The Hip in Fibrous Dysplasia

32

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Introduction

Fibrous dysplasia (FD) is a benign tumor-like condition caused by a genetic mutation resulting in the normal intramedullary trabecular architecture of bone being replaced by an immature and random network of fibro-osseous tissue. The individual works of Louis Lichtenstein, MD and Henry Jaffe, MD in the 1930s lead to the discovery of FD as a unique pathologic entity [1]. The pathologic bone is weaker than physiologic bone and can lead to pain, deformity, and pathologic fracture. Three clinical presentations of the disease exist: (1) monostotic fibrous dysplasia (lesion in a single bone), (2) polyostotic fibrous dysplasia (lesions in multiple bones), and (3) McCune-Albright syndrome (MAS). MAS is defined as the triad of polyostotic fibrous dysplasia, café-au-lait skin lesions, and a hyperfunctioning endocrinopathy—classically precious puberty in the young female. The hip is the most common location for FD to be identified, and also is the location at greatest risk for fracture. It is important for clinicians to be able to recognize and diagnose FD radiographically, and understand how to best manage children with these lesions.

Pathophysiology

FD results from a mutation in the GNAS gene, which codes for the ubiquitously expressed alpha subunit of the stimulatory guanine nucleotide-binding protein (Gsα-protein). In FD, an activating missense mutation results in the constitutive activation of the Gsα-protein, and uninhibited cyclic adenosine monophosphate (cAMP) production. The mutation occurs in the postzygotic embryo, and is a random mutation without familial inheritance [2, 3]. As the mutation occurs postzygotically, not all cells express the mutant genotype, and a mosaic pattern of wild type and mutant cells exists in the affected tissues. Mutation of the GNAS gene has variable clinical appearances. The phenotypic presentation of this mutation results from: (1) the point in embryologic development that the mutation occurs, (2) the tissues or organelles that the mutated cell migrates to, and (3) the consequence of constitutive activity of the Gsα-protein and overproduction of cAMP within the affected tissue [2]. FD and MAS are variable phenotypic expressions of the same genetic mutation. FD results from the constitutive expression of the Gsα-protein in bone marrow cells, whereas MAS syndrome results from the over production of cAMP in extra-osseous tissues such as the skin, the reproductive organs, the thyroid gland, the adrenal glands, and/or the pituitary gland.

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"Fibrous dysplasia and McCune Albright syndrome are variable phenotypic expressions of the same genetic mutation"

In bone marrow, the cAMP signaling pathway is responsible for the commitment of mesenchymal stem cells (MSCs) to differentiate into osteoblasts. The constitutive activation of the Gsα-protein, and overproduction of cAMP, results in the pathologic differentiation of MSCs to immature stromal cells. The mosaic cellular distribution of wild and mutant type cells within the bone results in the immature woven bone present in FD. Additionally, the mutant stromal cells produce fibroblast growth factor 23 (FGF-23). FGF-23 binds to receptors in the proximal tubules of the kidney down regulating a sodium phosphate co-transporter resulting in renal phosphate wasting. The greater the disease burden in FD, the greater the production of FGF-23, and the greater degree of osteomalacia secondary to hyperphosphaturia and hypophosphatemia. The FGF-23 protein is also recognized for its role in familial hypophosphatemic rickets [2–4].

The pediatric hip is the site of 91% of identified bone lesions in FD/MAS. The pathologic bone consisting of a mosaic pattern of immature stromal cells and mature osteoblasts in combination of global poor bone mineralization from the overproduction of FGF-23 results in biomechanically weaker bone. Hip fracture and progressive deformity with weight bearing are the major clinical concerns with these lesions. A recent study investigated the total number of mutated cells within the FD lesions and demonstrated an age-related decline of mutated cells. Once skeletal maturity is reached, the wild-type cells continue to self-renew and the mutated cells undergo apoptosis leading to relative normalization of the lesion [5].

In the skin, café-au-lait spots develop due to increased cAMP signalling and the overproduction of melanin. The increased melanin results from continuous activation of tyrosinase the rate-limiting enzyme in melanin production. The café-au-lait spots are usually midline and follow Blaschko's lines, which are the migratory lines of normal cell development in the skin [6].

In the ovaries, excess estrogen is produced due to estradiol producing ovarian cysts that develop from the uncontrolled activation of granulosa tissue by the cAMP pathway. This results in low levels of circulating luteinizing hormone (LH) and follicular stimulating hormone (FSH). The elevated levels of estradiol result in precocious puberty [6].

Mutant cells within the thyroid gland are responsible for the uncontrolled production of thyroid hormone, and potential goiter formation. The cAMP pathway is responsible for the production of thyroid hormone and the mutant cells constantly produce thyroid hormone irrespective of thyroid stimulating hormone (TSH). In the adrenal glands, cortisol is produced via the cAMP pathway, and mutant cells produce cortisol resulting in Cushing's syndrome. Finally, mutant cells migrating to the pituitary gland may produce excess growth hormone, resulting in acromegaly in adulthood [6].

Natural History

The natural history of FD is pathologic bone lesions present early in development, continue to enlarge as the patient is growing, and then stabilize or "normalize" in adulthood. 90% of bone lesions are present prior to 15 years of age [7]. Pain is the main presenting symptom that leads to identification of polyostotic FD, and 91% patients with polyostotic FD have a lesion in the proximal femur [8]. Monostotic FD typically presents with smaller bone lesions, often clinically benign, only being diagnosed incidentally. The proximal femur undergoes significant loading with weight bearing, and painful lesions or progressive hip deformity is what will guide surgical intervention.

