Fibrous dysplasia

Key concepts

● non-neoplastic condition where bone is replaced by expansile fibrous connective tissue

● malignant transformation to osteosarcoma or other sarcoma occurs in < 1%

● common sites of involvement: ribs, proximal femur, craniofacial bone

● may be monostotic, polyostotic, or part of McCune-Albright syndrome (triad: café au lait spots, endocrinopathy (e.g. precocious puberty) and polyostotic fibrous dyslpasia)

● common presentation: may be incidental, cosmetic, hearing loss, rarely visual loss

● treatment: the typical slow progression does not justify prophylactic surgery

Fibrous dysplasia (FD) is a non-neoplastic benign condition in which normal bone is replaced by fibrous connective tissue and immature woven bone that is weaker than normal bone and tends to expand. Most lesions occur in the ribs, proximal femur or craniofacial bones (especially the maxilla). Frequent femoral neck fractures can lead to a varus deformity (so-called “shepherd’s crook deformity”) Molecular genetics: FD is not heritable. It results from somatic activating mutations in the α sub- unit of the stimulatory G protein encoded by the GNAS locus at 20q13.2-q13.3.

Classification

Types of involvement

Patterns of involvement

3 patterns of involvement:

1. monostotic fibrous dysplasia (MFD): most common. The most frequent site of involvement is the zygomatic-maxillary complex

2. polyostotic fibrous dysplasia (PFD): 25% with this form have > 50% of the skeleton involved with associated fractures and skeletal deformities

3. PFD as part of McCune-Albright syndrome (and its variants).

Triad:

a) café au lait spots which tend to occur on one side of the midline and tend to be more jagged than those seen in neurofibromatosis and fewer in number

b) endocrinopathy:including precocious puberty(primarily in females)and growth hormone secretion

c) polyostotic fibrous dysplasia (PFD)

Skull involvement occurs in 27% of MFD. In PFD and MAS, craniofacial involvement occurs in 90% of cases and the anterior skull base is involved in > 95% [1].

Forms of fibrous dysplasia

3 forms of the FD lesions:

1. cystic (the lesions are not actually cysts in the strict sense): widening of the diplöe usually with thinning of the outer table and little involvement of the inner table. Typically occurs high in calvaria

2. sclerotic: usually involves skull base (especially sphenoid bone) and facial bones

3. mixed: appearance is similar to cystic type with patches of increased density within the lucent lesions.

Epidemiology

True incidence is unknown since many cases are asymptomatic. FD constitutes ≈ 7% of benign bone lesions. [2].

MFD is probably more common than PFD, but the actual ratio depends on the screening methodology. MAS is more common in females.

This disorder is usually diagnosed in childhood or early adulthood and can affect one or several bones.

Males and females of any race are equally affected.

Temporal bone involvement is the least frequently reported type, especially in children.

Etiology

It is a lesion of unknown etiology, uncertain pathogenesis, and diverse histopathology.

Clinical

Clinical manifestations of craniofacial fibrous dysplasia lesions include:

1. incidental finding (i.e., asymptomatic)

2. local pain or tenderness: the lesions are not tender, but overlying stretched periosteum may be. Associated aneurysmal bone cysts (ABCs) may be painful

3. local swelling (rarely: marked distortion resembling aneurysmal bone cyst)

4. changes due to facial deformity/asymmetry

a) cosmetic:frontal bossing,hypertelorism

b) orbital involvement may cause:proptosis,vertical dystopia(asymmetry in vertical alignment of the eyes), visual loss

c) nasal congestion

d) mandibular involvement: asymmetry which may produce malocclusion

5. may predispose to pathologic fractures when FD lesions occur in long bones

6. cranial nerve-related manifestations:

a) hearing loss:temporal bone involvement may obliterate the external auditory canal or may restrict the movement of middle ear ossicles. Temporal bone involvement occurs in > 70% of cases of craniofacial PFD and MAS and is uncommon in MFD [3].

b) visual loss: an uncommon but recognized sequela of FD as a result of compression of the optic nerve in the optic canal, more common in children

c) trigeminal neuralgia [4].

d) facial nerve palsy: rare.Compression typically occurs within Fallopian canal and/or IAC

7. seizures: rare presentation

8. serum alkaline phosphatase is elevated in about 33%, calcium levels are normal

9. darkened hair pigmentation overlying skull lesions

10. spontaneous scalp hemorrhages

11. rarely associated with Cushing'ssyndrome, acromegaly

Fibrous dysplasia causes abnormal growth or swelling of bone.

