INTRODUCTION

Fibrous dysplasia (FD) is a condition where normal bone is replaced with woven bone with interposed fibrous tissue in between [Figure 1]. It results from a defect in osteoblastic differentiation and proliferation resulting in abnormal fibro-osseous proliferation. It can be monostotic (involving single bone) monostotic FD (MFD) or polyostotic (involving multiple bones) polyostotic FD (PFD) or rarely can be a part of McCune-Albright syndrome. Similar calvarial hyperostosis can be found in Proteus syndrome also. FD is characterized by bony lesions and may be associated with endocrine and biochemical abnormality. Genetic mutation (GNAS1 gene) is linked up with this disease. FD is common in both the axial and appendicular skeleton.
Craniofacial bones are common locations of FDs mostly PFDs. They clinically present with cosmetic deformity, orbitocranial swelling, and dental malocclusion mostly. There can be associated pain, visual disturbance, hearing loss, nasal obstruction, and diplopia depending on the extent of involvement. FDs mostly develop and progress in the younger age group. Although MFD is less aggressive, slow progression even “burn out” up to adolescents, PFDs continue to progress over time and more symptomatic. On computed tomography (CT) scan, it has a ground-glass appearance with sclerotic/cystic/mixed pattern. Although conservative medical management is adopted in most nonprogressive asymptomatic cases patients, surgical resection with reconstruction whenever feasible and indicated is recommended and definitive for symptomatic cases.[21]

We present our experience of 21 such cases that were managed over 5 years along with short- and long-term outcomes.

MATERIALS AND METHODS

This is a retrospective study. Approval was taken from the Institutional Ethics Board. Data were collected for 21 symptomatic FD patients managed between 2014 and 2019. All endocrine and biochemical abnormalities were identified and corrected.

Inclusion criteria for surgical management:

The following criteria were included in the study:
1. Patient with cosmetic deformity wanting surgical treatment
2. Functional symptoms such as diminution of vision, diplopia, and hearing loss.

Inclusion criteria for medical management or observation:

The following criteria were included in the study:
1. Mild-to-moderate pain with slowly progressive disease or asymptomatic case
2. Lesions that are surgically not feasible to access
3. Patient not willing for surgery.

Preoperative symptoms were analyzed and appropriate indications were determined. All patients underwent preoperative craniofacial CT scan with three-dimensional reconstructions with bone windows.

In 16 out of 21 patients who were managed surgically, a standard bicoronal incision was taken in most patients and flap was raised. The underlying bony abnormality was defined all around and the entire abnormal areas were excised in the form of drilling/curettage en bloc or piecemeal. The defect was delineated all around and immediate reconstruction was performed in all cases. Reconstruction was done with split-thickness bone graft alone or in combination with polymethylmethacrylate (PMMA) cement or titanium mesh [Figures 2-5]. Intraoperative assistance from the plastic surgery team was taken whenever deemed needed. Subgaleal drain was placed and the wound was closed in layers.

In patients who were managed medically for pain (3/21), intravenous pamidronate (bisphosphonates) was given 1–3 mg/kg every 6 months–1 yearly. Vitamin D supplements were also given.

Two patients with holocranial/bilateral FD were managed with observation only. Clinical outcomes were assessed immediately as well as in short- and long-term follow-up over 1–4 years in both groups of patients [Table A].

RESULTS

A total of 21 patients were treated over 5 years. Among them, 6 (29%) were male and 15 (71%) females. The age group ranges from 12 to 55 years with a median age of 26 years [Table 1]. Cosmetic disfigurement was present in 15 of them (71%) involving one or more skull bone involvement (zygomatic/orbit/sphenoid/frontal/parietal). Two patients with nonprogressive PCFD with cosmetic deformity were managed with serial follow-up and ophthalmic and radiological examinations. Orbital displacement/visual disturbance was present in four of them (19%). Because of symptoms, 16 patients were treated surgically as per indication(s). Three patients (15%) with significant localized pain were managed medically with I.V. pamidronate and calcium and Vitamin D supplements [Table A].

All patients underwent cranio-facio-orbital CT scan with three-dimensional reconstructions with bone windows for ruling out other differential diagnoses (e.g., metastasis, meningioma-related hyperostosis, and bony tumors) and for surgical planning in indicated patients [Figures 2-5]. Contrast-enhanced magnetic resonance imaging (MRI) was also done in select cases to rule out other pathologies and to see optic nerve status. Monostotic type (MCFD) was in 10 cases (48%) and 11 were polyostotic (PCFD) (52%).