Bone pain and deformity result from the pathologic bone undergoing plastic deformation. The pain associated with these lesions forebodes pathologic fracture. Female patients have fluctuating levels of bony pain throughout their menstrual cycles, and increased levels of pain during pregnancy. Estrogen receptors are present in FD/MAS leading to lesion growth

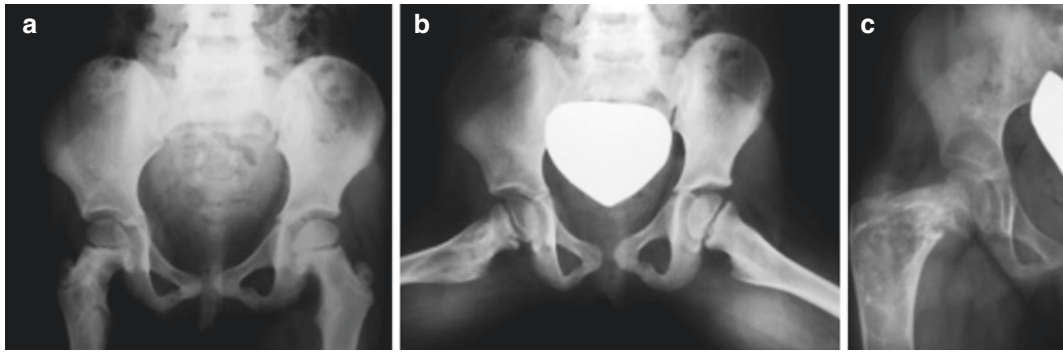

Fig. 32.1 AP radiograph of the pelvis demonstrating a child with fibrous dysplasia of the hips (**a** and **b**) that progresses to a "shepherd's crook" deformity over three years time (**c**)

and increased pain with increased levels of circulating estrogen [9]. Bone deformity is the result of aberrant remodeling following plastic deformation or abnormal bone growth. Bowing of the femoral diaphysis may occur with weight bearing. Classically, the shepherd's crook deformity is associated with FD, and is described as lateral bowing of the proximal femur, resembling a shepherd's crook on radiographs (Fig. 32.1).

Patient's clinical and functional outcomes are directly correlated with the total burden of disease. Specifically, increasing total disease burden and decreasing the femoral neck shaft angle correlate with worse Pediatric Outcomes Data Collection Instrument (PODCI) scores with regards to being able to perform in sports [10]. Patients with lesions present in greater than 60% of their osseous anatomy usually require an assistive device for ambulation [7, 11]. Additionally, with increasing disease burden the life-time fracture rate increases [12]. The greater the burden of disease results in greater renal phosphate wasting through production of FGF-23 and a mild form of rickets increasing the fracture risk. In general, monostotic FD has a more benign clinical course than polyostotic FD, and this is largely related to the respective disease burdens between these patients.

"The greater the burden of osseous disease in FD/MAS correlates with increased fracture risk, decreased PODCI scores, and increased need for ambulation with an assistive device".

FD lesions are benign lesions, and although rare, malignant transformation has been reported. The prevalence of malignant transformation ranges between 0.4 and 4% [13–16]. Osteosarcomas are the most common secondary sarcomas to develop, but fibrosacromas, chondrosarcomas, and undifferentiated pleomorphic sarcomas have been reported [14]. The facial bones and proximal femoral lesions are at greatest risk of malignant transformation. Clinically, malignant transformation should be suspected in individuals with enlarging masses and increasing pain at rest. The overall prognosis of a secondary sarcoma following FD is poor with a survival rate on average of 3.4 years [16].

The main course in the treatment of these patients is to prevent significant deformity and pathologic fracture. In the asymptomatic patient, the management includes surveillance of the lesion through radiographic and clinical assessment. However, in the large painful lesion of the proximal femur prophylactic surgical intervention is often warranted to prevent pathologic fracture.

Epidemiology

FD accounts for 5 to 10% of benign bone tumors, and is equally represented in males and females [17]. Bone lesions in FD/MAS present at a young age with 50% of total bone lesions being present by age 6, and 90% of lesions being present by age 15. Interestingly, 90% of craniofacial lesions

will present before 4 years of age [7]. Despite FD and MAS being different phenotypic expressions of the same genetic mutation the incidence of monostotic FD, polyostotic FD, and MAS are not the same. Monostotic FD is the most frequent presentation, representing 75–80% of cases, and MAS is the rarest of the clinical manifestations with a prevalence estimated to be between 1 in 100,000 and 1 in 1,000,000 [18].

Monostotic FD most commonly presents in the proximal femur (23%), the ribs (28%), and the craniofacial bones (20%) [8]. If FD involves multiple facial bones it is still considered monostotic disease unless other, non-facial bony lesions are identified. Monostotic disease generally has a more benign clinical presentation when compared to polyostotic disease and tends to be diagnosed incidentally. Polyostotic FD by definition has a minimum of two bony lesions and has been reported to involve up to 75% of the human skeleton. The multiple lesions may occur in a single limb termed monomelic or in different limbs termed polymelic. The most common sites of presentation in polyostotic FD include the femur (91%), tibia (81%), pelvis (78%), and foot (73%) [8]. Spinal lesions are present in 40–60% of patients with polyostotic FD, and patients may develop scoliosis [19]. McCune-Albright syndrome is the rarest presentation, and the bone lesions tend to be larger, more progressive, and associated with an increased number of complications.

Clinical Presentation

The clinical presentation of FD and MAS vary with MAS being associated with hyperfunctioning endocrinopathies and skin lesions in addition to bone symptoms. The clinical examination of the pediatric patient presenting with FD is largely non-specific, and the diagnosis of FD is made radiographically. Polyostotic FD patients typically will have clinical symptoms, but monostotic FD usually remains asymptomatic and is only diagnosed incidentally from radiographs obtained for other reasons. The history of a patient with FD will likely include mechanical pain at the site of the lesion that improves with rest or non-weight bearing. On examination, the patient may have pain or swelling at the site of the lesion. The pain and deformity may be very severe in the setting of pathologic fracture. Additional findings on physical exam can include bossing of the skull and prominent jaw with craniofacial FD, chest wall masses with rib FD, leg length discrepancy and an abnormal gait pattern with lower extremity FD, and evidence of painless or painful scoliosis from spinal FD. Patients may vary in age; however, the highest rate of fractures is observed between 6 and 10 years of age, which correlates with the ages of highest disease severity [12].

