REVIEW ARTICLE

Fibro-osseous lesions of the jaws: An insight

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Abstract

Fibro-osseous lesions of the jaws comprise a diverse group of conditions, which are characterized by replacement of normal bone by fibroblasts, collagen fibers, and mineralized tissue. The diagnosis based on microscopy alone is often impossible due to overlapping of histopathologic features. Adequate clinical and para clinical observations, such as patient’s age, sex, location of the lesion, duration of symptoms, imaging characteristics, and histologic findings are necessary to arrive at an accurate diagnosis. Certain cases present features that may be atypical and do not favor a definite diagnosis. Sound knowledge of various fibro-osseous lesions of craniofacial structures is critical for proper interpretation and diagnosis of these lesions. Despite striking similarity in the clinical, radiographic and to some extent the histologic patterns, the biologic behavior varies; so each lesion may require a different treatment approach. In this review, the most important and frequent features of the fibro-osseous lesions of jaws along with different classifications are discussed.

Keywords: Fibro-osseous lesions, fibrous dysplasia, jaws, ossifying fibroma

Introduction

Fibro-osseous lesions comprise a diverse group of pathologic conditions that include developmental lesions, reactive or dysplastic diseases, and neoplasms. Basically the term fibro-osseous lesion is a generic designation of a group of jaw disorders characterized by the replacement of bone by a benign connective tissue matrix. This matrix displays varying degree of mineralization in the form of woven bone or cementum-like round acellular intensely basophilic structures which are indistinguishable from “cementicles.”[1]

From a clinical standpoint, fibro-osseous lesions may be associated with significant cosmetic and functional disturbances or they may be completely asymptomatic localized lesions that are identified only on routine radiograph.[2] There are pronounced racial and sex predilections for a subset of fibro-osseous lesions that exclusively affect the jawbones, the osseous dysplasia, of which a hereditary form exists.[3]

Radiographically, fibro-osseous lesions may manifest as solitary, multifocal, or multi quadrant disease, they may be ill or well defined; they may have radiolucent, mixed radiolucent-radiopaque, predominantly radiopaque, or ground glass appearance and they may or may not be associated with the root apices of teeth.[4]

The gross appearance of fibro-osseous lesions also may vary depending on the lesion. Thus, most oral and maxillofacial pathologists would agree that definitive diagnosis of a fibro-osseous lesion requires correlation of the histologic appearance of the lesion with the clinical, radiographic, and intraoperative findings.[1,5]

Classification and Nomenclature of Fibro-Osseous Lesions

Since 1930’s, numerous classifications have been proposed and varieties of lesions have come under the umbrella of fibro-osseous lesion, which includes developmental lesions, reactive lesions, and benign fibro-osseous neoplasms. Historically, the nosology of fibro-osseous lesions has been fraught with inconsistency, confusion, and a seemingly endless array of terminology. However, a classification of fibro-osseous lesions proposed by Waldron has gained wide recognition over the years and remains, to date, the most accepted.[6]

Waldron (1985):
I. Fibrous dysplasia (FD)
   A. Polyostotic
   B. Monostotic
II. Fibro-osseous (cemental) lesions presumably arising in the periodontal ligament
   A. Periapical cemental dysplasia
   B. Localized fibro-osseous-cemental lesion (probably reactive in nature)
   C. Florid cement-osseous dysplasia (gigantiform cementoma)
   D. Ossifying and cementifying fibroma
III. Fibro-osseous neoplasms of uncertain or debatable relationship to those arising in the periodontal ligament
   A. Cementoblastoma, osteoblastoma and osteoid osteoma
   B. Juvenile active ossifying fibroma and other so-called aggressive, active ossifying/cementifying fibromas.