In the surgical group following surgical excision of the lesion, immediate reconstruction was done. Split-thickness bone graft alone was used in 10 cases out of 16 (63%) [Figures 2-4] and in combination with PMMA cement in 4 cases (25%) and titanium mesh in 2 cases (12%) [Table 2]. Cosmetic and clinical outcomes were assessed immediately after surgery and then on follow-up [Figures 3-5].

### Table 1 : Demographic distribution of patients.

| Age group   | Number of patients | Percentage |
|-------------|--------------------|------------|
| Below 20 years | 6                  | 28.5       |
| 20–40 years   | 12                 | 57.2       |
| 41–60 years   | 3                  | 14.3       |
| Total        | 21                 |            |
In medically managed patients after ruling out other endocrine (parathyroid hormone, calcitonin, etc.) and biochemical (serum calcium, serum phosphate, etc.) abnormalities, intravenous pamidronate (1–3 mg/kg) 6 months–1 yearly until pain subsides along with Vitamin D and oral calcium supplements was given. Regular follow-up was done thereafter.

Histopathological analysis was done in operative samples and all cases showed a varying amount of spindle cells and trabeculae of immature woven bone [Figure 1].

Complications and follow-up

In surgically treated patients, one patient had persistent subgaleal collection which was managed by compression bandage and anti-inflammatory medication. Another patient experienced postoperative new-onset seizure that was managed by anti-seizure drugs.

Surgically managed patients were followed up over a period ranging from 12 to 48 months with an average follow-up period of 24–30 months [Table A]. Only one patient with preexisting visual impairment did not improve after surgery and remained the same. All other 15 patients had a good cosmetic outcome and improvement in visual symptoms on follow-up. One patient had recurrence by the 3rd year who was reoperated. The longest follow-up available is for two patients with 45 and 48 months, respectively. Both are doing well.

In conservatively managed group, patients remained symptom free and nonprogressive disease over 18–24 months follow-up.

DISCUSSION

FD is a relatively uncommon condition and there is a relative dearth of studies on this topic in the neurosurgical literature. Its treatment is also controversial with many in favor of expectant/medical management. Surgical treatment whenever done can be accompanied by a staged reconstruction later or immediately at the time of first surgery. We here have presented our experience of single-stage surgery of these lesions in 16 patients as well as conservative treatment in appropriate cases.

FD is benign pathology of bones defined by Reed as an “arrest of bone maturation in woven bone with ossification resulting from metaplasia of a nonspecific fibro-osseous type”. The term FD was coined by Linchiestien and Jaffe (1942). FD is classified as monostotic type (MFD) (involving single bone) and polyostotic type (PFD) (multiple bones). Monostotic type (60–70%) is more common and commonly asymptomatic seen in early adulthood.[20]

Appendicular bones (tibia and femur), ribs, and craniofacial bones are more commonly involved. PFD (50–70%) is the most common presentation in craniofacial involvement. MFD comprises 10–30%. FD incidence is almost the same in both genders with slight female predilection. FD presents in late 20s and 30s after puberty when bone maturity occurs. It involved membranous bone more readily than cartilaginous bones. Malignant transformation occurs in <1% of cases.[12,15,18]

Craniofacial FD (CFD) usually presents with multiple adjacent skull and face bones; however, other body skeletons are not involved generally.[10]

Eversole et al.[7] classified the craniofacial type as polyostotic because many bones of the craniofacial complex are involved that are separated from each other only by sutures. The polyostotic type may be divided into three types:

1. CFD, in which only the bones of the craniofacial complex are affected
2. Lichtenstein-Jaffe type, in which multiple bones of the skeleton are involved with café-au-lait pigmentation of the skin and rare endocrinopathies in a few of these patients; and
3. Albright's syndrome, characterized by the triad of polyostotic FD (mostly unilateral), café-au-lait pigmentation of the skin, and various endocrinopathies. Another very rare and special form is the Mazabraud syndrome, describing an association of the FD with soft-tissue myxomas.

Table 2: Reconstruction materials used.

| Reconstruction                  | Number of patients | Percentage |
|---------------------------------|--------------------|------------|
| Split-thickness bone graft      | 10                 | 62.5       |
| Bone graft and PMMA cement     | 4                  | 25         |
| Bone graft and mesh             | 2                  | 12.5       |
| Total                           | 16                 |            |

PMMA: Polymethylmethacrylate

Figure 1: Histopathology.
Etiology

Genetic changes lead to FD. Culprit mutation (missense) affecting the GNAS1 gene located at chromosome 20q13 has been implicated. Persistent activation of adenyl cyclase and increase cellular cAMP due to mutation causes abnormal bone formation and resorption of normal bone by increasing interleukin (IL)-6.\textsuperscript{[22]}

Diagnosis

CFD generally presents with painless/painful bony enlargement with facial/cranial asymmetry. Involvement of orbit, skull base, neural foramina, and calvaria leads to seizures, visual diminution, diplopia, proptosis, hearing loss, etc.\textsuperscript{[6,7]}

Differential diagnosis includes various skull tumor/lesions such as simple bone cyst, giant cell tumor, fibroxanthoma,
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Patients’ age, sex, and radiological features (X-ray, CT, and MRI) were assessed. A thin bony cortex was seen with well-defined borders and ground-glass appearance. Three distinctive patterns on CT were seen – (1) Scattered lesion with bony expansion (Pagetoid), (2) homogeneous with ground-glass appearance (sclerotic), and (3) low density with sclerotic margin (cystic).