MAS presents earlier than FD, and the first clue is the presence of café-au-lait spots that are present at birth or soon thereafter. The hyperpigmented skin lesions have a jagged boarder and are termed “coast of Maine” lesions (Fig. 32.2); in contrast café-au-lait lesions in Neurofibromatosis type one (NF-1) which have smooth boarders and are termed “coast of California” lesions (Fig. 32.3). The presence of café-au-lait skin lesions should raise suspicion for an underlying genetic abnormality, and a work up may be undertaken by the patient’s pediatrician or geneticist to rule out possible conditions including NF1, MAS, Fanconi anemia, and tuberous sclerosis. In MAS, the location of the skin lesions nor the size of the skin lesions correlate to underlying bone lesions [2]. The original description of MAS in the 1930s defined the syndrome as a triad of polyostotic

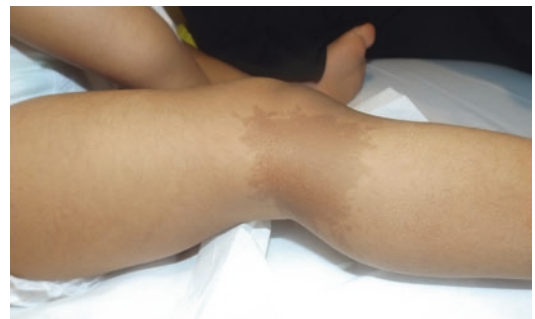

Fig. 32.2 The café-au-lait spots with a jagged boarder and are termed “coast of Maine” are typical of FD

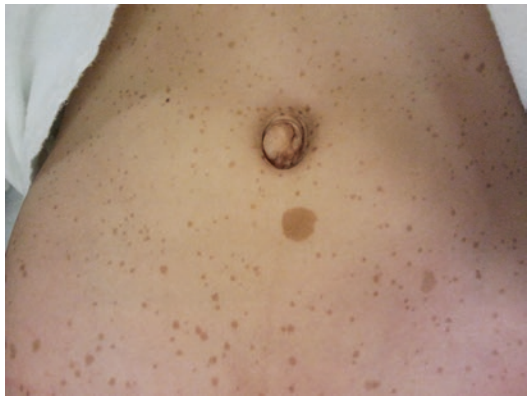

Fig. 32.3 The café-au-lait lesions in Neurofibromatosis type one (NF-1) which have smooth boarders and are termed "coast of California" lesions

FD, café-au-lait skins lesions, and precocious puberty [20, 21]. Evolution of the understanding of the disease has expanded the definition to include numerous hyperfunctioning endocrinopathies. Precocious puberty presents in 80% of female patients as intermittent vaginal bleeding prior to menarche. Ultimately, precocious puberty in males and females results in early physeal closure and reduced adult height. Other commonly associated endocrinopathies include hyperthyroid, Cushing's syndrome, growth hormone excess, and hypophosphatemia [6]. The diagnosis of MAS is made in a patient that has two characteristics of the syndrome including polyostotic FD, café-au-lait skin lesions, hyperthyroid, Cushing's syndrome, precocious puberty, hypophosphatemia, or excessive growth hormone.

A patient presenting to the orthopaedic clinic is likely being referred for evaluation or surveillance of identified or potential bone lesions of polyostotic FD that are present in MAS. The first step in the work up of a patient with MAS is to perform a clinical exam looking for a limp, bone pain, or limb length discrepancy. In patients younger than 5 years of age with a high clinical suspicion for a bone lesion a skeletal survey should be obtained. Additionally, serum phosphate levels can be ordered, although this is typically performed by an endocrinologist or pediatrician. In patients younger than 5 years of age, with a low clinical suspicion of a bone lesion, these patients should be followed with periodic clinical exams. Once the patient has reached 5 years of age a bone scan should be obtained in both symptomatic or asymptomatic patients with MAS to assess for bone lesions. Plain radiographs should be considered in areas of increased uptake with the bone scan [2].

Histology

Although the diagnosis of FD can often be made by the clinical history and radiographic examination of the patient, in unclear situations a biopsy can be obtained. Microscopically, the appearance of FD is a moderately cellular whorled or storiform fibrous stroma with randomly organized curvilinear trabeculae of woven bone, referred to as a "Chinese writing pattern" (Fig. 32.4) [22]. One key aspect of FD is that the spindle shaped fibrous stromal cells have no indication of malignancy or cellular atypia such as pleomorphism, abnormal nuclear to cytoplasm ratio, and increased number of mitoses. Additional histologic characteristics of FD is that the trabeculae of woven bone are devoid of osteoblastic rimming [22, 23].

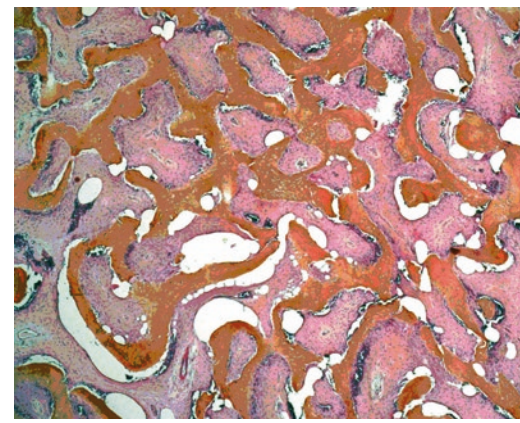

Fig. 32.4 Histologic features of fibrous dysplasia. Randomly organized trabeculae in the background of primitive mesenchymal tissue,. There is an absence of osteoblasts rimming the trabecular bone that helps in diagnosing FD from other pathologic entities

Differential Diagnosis

The clinical presentation of FD is non-specific, and although the radiographic and histologic work up help to make the diagnosis other pathologic lesions have similar findings and need to be considered in the differential. The differential should include ossifying fibroma, unicameral bone cyst, non-ossifying fibroma, adamantinoma, and low-grade osteosarcoma.

