Treatment of Pathological Fracture of Femur in Mc-Cune Albright Syndrome Using A Custom Made Intramedullary Nail - A Case Report

Dr. Nikhil Das Bhat¹, Dr. Anudeep.N. Naik²

Department of Orthopaedics, Kempegowda Institute of Medical Sciences and Research Center, Bangalore *Corresponding Author: Dr. Anudeep.N. Naik

ABSTRACT:-

Introduction: Mc cune Albright syndrome is a rare and heterogeneous disease with estimated prevalence between 1/100,000 and 1/1,000,000. The clinical condition is caused by rare sporadic genetic mutation characterized by Fibrous Dysplasia, where there is a replacement of normal bone by fibrous tissue, cafe au lait spots. The surgical management of Fibrous Dysplasia is technically challenging. The new bone formed after fractures are dysplastic, thus recurrent fractures and deformity should be expected. The proximal femur is very commonly involved in this disease and presents the most unique reconstruction challenges.

Case Presentation: We describe a 14 year old boy with mc cune Albright syndrome with polyosteotic Fibrous Dysplasia, with series of pathological fracture of femur. Patient was managed using a custom made intra medullary nail after series of re-fracture and other modalities of treatment.

Conclusion: A Fibrous Dysplasia lesion of the proximal femur is known to be associated with more pain, fractures and especially with more deformity than any other skeletal localization of the disease. Management especially in children/ pediatric age group must include treatment and prevention of pathological fracture and also use tailored devices, to provide stability, and also tackle the varus deformity associated with the condition.

Keywords: Fibrous Dysplasia, Mc-Cune Albright syndrome.

I. INTRODUCTION

Mccune-albright syndrome is a rare genetic disorder with typical skeletal and endocrine manifestations. Mccune Albright Syndrome(MAS) was defined as a triad of fibrous dysplasia (FD), café-au-lait macules and endocrine disturbances, most notably precocious puberty but any combination of one or more of the typical features of MAS (FD, café-au-lait macules, and/or hyper functioning endocrinopathies such as gonadotropinindependent precocious puberty, hyperthyroidism, growth hormone excess, etc.) Warrants the diagnosis of MAS¹.

MAS has to be differentiated from Neurofibromatosis the café au lait macules of MAS have irregular border (coast of Maine) located at nape of the neck and the crease at the apex of the buttocks and mostly do not cross the midline while NF have a smooth border(coast of California). In MAS, the skeletal disease (Polyosteotic FD) almost always involves one or both proximal femurs and/or the skull base, as well as other locations. Skeletal involvement in NF is uncommon and usually involves the diaphysis of the long bones, especially the tibia, often leading to pseudoarthrosis^{2,3}

FD (FD) is a genetic, non-inheritable congenital skeletal disorder characterized by thinning of the cortex. The disease, which was first reported by Von Recklinghausen in 1891, was later described by Lichtenstein in 1938and subsequently in 1942 along with Jaffe⁴. The term Jaffe-Lichtenstein syndrome is sometimes used synonymously with monostotic FD or to denote cases of polyostotic FD with café au lait spots, but no endocrine dysfunction. The clinical spectrum of FD varies widely, including single bony lesions (*monostotic FD*), multiple lesions (*polyostotic FD*). The polyostotic form manifests earlier, usually in children younger than 10 years; has a more serious prognosis; and frequently affects the maxilla or other craniofacial bones, ribs, femur, or tibia. Because of the weight-bearing forces acting on the lower extremities, the femur is most prone to deformities and fractures, ultimately resulting in the pathognomonic feature of FD of the proximal femur; the 'shepherd's crook' deformity⁵. Typically a child with FD will consult the orthopedic surgeon for complaints of pain, limp, or management of a pathologic fracture through an area of FD³. Epidemiology

The estimated prevalence is between 1/100,000 and $1/1,000,000^2$. This is more common in females than males (10:1) and more likely to cause precocious puberty in girls. Etiology

The observation that the G protein/camp/adenylate cyclase signalling pathway was central to all of the tissues involved in MAS eventually led to the discovery that mutations in the regulatory Gs α protein (encoded by the *GNAS* gene ,The *GNAS1* gene is located at chromosome 20q13.2-13.3) were the underlying molecular aetiology of MAS. In all published cases of MAS, PFD. More recently, mutations at the Q227 position have been found in association with FD⁶. This results in increased intracellular levels of camp in bone forming cells, leading to local replacement of lamellar bone with ill-woven, under mineralized (fibrous) tissue of poor quality in affected parts of the skeleton, associated with clinical manifestations of pain, deformity and pathological fractures⁶.