Histopathological diagnosis is confirmatory and useful to rule out any malignancy.

Management
CFD management includes conservative approach with observation and follow-up, medical management, and...
and petrous temporal bones (ZONE 3 Chen YR, Noordhoff, 1990) are advised to be managed with observation only as surgery can cause more harm [Figure 6].[8,21]

Medical treatment, still not promising in the management of FDs and still under evaluation, is based on control of pathophysiology of abnormal bone formation and raised osteoclastic activity and decreasing local pain due to this. This includes bisphosphonates, more appropriately pamidronate intravenous 60 mg/day for 3 days repeated in every 6 months–1 year. Calcitonin is another drug used by some clinicians. Vitamin D and calcium supplements also used in selected patients.[17]

Surgery is the mainstay treatment in selected patients with CFDs. Radical surgery with excision is one option not feasible many times due to diffuse involvement and adjacent neurovascular structure.[2] We had such a patient where we took a wait and watch policy.

Conservative surgery including bone remodeling and recontouring is performed most of the times to correct cosmetic deformities and functional deficit due to neural foramina or orbital involvement. The risk of recurrence (15–20%) and less likely malignant transformation (0.4–4%) is possible in conservative approach which can be minimized by performing primary surgery after pubertal growth and bone maturity and regular follow-up by clinical, radiological (CT/ MRI/X-ray), and biochemical (serum alkaline phosphatase is raised in recurrence) examination.[16]

Couldwell et al.[5] reported three cases of symptomatic CFD that was operated by single-stage or two-stage procedures. All patients had improvement in their symptoms after surgery. We had similar results in our study.

Lei et al.[14] published a series of 12 operated patients with cranial FD where they showed that in indicated patients, complete excision with reconstruction is feasible in one stage like we have shown in our study. Like in our study, they also used autologous bone as well as artificial mesh.

Adada and Al-Mefty[1] showed that in clival FD, surgery is indicated only when there is compressive cranial nerve palsy and conservative treatment otherwise. We had one case with holocranial FD (with clival involvement) in which case, we took a wait and watch policy.

Valentini et al.[21] experienced that there is no specific treatment exists for FD. Radical resection is the only technique to obtain a complete resolution of FD. Wait-and-see is indicated in cases of stable lesions which cease to grow once the patient reaches puberty. Reconstructive techniques allow obtaining adequate aesthetic and functional results. Our study matches this philosophy.

Lee et al.[13] recommended observation for skeletal maturity in prepubertal patients for slowly growing lesions. Adult patients with bone maturity and with active disease (rapid
growth, new onset of pain or paresthesia, and visual or hearing change) need urgent surgical management. We have selected our patients for surgery by a similar approach. They also highlighted that the management of FD needs a multidisciplinary approach as echoed in our study.

Zanotti et al.[23] in their study have analyzed the different materials used for calvarial reconstruction and showed that custom-made implants are the most favorable and synthetic materials such as PMMA, HA, and PEEK have their own merits and demerits. In our series, we have not encountered any implant-related complications so far. With the arrival of augmented and virtual reality, cranial reconstruction will be a more sophisticated undertaking.

Limitations
The retrospective nature of this study is a limiting factor. Long follow-up has been done to compensate for the nature of the study. Another factor is the number of patients. However, given the dearth of adequate neurosurgical literature on this subject matter, our number is respectable.

CONCLUSION
CFD is complex lesions which range from asymptomatic (nonprogressive) to cosmetic disturbances, pain, neurological, ophthalmological, ENT, and dental symptoms in progressive disease. Age and symptoms should be considered before deciding management; however, single-stage surgical management of symptomatic CFD with immediate reconstruction in selected patients is feasible and safe with good short- and long-term outcomes. However, given the variable natural history of the disease, regular follow-up and long-term surveillance are needed.

Declaration of patient consent
The authors certify that they have obtained all appropriate patient consent.

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Nil.

Conflicts of interest
There are no conflicts of interest.

Ethical approval
All procedures performed in this study were per with the ethical standards of the Institutional Research Committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

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