Osteofibrous dysplasia, or ossifying fibromas, and adamantinomas are tumors, which presents along the anterior cortex of the tibia. Children with an osteofibrous dysplasia lesion or an adamantinoma may present with anterolateral bowing of the tibia. These lesions are intracortical and multiloculated, which helps to differentiate them from the intramedullary based lesions in FD [23]. Adamantinomas are often described as having a "soap bubble" appearance from the multiloculated lytic lesions with sclerotic septae [24]. Histologically, the appearance of osteofibrous dysplasia is nearly identical to FD with the only difference being the presence of osteoblasts rimming the trabecular bone in osteofibrous dysplasia, which are not present in FD. Adamantinomas on histology have keratin positive epithelial cells, which differentiates them from ossifying fibromas and FD [25]. FD, osteofibrous dysplasia, and adamantinoma lesions may all present in the tibia, and can be difficult to distinguish. Adamantinomas are low-grade sarcomas with the ability to metastasize and are locally aggressive, and the treatment of these lesions is wide resection.

Unicameral bone cysts (UBCs) present in childhood, most commonly at the proximal humerus, but other common locations include the proximal femur, distal tibia, and calcaneus. Radiographically UBCs tend to be more radiolucent, have greater thinning of the cortex, and tend to be more expansile than FD lesions. In difficult to differentiate lesions on plain film, a MRI should be obtained [26]. Non-ossifying fibromas are very common benign fibrous lesions of bones. They originate in the metaphysis, are asymptomatic, and regress with age. On radiograph, they tend to be well demarcated, eccentric lesions that enlarge with skeletal growth. As patients approach skeletal maturity the lesion begins to ossify. In addition, these lesions are often intracortical, which aids in differentiating them from FD [27].

Low grade central intramedullary osteosarcomas are rare osteosarcomas, representing less than 2% of osteosarcomas, that present during the third decade of life [28]. Most commonly these lesions are seen at the distal femur or proximal tibia. On plain films these lesions present as large intramedullary lesions that resemble FD. Distinguishing features on radiograph include areas of cortical disruption and extension of the lesion to the knee articular cartilage [29]. MRI may help to identify cortical disruption in low grade intramedullary osteosarcomas not visualized on plain film. Histologically, these low-grade osteosarcomas present with variable amounts of bone production in a fibrous background. The key aspects in defining these osteosarcomas from FD histologically are the presence of permeation into surrounding tissue, cytologic atypia, increased mitotic activity, and unique patterns of bone production [29].

Essential Clinical Tests

- History patients present with pain and/or deformity
- Exam should focus on gait, tenderness, and deformity
- MAS exam features include café-au-lait spots, cushingnoid appearance, precocious puberty

Imaging

The initial imaging work up consists of X-ray imaging, and unlike many pathologic lesions the diagnosis of FD can be made by radiographs alone. In physiologic bone, the trabecular bone organizes itself into a pattern to best resist extrinsic forces (Wolffs law), one example being the organization of trabecular bone in the proximal femur to resist weight bearing. This pattern of trabeculae results in the normal, heterogeneous, radiographic appearance of bone. In FD, this physiologic trabecular bony pattern is replaced by random fibro-osseous tissue, and radiographically this pathologic tissue

is homogenous, radiolucent, and has a "ground glass" appearance [30]. FD lesions are well circumscribed with a reactive rim referred to as the "rind sign" radiographically. The lesions are intramedullary, and do not expand beyond the outer cortex of bone. Endosteal scalloping of the inner cortex may be present, and bony expansion may occur. Focal areas of cartilage may be present within the lesion, and this is represented as punctate foci on radiographs [23]. The shepherd's crook is a radiographic finding pathognomonic for FD, and results from combined coxa vara and bowing deformity of the proximal femur giving the bone the radiographic appearance of a shepherd's crook [31].

Radiographic classifications of proximal femur FD has been described in the literature. The first classification breaks proximal femur lesions into 5 groups based on the presence of three factors: (1) coxa vara, (2) proximal femur bowing deformity, and (3) cortical weakness defined as >50% cortical involvement (defined by axial CT scan) [32]. Type 1 lesions are lesions with greater than 50% cortical thickness without deformity. Type 2 lesions are without deformity, and have >50% cortical involvement. Type 3 lesions have coxa vara without bowing of the proximal femur. Type 4 lesions have proximal femoral shaft bowing with a normal neck-shaft angle. And Type 5 lesions have coxa vara and proximal femoral bowing, the sheperd's crook deformity. In this study, type 1 lesions were managed successfully without surgery, and the remaining types received surgical correction of the deformity.

The second classification system divides the proximal femur lesions into six types. The first three types are devoid of proximal femur bowing, and type 1 has a normal neck-shaft angle, type 2 has coxa valga, and type 3 has coxa vara. Types four, five, and six have proximal femur bowing, and type 4 has a normal neck-shaft angle, type 5 has coxa valga, and type 6 has coxa vara. The authors concluded that in types 1 and 2 FD lesions do not progress, but progression should be anticipated for types 3 to 6 [33].

"The diagnosis of FD is made from plain radiographs, and MRI should only be obtained for surgical planning or to rule out malignant transformation".

Advanced imaging is not mandatory to make the diagnosis of FD, but are often obtained to better define the lesion. On MRI the lesions are hyperintense on T2 weighted sequences, and hypointense on T1 weighted sequences [30]. MRI is useful in determining the extent of the disease for possible surgical planning, for assessing for soft tissues involvement, and for ruling out potential malignant pathology. Malignant transformation of FD is rare; however, a MRI should be obtained if there is clinical suspicion of transformation. MRI will demonstrate cortical involvement and spread of the lesion into adjacent soft tissues.