Fibrous dysplasia can occur in any part of the skeleton but the bones of the skull, thigh, shin, ribs, upper arm and pelvis are most commonly affected. Most lesions are monostotic, asymptomatic and identified incidentally and can be treated with clinical observation and patient education.

Optic neuropathy in fibrous dysplasia (FD) is more common in patients with growth hormone excess [5] [6].

Fibrous dysplasia (FD) of the skull base can manifest with optic nerve compression. As most patients initially do not experience vision loss, controversy exists whether to proceed with prophylactic surgical decompression or elect for conservative observation.

Optical Coherence Tomography (OCT) may be a valuable imaging modality to monitor patients with fibrous dysplasia for development of optic neuropathy during periods of conservative watchful waiting.

Diagnosis

A major objective is to determine if the patient has a single lesion (MFD) or multiple lesions as in PFD or MAS.

1. history: ● onset and nature of symptoms

● rapidity of progression

● history of pathologic fractures (clue for other FD lesions)

● indications of endocrinopathies: age of menarche in females (R/O precious puberty), growth abnormalities (R/O growth hormone excess)

2. physical exam: look for and ask about skin discoloration (café-au-lait spots)

3. diagnostic studies:

● skeletal survey (total body X-rays) or bone scan if additional lesions are suspected ● non-contrast head CT with thin cuts: characteristic ground glass appearance of craniofacial FD on X-rays and CT is due to the thin spicules of woven bone. With age, lesions morph into a mixed radio-dense/radio-lucent appearance. In prepubertal patients with PFD or MAS a homogeneous radio-dense appearance is more common.

● panorex and/or dental films when there is involvment around the teeth

Differential diagnosis

Osteoma.

Hyperostosis frontalis interna.

Natural history

FD lesions are usually slowly progessive. Rapid progression may occur:

● infrequently, in PFD or MAS prior to puberty. Progression usually slows when skeletal maturity is reached.

● malignant transformation: occurs in < 1% of cases [7].

Typically to osteosarcoma, but other sarcomas are possible (fibrosarcoma, chondrosarcoma…)

● associated expansile lesions:

○ aneurysmal bone cyst (ABC)

○ mucocele: when the ostium to a sinus becomes occluded by fibrous overgrowth

● osteomyelitis: often difficult to cure in the presence of FD

The most disfiguring and symptomatic lesions occur in patients with poorly controlled excess growth hormone (GH). [8)]

Therefore excess GH should be managed aggressively

Craniofacial FD may be categorized as [9)]

1.-quiescent: no progression. Typically with smaller lesions

2.-non-aggressive: slow growing

3.-aggressive: rapid growth, associated pain, pathologic fractures, malignant transformation…

Management

Observation is often the best first management option. If possible, wait for skeletal maturity (around age 10–12 years).

Cure may be possible with smaller lesions in MFD but is unlikely with PFD or MAS. Local procedures (mostly orthopedic) are used for deformities or bone pain that is refractory to other treatment. Incompletely resected lesions are subject to regrowth.

Consult an endocrinologist if there is any suspicion of endocrinopathy.

Biopsy of an accessible lesion by the appropriate surgical specialist should be considered when the diagnosis is in doubt.28 Bleeding may be brisk due to vascularity. Biopsy does not promote growth of the lesion. Histology does not predict biological behavior.

