maxilla; G Protein; geneGNAS; Subtotal Maxillectomy

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Introduction

Fibrous dysplasia (FD) is a non-malignant condition in which normal bone and marrow are replaced by fibrous tissue and haphazardly distributed woven bone [1, 2]. Patients may exhibit involvement of one bone (monostotic FD; MFD), multiple bones (polystotic FD; PFD) or they may have McCune-Albright syndrome (MAS), which has been classically defined by the triad of PFD, café-au-lait skin macules and endocrinopathies, including among others, precocious puberty [3]. FD is caused by somatic activating mutations in the α subunit of the stimulatory G protein encoded by the gene GNAS [4, 5]. MFD is reported to be the most common manifestation of the disease, in some references it is estimated to occur four times more often than PFD [6]. However, in other series PFD is reported to be more common than MFD [7, 8]. While the prevalence of MFD is probably greater than PFD, in none of the studies that define the relative prevalence of MFD versus PFD have the subject’s undergone thorough skeletal and/or endocrine screening to determine the full extent of the skeletal and/or endocrine involvement. The most common locations are the craniofacial bones, proximal femur, and rib [2, 8, 9]. In MFD, the zygomatic-maxillary complex is reported to be the region most commonly involved [10]. In the less prevalent PFD and MAS, the craniofacial region is involved in 90% of the cases and the anterior cranial base is involved in over 95% of cases [11]. Depending on the type and location of FD, the signs and symptoms vary and include facial deformity and asymmetry, vision changes, hearing impairment, nasal congestion and/or obstruction, pain, paresthesia, and malocclusion. Many patients are asymptomatic and the diagnosis is made when a family member, friend or health care provider who has not seen the patient for a period of time notices asymmetry, or there is an incidental abnormality noted on dental or panoramic x-rays or on a head and neck computed tomogram (CT). Uncommonly, in young children and pre-pubertal adolescents, the lesions may demonstrate rapid growth, cortical bone expansion and displacement of adjacent structures such as the eye and the teeth. In some patients, rapid growth is associated with other pathological lesions such as aneurysmal bone cysts (ABC) or mucoceles [11, 12] more rarely with malignant transformation. Malignant change to osteosarcoma or other forms of sarcoma has been reported to occur in less than 1% of cases of FD [11, 13]. In addition, in the NIH Screening and Natural History Study of Fibrous Dysplasia (SNHFD, protocol 98-D-0145) has documented persistent active disease and pain into adulthood in some patients. Based on >25 years of observation at the NIH, it appears that MFD, does not progress to PFD and neither progress to MAS [14].