In children greater than 5 years of age and diagnosed with MAS a bone scan is recommended. FD lesions will have increased uptake on bone scan, and the extent of the disease can be confirmed by this examination [2]. Following bone scan individual lesions can be further investigated with X-ray or advanced imaging. There are case reports in the literature of FD mimicking metastatic disease on bone scan, and it is important to further investigate the areas of increased uptake with additional imaging.

Essential Imaging Tests and Measurements

- Radiographs are the gold standard to diagnose FD
- "Ground glass appearance" and "rind sign" are classic X-ray findings
- Well circumscribed lesions that do not expand beyond the outer cortex of bone, may be expansible and have endosteal scalloping
- On MRI, hyperintense T2 and hypointense T1.
- In polyostotic FD and MAS bone scans should be obtained in children >5 years of age to fully classify extent of osseous involvement

Non-Operative Management

Orthopaedics management of FD ranges from observation to surgical deformity correction. The non-operative management of patients with

FD involves observation and surveillance and potentially anti-resorptive medical therapy. Non-operative management of proximal femur FD is reserved for small asymptomatic lesions. Bone pain is a major reason for treatment in FD. In general, bone pain will increase as the patients get older. In a study assessing bone pain 50–60% of patients 11–30 years of age reported bone pain, and greater than 85% of patients greater than 30 years of age reported bone pain [34].

There is no universally effective medical management, although bisphosphonate therapy is advocated for the treatment of bone related pain. In FD there is prominent osteoclastogenesis, and bisphosphonates potentially minimize bone turnover decreasing pain. The initial studies investigating bisphosphonate therapy for FD demonstrated improved bone pain with inconsistent mineralization observed radiographically. These studies all used relatively high dose intravenous pamidronate for medical therapy [35–38]. In 2014, a randomized, double blind, and placebo-controlled study investigated oral alendronate treatment for FD and found no improvement in regards to bone pain or radiographic appearance with bisphosphonate use [36]. Summarizing this data, high dose intravenous bisphosphonate therapy may aid in alleviating bone pain, however oral bisphosphonate therapy does not improve bone pain. In addition, there is no strong evidence that bisphosphonate therapy alters the mineralization of a FD lesion. More recently, a single case report for the use of Denosumab, a RANKL antibody, in FD was published. This case report demonstrated improved bone pain and decreased lesion expansion; however, this case was complicated by rebound osteoclast activity with profound hypercalcemia following discontinuation of the drug [39].

Essential Non-Operative Management Methods

- Small and asymptomatic proximal femur lesions may be managed with observation and periodic surveillance
- High dose bisphosphonate therapy may be considered for the alleviation of bone pain

Operative Management

Fracture prevention and the decision as to when to prophylactically stabilize these lesions remains one of individual preference. Observation is appropriate for a lesion discovered incidentally that is asymptomatic. Surveillance radiographs should probably not be obtained at every visit, but should be repeated for a worsening clinical exam. Any new clinical symptoms of worsening pain and deformity need to be addressed seriously as these both likely indicate plastic deformity within the lesion, and possible impending fracture. The peak fracture risk occurs between 6 and 10 years of age with a risk of 0.38 fracture per patient per year [12]. Utilizing this data, prophylactic fracture fixation would have to occur at an early age to be effective, which possess unique challenges with the degree of skeletal growth remaining for the patient. Children who present with a stress fracture need to be surgically stabilized to prevent overt fracture from occurring. Relative surgical indication for prophylactic fixation includes worsening pain with weight bearing.

In the surgical planning phase of fracture fixation for FD some general principles should be considered, (1) poor bone quality leads to cortical cut-out of plate and screw devices, and intramedullary (IM) devices should be used when able, (2) bone-graft is resorbed and does not incorporate into the host tissue, and (3) periods of non-weight bearing weaken the surrounding bone and lead to increased fracture risk. Historically, the use of curettage and bone grafting was recommended for FD lesions. However, it has since been shown that both autograft and allograft fail to incorporate with resorption of the graft material. Leet and colleagues reviewed 54 bone-grafting procedures in patients with a mean age of 13 and demonstrated a 75% rate of graft resorption. No statistically different resorption rate was found between different graft materials. One interesting finding was that for the 25% of patients with graft survival, these patients were greater than 20 years of age [40]. In adults, with monostotic FD cortical allograft struts have been shown to incorporate with greater efficiency, and in this population grafting remains an option.

"Bone grafting becomes resorbed and replaced with dysplastic bone and should not be used in the treatment of pediatric FD".

Deformity correction is most frequently discussed for coxa vara of the proximal femur or the pathognomonic shepherd's crook deformity. The weakened and dysplastic proximal femur develops coxa vara of the neck-shaft angle bowing of the proximal third femur over time with weight bearing. This deformity is progressive, and even following surgical correction, tends to recur [41, 42]. Most authorities recommend deformity correction for neck-shaft angles that have progressed to less than 110–120 degrees. To correct the deformity a valgus corrective osteotomy is used in combination with a medial displacement femoral shaft osteotomy. In severe deformities two valgus osteotomies may need to be performed to correct both the coxa vara and proximal femur bowing. Over correction of the varus deformity is typically recommended in younger patients aiming for a neck-shaft angle close to 160–170 degrees (Fig. 32.5). This overcorrection will allow for some recurrent deformity and may delay a subsequent surgery. In addition, instrumentation is required to cross the femoral neck in order to prevent deformity recurrence.