Diagnosis

Diagnosis of MAS is usually established on clinical grounds².

Plain radiographs are often sufficient to make the diagnosis of FD. Isotopic bone scans are the most sensitive tool for detecting the presence of FD lesions. FD has a typical appearance on radiographs described as "ground glass." In general, lesions in the long bones have a "lytic" appearance. The lesions usually arise in the medullary cavity and expand outward replacing normal bone, which results in thinning of the cortex. Due to the fact that these lesions are under mineralized the bones are "soft" and prone to deformation, as exemplified by the classic "shepherd's crook" deformity of the proximal femur. FD lesions typically become less active in adulthood³.

Biopsy and/or molecular diagnosis are rarely needed especially in polyosteotic type.One characteristic of FD bone is the absence of the lamellation pattern seen in normal bone under polarized light. The histopathological description of FD is often described as a "Chinese writing" pattern, and with special preparation and stains used to detect mineralized and unmineralized tissue, extensive areas of unmineralized osteoid are evident²

II. CASE PRESENTATION

A 10-year-old male presented in the emergency department with a history of RTA to the right thigh. Immediate assessment showed that he was hemodynamically stable, and showed no signs of closed head or chest or blunt abdominal trauma. The affected thigh was deformed suggesting a femoral fracture. The affected extremity was splinted, and radiographs obtained, which showed an oblique fracture of the mid-femoral shaft.Patient was operated with CRIF with TENS nail to left femur, post-operative period was uneventful. Patient was asymptomatic and mobile for 3 years. Implant removal was done on 20/5/17.

Ist presentation-Patient sustained refracture shaft of left femur after a trivial trauma, but during this presentation, deformity and ground glass appearance of femur was noted. Patient was operated with ORIF with DCP plate and screw (9/5/18) due to difficulty that was faced during previous tens nailing procedure. Patient was mobilized with non weight bearing walker support and was started on physiotherapy.

Implant failure-Patient was asymptomatic for 2 months, following which patient gives history of swlling in the left thigh, later was found to have implant failure/ back out. Patient was operated with implant removal, ORIF with LCP plate and circlage wires, and immobilized with above knee cast.(20/06/18)

2nd refracture- Patient complained of severe pain while he sat up from a supine position and was found to have peri prosthetic proximal fracture of left femur, patient was operated with implant removal and ORIF with tailored recon nail to left femur. Patient currently is allowed to do weight bearing mobilization and x-ray shows no deformity.

Investigations and clinical findings

Blood routine –normal; ESR- normal; LFT- normal; TSH – normal; Alkaline phosphatase-147 u/l;Serum.Calcium-9.7;café-au-lait spots- Along left side of the body, with charactristic irregular borders, X-ray showed- *ground glass appearances, with "shepherd crook"* deformity in femur

• No signs suggestive of precocious puberty.(precocious puberty (PP) in girls is common, PP in boys is less common), No signs cranio facial involvement, no facial asymmetry, hearing impairment.

• Larger lesions with cortical thinning and a ground glass appearance usually do not require a biopsy to confirm diagnosis of FD.

III. DISCUSSION

Patient in our study was operated with TENS for fracture shaft of femur at the age of 10, showed good healing, with no progression in neck shaft angle, patient on contrary was asymptomatic without pain for a period of 1 year. After the refracture after a trivial fall an attempt at TENS was tried, but was abandoned due to difficulty in passing the nail, hence was tried with plate and screw in order to prevent further deformity. Patient suffered implant failure due to inadequate bone stock and after that had peri prosthetic fracture. All the above mentioned fracture was in shaft of femur. Regular intramedullary nail by conventional approach would compromise the open physis. After patient suffered peri prosthetic fracture, a custom made RECON nail was

introduced through the fracture site without hindering the physis in a retrograde manner⁷. Patient has no complaints in the contralateral limb, but is at high risk of pathological fracture. Follow up of the patient is done regularly; FD is considered a static disease after skeletal maturity. Hence close watch over patient is essential⁸.