Case Report

A 10-year-old boy reported to our hospital with a painless, diffused, progressive swelling over right side of the face. As per the history given by the patient the swelling was initially of the size of a peanut which within the period of 6 months increased rapidly to present size. On clinical evaluation a diffused
swelling extending from right infraorbital margin to inferior border of the mandible (craniocaudally), mediolaterally from ala of the nose to tragus of right ear (Figure 1). Extra oral clinical examination reveals obstruction of right nostril completely. The patient was suffering from eye symptoms like epiphora and proptosis with no signs of diplopia, with no history of paresthesia (Figure 2). Intraoral examination reveals the tumor extending from right maxillary central incisor extending to the posterior border of maxilla; swelling is so extensive obliterating the right upper buccal vestibular region (Figure 3). Patient medical, family and social history was unremarkable. There was no history of trauma. During taking an incisional biopsy the bleeding was significant and diagnosed as MFD. The patient was subsequently admitted to the hospital and taken for surgery under general anesthesia. The treatment has been planned to do the subtotal maxillectomy and ligation of the terminal branch of external carotid artery like (maxillary artery and superficial temporal artery and vein.) The treatment has been accordingly planned to resect the tumor en bloc in Toto. The Fibrous dysplasia created a cleavage between a healthy bone and tumor margins. By seeing the socio economic condition, the patient doesn’t afford the cost embolization of the terminal branches of the external carotid artery, so the treatment has been planned to ligate the terminal branches of the external carotid artery and enbloc resection of the tumor. By taking the consent of the patient considering the age of the patient and the present reports of CBC the hemoglobin was 8 gm. /dl, it is decided to give extra oral incision and to ligate the external carotid artery in retromandibular fossa and resection of the tumor intra orally. The complication has been explained to the patient like diplopia, paresthesia, facial nerve paralysis, hematoma, infection, facial aesthetic deformity, meningitis and consent taken. The resection of tumor has been done and the peripheral margins of the tumor like inferior margin of the orbit, infra temporal fossa, nasal cavity and its posterior extension to pharynx, nasolacrimal duct has been sent for frozen sections. As per the reports of frozen section the tumor is resected successfully and the peripheral margins are free of the lesion. During resection the Pterygoid hammulus is exposed intraoral and the reconstruction of the pterygoid hammulus has been done by pedicled buccal fat pad and remaining defect covered with split thickness skin graft. The defect has been packed with sterile gauze. Intraoperative the total blood loss was about 150ml of blood which was replaced inter and post operatively with 2 units of packed cell volume. As previously decided in treatment plan the intra oral impression has been taken and the obturator has been prepared previously. After removal of the sterile pack the defect has been carefully examined and the obturator is fixed with the help of Adams clasp. Patient responded well to surgery postoperatively without any complication as explained to patient. Preoperatively the Intraocular pressure of the Right eye when checked with schiotz tonometer was increased to 24mmhg with 5.5gmwt which after surgery decreased to 20mmhg due to resection of the tumor. Tumor was extending into the ethmoid sinus invading the cribriform plate of ethmoid which resulted in CSF leak when the tumor was resected. The cribriform plate of the ethmoid has been invaded by the tumor and the reconstruction of cribriform plate has been done by the chin graft. Postoperatively after 5 days the CSF rhinorrhea is stopped. Ryles tube feeding was started to
the patient postoperatively to avoid infection. After review of 3 months, 6 months there was no complication present. As per the socio economic condition of the patient it is not possible to reconstruct the defect with micro vascular graft. So the patient has been reviewed after 6 months (Figure 6) and planned for reconstruction of the floor of the orbit and maxilla. Patient had epiphora from Right eye and when checked for exophthalmos of Right eye with Lueddes exophthalmometer it showed proptosis of Right eye by 24mm as compared to Left eye. Vision in Right eye was normal 6/6. There were no signs of exposure keratopathy.

**Investigation**

1. On radiological examination CT scan shows a swelling of size 29 x 50.5mm, multilocular, expansile, lytic lesion involving the anterior wall of the right maxillary sinus medially the tumor extending into the right nostril and obstructing the right nasolacrimal duct, cribiform plate of ethymoid superiorly the tumor was perforating the floor of the orbit, the posterior limit of the tumor up to infratemporal fossa. The tumor shows foci of calcification with no intracranial abnormality (Figure 4).

2. All the investigations like complete blood picture Hb-8gm./dl, serum electrolytes, blood grouping, prothrombin time, plasma thromboplastin time, INR, parathyroid hormone, calcium, phosphorus, serum alkaline phosphatase are within normal limits.

3. Incision biopsy performed. Histopathological examination (HPE) report suggestive of Fibrous dysplasia. As per histopathological report showing the aggressive monostotic fibrous dysplasia reveals irregular bony trabeculae with osteoblasts surrounded by interlacing bundles of monomorphic spindle cell, the fibroblast exhibit uniform spindle to star shaped nuclei. The bony trabecular assume bizarre irregular shapes likened to Chinese character (Figure 5).

4. Excisional biopsy confirmed the report of the incisional biopsy.

*Figure 1* Facial Profile  
*Figure 2* Lateral Profile  
*Figure 3* Intraoral Profile
Figure 4 Computed Tomogram showing extension multilocular, expansile, lytic lesion involving the anterior wall of the right maxillary sinus medially the tumor extending into the right nostril and obstructing the right nasolacrimal duct, cribiform plate of ethmoid superiorly the tumor was perforating the floor of the orbit, the posterior limit of the tumor up to infratemporal fossa. The tumor shows foci of calcification with no intracranial abnormality.