IM fixation is preferred over extramedullary plate fixation to maintain post-surgical correction and allow shared weight bearing; however, this can be problematic in growing children. As an alternative, a corrective osteotomy can be performed in a staged manner. Initial fixation is obtained using a blade-plate or screw-plate construct, and later converting to an intramedullary (IM) device once the desired correction is achieved and the patient approaches skeletal maturity [41]. The instrumentation (plate or IM rod) should span the entire abnormal bone. Fixation should span the femoral neck to protect the neck from fracture and prevent deformity recurrence, but such instrumentation is problematic in growing children due to the open capital physis. As such, novel fixation using smooth fixation across the growth plate into the femoral head and a growing rod in the femur have been used (Fig. 32.5). The bone around the proximal femoral growth plate is the strongest area for fixation, but screw fixation in young children (under six to eight) can lead to growth arrest and progressive overgrowth of the greater trochanter and thus relative deformity recurrence. The use of smooth fixation across the proximal femoral growth plate have been devised, such as K-wire fixation. Unfortunately, devices that can directly link these to an IM rod are lacking. A growing rod is especially useful in younger children. Once the children are old enough that screw fixation across the proximal femoral epiphysis can be safely undertaken hybrid devices can be considered (the distal end of a growing rod construct and the proximal hardware being a reconstruction nail) (Fig. 32.6). Once children become skeletally mature, conversion to more traditional fixation is often warranted (Fig. 32.7). An additional technique that can be considered to assist in holding the proximal femur out of varus is using a trochentaric entry rod with a piriformis start point into the piriformus fossa, thus adding to the maintenance of correction.

Essential Surgical Techniques

- Prophylactic fixation with an antegrade IM device should be utilized for lesions without deformity
- Bone grafting is not effective in FD
- A valgus osteotomy at the vertex of the deformity is used to correct the deformity
- Fixation needs to cross the femoral neck, ideally with smooth pins, to prevent future fracture and deformity recurrence
- Staged surgery is often utilized with hybrid or growing rod constructs used initially being replaced by traditional IM rods once skeletal maturity is reached

Operative Pitfalls

- Following surgery, the bone heals with dysplastic bone and recurrence of the deformity is common
- Growth arrest of the proximal femoral physis may occur with fixation across the growth plate
- Prophylactic fixation is preferred, and proximal femur pathologic fracture is associated with avascular necrosis and non-union

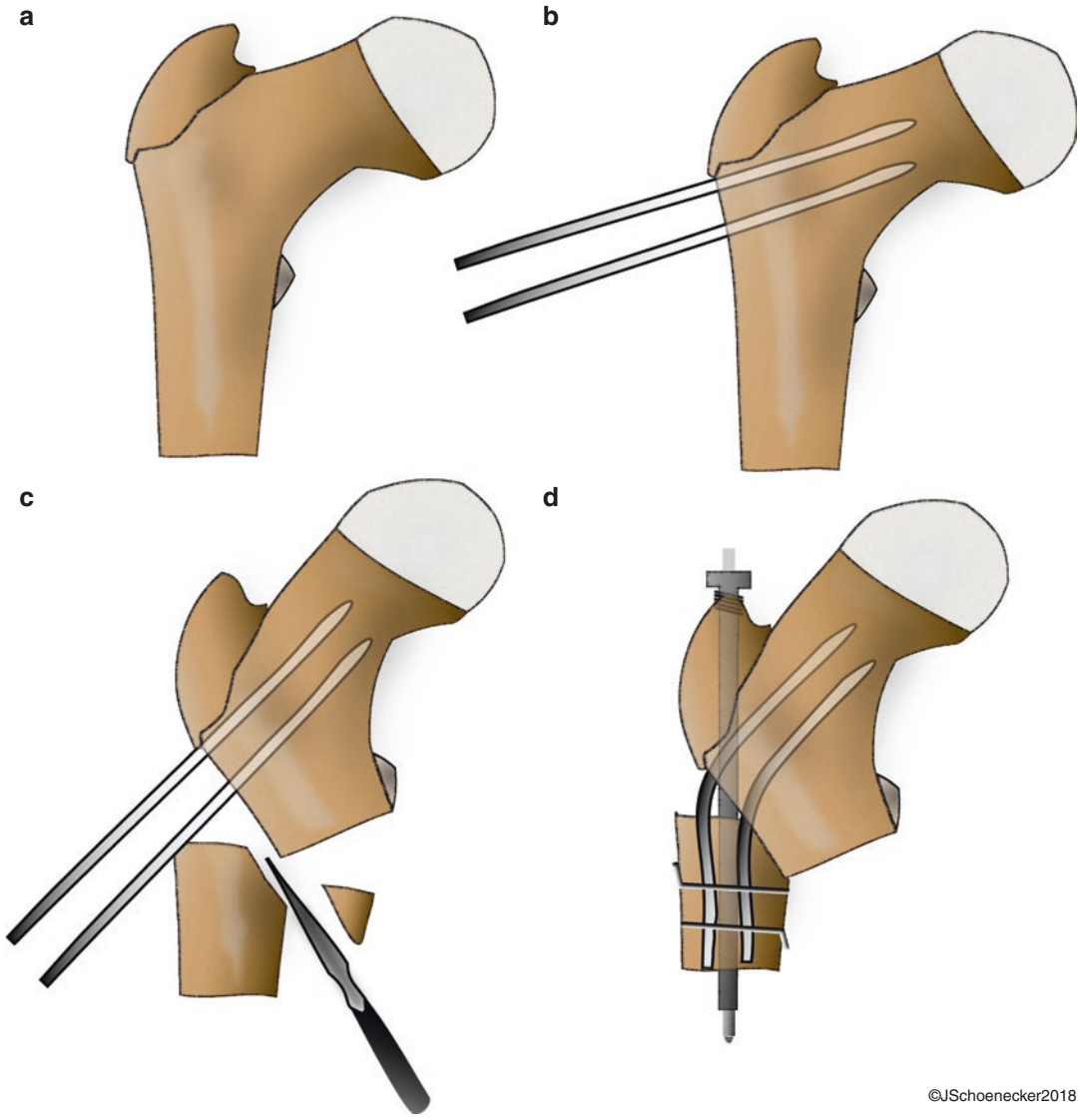

Fig. 32.5 Surgical approach to fix a "shepherd's crook" deformity in a growing child. (**a**) typical deformity. (**b**) Placement of K-wires into the head. (**c**) Osteotomy of the proximal femur, and (**d**) fixation of the k-wires and placement of an intramedullary rod