Treatment of PFD in children during the growing years is often very challenging. In the absence of a fracture or symptoms, the follow-up for a child with FD consists of twice yearly clinical evaluations and radiological evaluation if lesion is noted in proximal femur. Most patients will develop fractures and long bone deformity in the absence of surgical intervention. (Limb length discrepancy can be an early sign of progressive deformity¹.

As the growth of the femur has to be accounted in the placement of internal fixation to avoid damage to the growth plate or to the pediatric vascular circulation of the proximal femur.Standard intramedullary devices used in adults will generally not fit into the small femoral shaft of children, ruling out their use in most young children, especially in growing patients with an open physis. Titanium elastic nails (TENS) have frequently been used to address fractures, and although most fractures show good healing, the tens will not prevent any subsequent fracture or the progression of deformities and should therefore not be used in the proximal femur of young patients with FD⁵.

- The indications for surgical treatment ^{1,5}
- 1. Symptomatic FD lesion of the proximal femur extending beyond the femoral neck,
- 2. A fracture with displacement
- 3. Severe deformity of the proximal femur.
- 4. Neck shaft angle <120 degree

There has been a gradual inclination towards intramedullary nails due to its use in extensive lesion, a better outcome in both pediatric and adult group of patients and intramedullary nails offer the advantage of being minimally invasive and being more frequently used in general trauma unit, providing an osteotomy is not require⁵. The use of internal fixation devices may allow early weight-bearing. Prolonged non-weight-bearing treatment following surgery will only aggravate the preexisting bone weakness.

Use of typical plate and screw devices is discouraged, unless screws can be placed outside the FD lesions obtaining purchase in normal cortical bone. Screw failure is extremely likely if the screws are placed into FD bone and should be used with caution only in selected patients with adequate cortical bone⁵. In cases where the neck-shaft angle has become severely deformed, single-staged correction may not be feasible, staged procedures using screw-plate devices to achieve partial correction may be used and later converted to IM devices⁵.

Use of bone graft still remains controversial and the indications are very slim in a setting of FD. Allogeneic strut grafts ban be used in management of impending fractures and of pain due to FD of the proximal femur in selected cases,

- 1. If no history of a pathological fracture of the proximal femur,
- 2. There should be enough bone stock proximal in the femoral neck to anchor the strut graft,
- 3. There should be no indication for a valgus osteotomy.

4. FD lesion should not extend to the femoral shaft 5^{-1} .

Bisphosphonates are effective in relieving bone pain associated with FD, but their role in altering the course of the disease is still remains questionable. The medical management of the MAS is more important in treating the endocrinopathies, as the associated endocrinopathies (i.e. Hyperthyroidism, phosphate wasting, increased GH) often lead to decreased bone strength both in FD affected bone and in the surrounding "unaffected" bone. Drugs like Toclizumab and Denosumab (Monoclonal antibody) are being studied as a potential therapy for FD. Toclizumab acts by blocking their activity of IL-6, a protein that is realized in excess from the FD bone and stimulates bone resorption. Denosumab is approved for treatment of osteoporosis⁹.

IV. CONCLUSION

• The patient was diagnosed with mas syndrome at 14 years of age based on the association of café-aulait spots and radiological signs of polyostotic FD. This comprehensive pathological study of a single patient highlights the complex clinical profile of mas and illustrates modalities of treatment in pathological fracture of child with FD.Given these characteristics of FD, patients with this disease should be followed carefully over the long term.Regardless of the choice of treatment, it is important to appreciate that the risk of failure or of recurrence and the need for revision surgery is high in young and growing patients and that in pediatric patients there is a need for a tailored device providing stability and preventing further deformation of the femur.

V. CLINICAL MESSAGE

It is important to identify MAS, routine clinical and radiological examination is necessary in asymptomatic patients. Intra medullary nails are preferable in symptomatic patients and those associated with fracture.

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Figures:

Figure 1: café au lait spots

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Figure 2: poly-osteotic involvement, with ground glass appearance, Shepherd crook deformity and thinned out cortex.



Figure 3: pathological fractures and chronological presentation



Figure 4: custom retro grade nailing with IMIL



Figure 5:12 weeks follow up



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