Figure 5 Histopathological features suggestive of Fibrous Dysplasia Fibroblasts within woven cancellous bone

Figure 6 OPG showing 3 months Postoperative
Differential Diagnosis

The primary Differential Diagnosis for Fibrous Dysplasia of jaw is ossifying fibroma. Clinical, radiographic and microscopic features must be considered together in order to distinguish these processes most accurately. In general lesion diagnosed as ossifying fibroma has a thin bony shell and a distinct boundary seen in Radiograph. Whereas the two lesions were based only on histologic criteria. Fibrous dysplasia way reported to contain only woven bones without evidence of osteoblastic rimming of bone. The presence of mature lamellar bone was believed to be characteristic of ossifying fibroma. Most authorities now acknowledge that criteria are unreliable because both types of bone may be found in either lesion [15]. Sign and symptoms of fibrous dysplasia and sclerosing osteomyelitis of Garre may be clinically distinguishable. Radiographically both diseases may produce appearances characterized by region of sclerosis with or without osteolytic area with enlargement of jaw. The enlargement in sclerosing osteomyelitis is due to periosteal new bone formation. Where as in fibrous dysplasia it is the result of appositional bone formation on the outer side of cortex secondary to remodeling of the endosteal erosion. Histologically garre osteomyelitis is characterized by dense mass of sclerotic bone in fibrous marrow with chronic inflammatory cell infiltrate. Paget’s disease share some feature of fibrous dysplasia, but it occurs in a much older age group and typically exhibit a bilateral distribution. Alkaline phosphatase levelis characteristically in Paget’s disease [16]. A related disorder, cherubism, is manifest by expansile, multiloculated, radiolucent fibro-osseous lesions with multiple giant cells located bilaterally and symmetrically in the jaws.

Outcome and Follow up

After 6-month follow-up period, no sign of recurrence was observed. The patient continues to be on regular follow-up.

Discussion

Craniofacial FD is a genetic nonhereditary disease that has a benign course in most patients. It can progress beyond puberty, and there is no correlation between age and clinical course. Cranial nerve involvement is rare in this population. The presence of mucoceles or bone cyst may increase the risk of visual deterioration caused by optic nerve compression. The absence of level-I evidence on the management of patients with FD makes it difficult to decide on the optimal patient management. It is difficult to predict which patient will progress to have a debilitating disease. Considering the risk of surgical injury to the ON together with the unknown course of the disease, the possibility of an adverse outcome must be considered seriously before operating on asymptomatic patients. The accumulated experience Fibrous Dysplasia 897 reported in the literature revealed in the authors’ meta-analysis shows no difference in the visual deterioration rate between prophylactically and therapeutically
decompressed nerves. The significantly lower rate of adverse visual outcome in conservatively treated patients suggests that performing decompression in asymptomatic patients unnecessarily puts the ON at risk. Moreover, the prevalence of visual deterioration during follow-up is rare, even in patients with MAS who usually exhibit a more aggressive course of disease. In conclusion, published data and the authors’ meta-analysis suggest that symptomatic patients with ON involvement can safely be managed by an endonasal surgery directed toward partial decompression of the optic canal. Early diagnosis and treatment was necessary in this case to avoid the further complications of the tumor like intracranial involvement, cranial nerve damage, orbital involvement, optic nerve damage, skull base involvement, oropharyngeal obstruction and enigmatic complications. So early diagnosis and aggressive surgical intervention is necessary in this type of cases. The ligation of terminal branches of external carotid artery was done to prevent the further blood loss. Genetic studies involving mutation of GNAS genes is therefore necessary to prevent this debilitating condition affecting early age group from occurring and early diagnosis and treatment techniques should be researched through genetic study. The incidence of malignant transformation of FD is 0.4% [16, 17].

Learning Points

1) Aggressively screen for and manage endocrinopathies (particularly growth hormone excess).
2) Active disease (rapid growth, new onset of pain or paresthesia, visual or hearing changes) warrants an immediate surgical referral and evaluation.
3) A bone biopsy should be obtained if there is any doubt about the diagnosis. If the lesion is in a site that cannot be biopsied due to unacceptable risks, history, clinical examination and radiographic diagnosis may be adequate for diagnosis.
4) What pharmacologic or molecular therapies may reverse the effects of the abnormal gene products in FD?
5) Does the detectability of a Gs mutation in a fibro-osseous lesion predict clinical behavior?
6) Is mutation testing a necessary component of FD evaluation and gene therapy necessary?

References