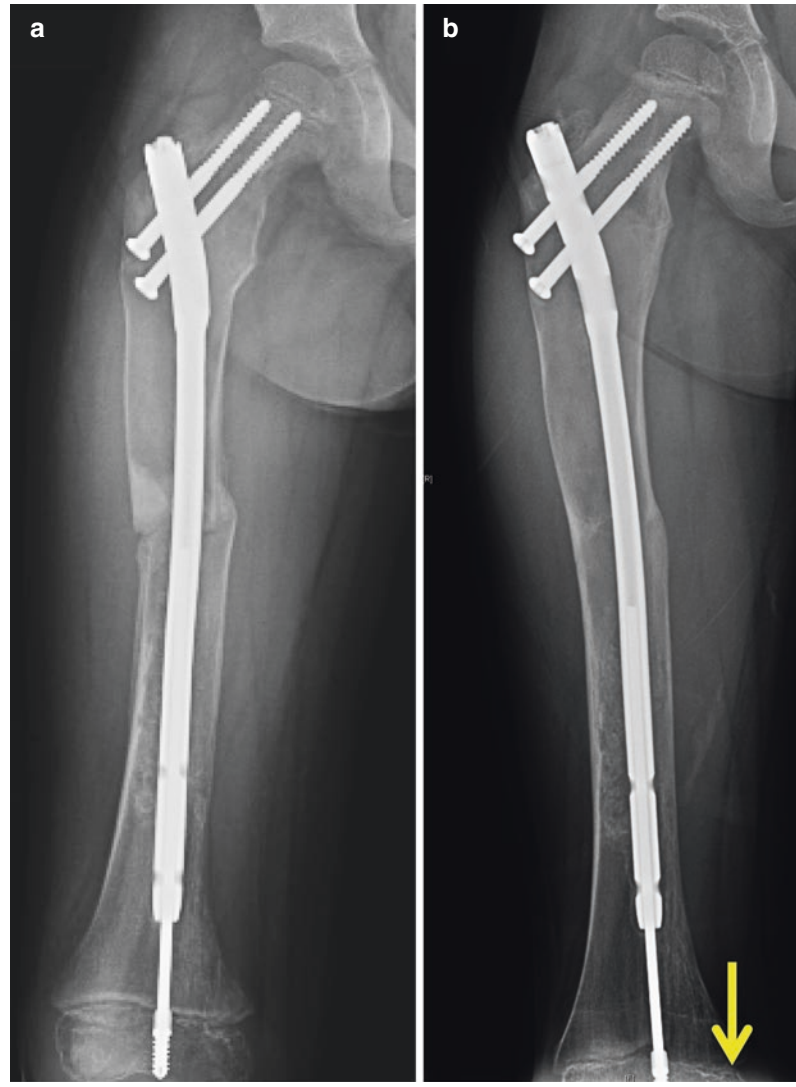

Fig. 32.6 Ruse of hybrid constructs in growing children. Proximal fixation using a standard nail with the distal end of a growing rod used to hold the fixation of the entire bone with growth. (**a**) At time of initial surgery, and (**b**) after two years showing expansion of the growing rod

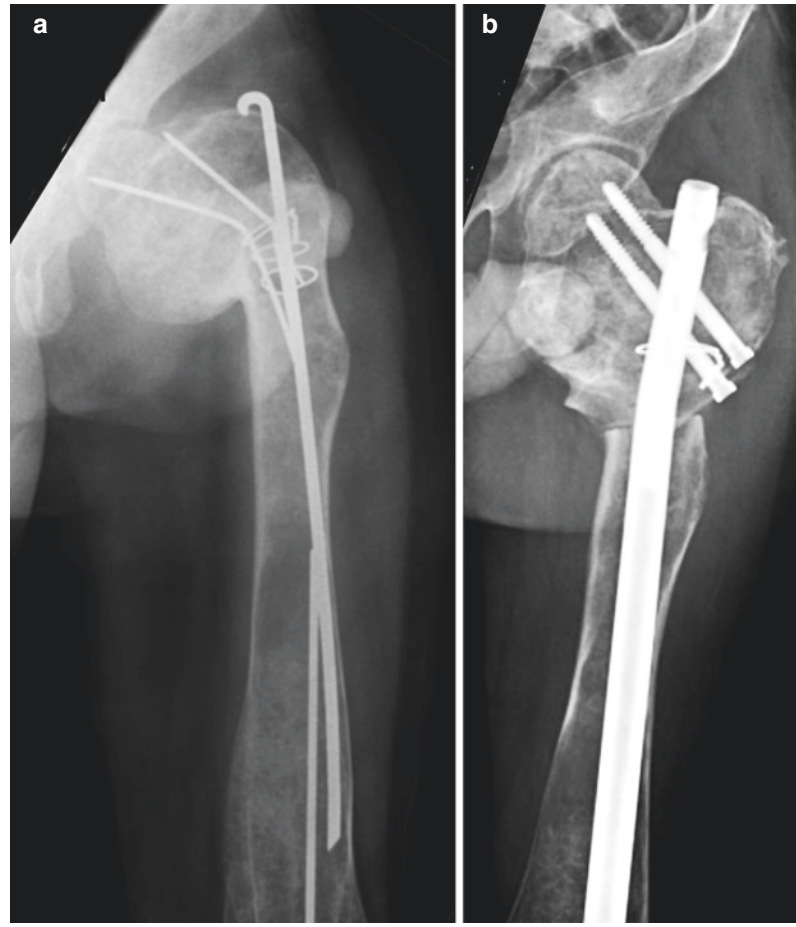

Fig. 32.7 Revision of childhood fixation when skeletally mature. (**a**) Presentation at skeletal maturity. (**b**) Use of a trochanteric entry rod inserted into the piriformis sinus to hold the correction

Classic Papers

Lichtenstein, L., Polyostotic Fibrous Dysplasia. Arch Surg, 1938. 36: p. 874–98. This was the article that first described fibrous dysplasia as a unique pathologic entity. The article describes the findings of two pathologists, Drs. Lichtenstein and Jaffe, as they first describe fibrous dysplasia.