Quiescent craniofacial lesions without complaints of facial deformity may be monitored with annual evaluations which should include: patient-reported symptoms, neurologic exam including sensory testing, photographs and facial CT for the first 2 visits and then less frequently based on prior CT results and clinical findings.

Non-aggressive or quiescent lesions producing bothersome facial disfigurement may be treated by a craniofacial surgeon. If practical, it is best to wait until the patient reaches skeletal maturity. When optic canal involvement is documented, annual ophthalmological exams should be conducted. The diagnosis of optic neuropathy is made when there is a visual defect or if 2 out of 3 exams (contrast sensitivity, color vision, and funduscopic exam) are abnormal. Optic neuropathy in FD is more common in patients with growth hormone excess [10) 11)].

Evidence suggests aggressive management of GH excess reduces the risk of optic neuropathy. When there is temporal bone involvement, regular otolaryngology exams (including microscopy for EAC stenosis) should be performed to maintain patency of EAC (from bone, cerumen or the rare cholesteatoma). Annual audiology evaluations are recommended during periods of active lesion growth. Pain is a common complaint and is more prevalent in the lower extremities than with craniofacial involvement. It does not correlate with disease burden.

Calcitonin may be used for widespread lesions with bone pain and/or high serum alkaline phosphatase levels. Bisphosphonates (e.g. alendronate, pamidronate or zoledronic acid): mixed results for

craniofacial pain control and growth rate reduction in FD.

RANK ligand inhibitors e.g. denosumab: uncertain role in FD [12)]

✖ Radiation therapy is not recommended (risk of XRT induced tumors).

Treatment

There is no known cure.

Neurosurgical involvement, may be required for skull lesions producing refractory pain or neurologic symptoms or for rapidly growing associated lesions (e.g. ABC). Calvarial lesions may be treated with curettage and cranioplasty. Once the dysplastic bone is disconnected from the skull, the loss of vascular supply usually renders it inactive. Skull base lesions often require a multidisciplinary approach. Acute visual deterioration associated with an expansile lesion near the optic canal should be treated with high-dose glucocorticoids and rapid surgical decompression [13)].

However, vision is usually preserved despite optic canal narrowing with FD [14)] and visual loss may follow injudicious surgical intervention due to the intolerance of the optic nerve to surgical trauma. Rule out other possible explanations for a visual loss before operating.

Image guidance may be helpful when drilling down exuberant bone to decompress the optic canal. Copious irrigation (e.g. with irrigating drill) is critical to avoid thermal damage. Endoscopic techniques may be useful adjuncts, but distorted anatomy requires an experienced practitioner.

Case reports

A 16-year-old male patient presented with painful swelling on his left eye that had persisted for 2 days. Transnasal endoscopic drainage of the left orbital subperiosteal abscess was performed and progressive improvement of the swelling of the left eye was noted. After the acute phase, transcranial removal of the sinonasal bony lesion and mesh reconstruction of the left orbital wall were performed. There has been no progression of FD to date, with 24 months of follow-up.

After the acute phase, radical excision with reconstruction or debulking surgery after skeletal maturation may prevent recurrence. Although malignant transformation is rare, long-term follow-up is necessary for FD [15)].

A 21-year-old woman who had presented with acute worsening visual loss secondary to hemorrhagic fibrous dysplasia with ensuing optic nerve compression. Emergent surgical decompression resulted in rapid improvement of her visual dysfunction. The pathological features demonstrated a mixed pattern of woven bone in a fibrous background and secondary aneurysmal bone cyst-like changes.

Hemorrhagic transformation of craniofacial FD remains rare but can present with acute neurologic deterioration. Rapid diagnosis and treatment can allow reversal of patient morbidity. We have also

included Supplementary Video 1 to illustrate the surgical principles, and we review the reported data of similar cases [16].

Guatta and Scolozzi, report the successful treatment of severe fronto-orbital asymmetry in a 20-year-old man with fibrous dysplasia by bone recontouring using a specific approach combining “mirroring” virtual computational planning with intraoperative guided surgical navigation [17].

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