Albright F, B.A., Hampton AO, Smith P, Syndrome Characterized by Osteitis Fibrosa Disseminata, Areas, of Pigmentation, and Endocrine Dysfunction, with Precociuos Puberty in Females. N Engl J Med., 1937. 216: p. 727–746. This article by Dr. Albright describes the classic triad of McCune Albright syndrome presenting five patients, and including patients that had been previously described by Dr. McCune earlier in the same year. This was the classic first article describing the clinical features of McCune Albright syndrome.

Weinstein LS, Shenker A, Gejman PV, Merino MJ, Friedman E, Spiegel AM, Activating mutations of the stimulatory G protein in the McCune-Albright Syndrome. N Engl J Med., 1991. 12;325(24):1688–95. This is the classic article initially describing the missense mutation responsible for FD and MAS. Polymerase chain reaction (PCR) was used to identify the missense mutations within exons 8 and 9 of the Gs alpha gene responsible for overactivation of the cAMP pathway leading to the clinical manifestations of MAS and FD.

Key Evidence

Kuznetsov, S.A., et al., Age-dependent demise of GNAS-mutated skeletal stem cells and "normalization" of fibrous dysplasia of bone. J Bone Miner Res., 2008. 23(11): p. 1731–40. doi: https://doi.org/10.1359/jbmr.080609. This study investigated the number of mutated cells in FD lesions as children aged and found an inverse correlation of the number of mutated cells and older age. From this article evolved the novel concept of "normalization" of FD lesions. Mutated cells fail to self-renew, and eventually are removed via apoptosis.

Hart E, K.M., Brillante B, Chen C, Ziran N, Lee J, Feuillan P, Leet A, Kushner H, Robey P, Collins M, Onset, Progression, and Plateau of Skeletal Lesions in Fibrous Dysplasia and the Relationship to Functional Outcome. Journal of Bone and Mineral Research, 2007. 22(9). This study demonstrated that 90% of the entire extremity disease burden is present by 15 years of age with greater than 50% of the disease burden being present by six years of age. 90% of Craniofacial FD is present by four years of age. The average disease burden, as assessed by bone scan, was 64% for patients requiring an assistive device for ambulation compared to 23% for those ambulating without assistance.

Leet A, W.S., Kushner H, Brillante B, Kelly M, Robey P, Collins M, The Correlation of Specific Orthopaedic Features of Polyostotic Fibrous Dysplasia with Functional Outcomes in Children The Journal of Bone and Joint Surgery, 2006. 88(4): p. 818–823. This study compared the disease burden of FD to functional outcomes, using the Pediatric Outcomes Data Collection Instrument score. Femoral neck shaft angle and overall disease burden correlated with worse functional outcome scores. The sports score and happiness score were statistically impacted.

Leet A, C.C., Kushner H, Chen CC, Kelly MH, Brillante BA, Robey PG, Bianco P, Wientroub S, Collins MT, Fracture Incidence in Polyostotic Fibrous Dysplasia and the McCune-Albright Syndrome. J Bone Miner Res, 2004. 19(571–7). This study assessed risk factors for pathologic fracture in 35 patients with FD. The proximal femur is the site with the greatest risk for fracture. The peak fracture rate occurred between six and 10 years of age. Patients with hypophosphatemia were at increased risk for fracture, and fracture occurred at a younger age.

Chapurlat RD, Hugueny P, Delmas PD, Meunier PJ, Treatment of Fibrous Dysplasia of Bone with Intravenous Pamidronate: Long-term Effectiveness and Evaluation of Predictors of Response to Treatment. Bone, 2004. 1: p. 235–42. 58 patients were treated with IV pamidronate every 6 months for an average of 50 months. The results demonstrated that pain scores decreased in 44 patients, biomarkers of bone turnover were reduced, and radiographic improvement of the lesion was observed in 50% of patients. Authors concluded that pamidronate was safe, and cold be used to decrease bone pain associated with FD.

Boyce, A.M., et al., A randomized, double blind, placebo-controlled trial of alendronate treatment for fibrous dysplasia of bone. J Clin Endocrinol Metab., 2014. 99(11): p. 4133–40. doi: https://doi.org/10.1210/jc.2014-1371. Epub 2014 Jul 17. A randomized controlled trial of 40 patients with polyostotic FD. The patients were grouped to either receive oral alendronate or act as a control group. At the conclusion of the two year study, the alendronate group had improved bone mineral density and decreased bone turn over markers. Pain and functional parameters were not clinically significant between the groups.

Leet, A.I., et al., Bone-Grafting in Polyostotic Fibrous Dysplasia. J Bone Joint Surg Am., 2016. 98(3): p. 211–9. doi: https://doi.org/10.2106/JBJS.O.00547. A study of 23 patients with 52 bone grafting procedures were analyzed using Kaplan Meier statistics to evaluate for graft survival. The study demonstrated a 50% graft survival rate at a 14 year follow up. The authors concluded that implant support is necessary to maintain bone mechanics.

Take Home Messages

- Fibrous dysplasia is a relatively common benign condition of the bone typically diagnosed in the pediatric patient.
- It remains important for the physician to diagnose fibrous dysplasia, and monitor the patient appropriately to prevent pathologic fracture.
- In general, once an individual with fibrous dysplasia reaches skeletal maturity, the lesions stabilize and rarely do new lesions present.
- Despite our understanding of the underlying pathophysiology of this condition, there remains no curative treatment options, and medical management focuses on pain relief, deformity correction, and fracture prevention.
- Hip deformity is common and surgery focuses on deformity correction and intramedullary fixation.

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