Waldron (1993):
I. FD
II. Cemento-osseous dysplasia
   A. Focal cemento-osseous dysplasia
   B. Periapical cemento-osseous dysplasia
   C. Florid cemento-osseous dysplasia.
III. Ossifying fibroma

Slootweg and Muller (1996):
1. Group I: FD
2. Group II: Juvenile ossifying fibroma
3. Group III: Ossifying fibroma

Group IV: Cemento-osseous dysplasia

Brannon and Fowler (2001):
I. FD
   A. Monostotic
   B. Craniofacial
   C. Polyostotic
   D. McCune-Albright syndrome
II. Ossifying fibroma and juvenile ossifying fibroma
III. Osseous dysplasia
   A. Periapical
   B. Focal
   C. Florid
   D. Familial gigantiform cementoma (FGC)

Speight and Charlose (2006):
I. Fibrous dysplasia
   A. Monostotic FD
   B. Polyostotic FD
   C. Craniofacial FD
II. Osseous dysplasia:
   A. Periapical osseous dysplasia
   B. Focal osseous dysplasia
   C. Florid osseous dysplasia
   D. FGC
III. Ossifying fibroma:
   A. Conventional ossifying fibroma
   B. Juvenile trabecular ossifying fibroma (TJOF)
   C. Juvenile psammomatoid ossifying fibroma (PJOF)

Eversole (2008):
I. Bone dysplasia
   A. FD
      i. Monostotic
      ii. Polyostotic
      iii. Polyostotic with endocrinopathy (McCune-Albright)
   iv. Osteofibrous dysplasia
   B. Osteitis deformans
   C. Pagetoid heritable bone dysplasia of childhood
   D. Segmental odontomaxillary dysplasia
II. Cemento-osseous dysplasia
   A. Focal cemento-osseous dysplasia
   B. Florid cemento-osseous dysplasia
III. Inflammatory/reactive processes
   A. Focal sclerosing osteomyelitis
   B. Diffuse sclerosing osteomyelitis
   C. Proliferative periostitis
IV. Metabolic disease: Hyperparathyroidism
V. Neoplastic lesions (Ossifying fibromas)
   A. Ossifying fibroma NOS
   B. Hyperparathyroidism jaw lesion syndrome
   C. Juvenile ossifying fibroma
      i. Trabecular type
      ii. Psammomatoid type
   D. Gigantiform cementomas

Discussion
Regardless of the subtype, all fibro-osseous lesions demonstrate replacement of normal bone by fibrous connective tissue with an admixture of the mineralized product including osteoid, mature bone, and/or cementum like calcifications. Thus, histologic diagnosis of a fibro-osseous lesion is in many cases, relatively complicated.

I. FD

FD is a benign fibro-osseous disease frequently affecting the jaw bones and represents about 5% of all benign bone tumors. It is postulated to occur as a result of a developmental failure in the remodeling of primitive bone to mature lamellar bone leaving a mass of immature isolated trabeculae enmeshed in dysplastic fibrous tissue that undergo turn over constantly but never (or very, very slowly) complete the remodeling process. In addition, the immature matrix does not mineralize normally. It was said to be a hamartomatous fibro-osseous lesion not of periodontal ligament origin.

FD is classified by Waldron as being monostotic when it affects a single bone or, less commonly, polyostotic when it involves multiple bones concomitantly. Two apparently separate types of polyostotic FD are described:

1. FD involving a variable number of bones although most of the skeleton is normal, accompanied by pigmented lesions of the skin or cafe-au-lait spots (Jaffe’s type).
2. An even more severe porous dysplasia involving nearly all
bodies in the skeleton and accompanied by pigmented lesions of the skin, and in addition, endocrine disturbances of varying types (Albright’s syndrome).

(a) Monostotic FD

Monostotic presentation is more frequent, and lesions enlarge in proportion to skeletal growth accounting for 80-85% of cases of FD.[4] This is seen with approximately equal frequency in males and females in their first or second decades of life. It is usually insidious in onset and manifests clinically as a slow-growing, painless expansion of the involved bone monostotic FD commonly occurs in the rib (24%), femur (17%), tibia (13%), mandible (12%), and maxilla (12%).[9] In the skull, it commonly involves the ethmoid, sphenoid, frontal, and temporal bones in decreasing order, respectively.[10]

Maxillary involvement, specifically posterior maxilla is more common than mandibular. The clinical term “leontiasis ossea” has often been applied to cases of FD which affects the maxilla or facial bones and give the patient a leonine appearance.[11]

(b) Polyostotic FD

Involvement of two or more bones is termed polyostotic FD accounting for approximately 20-30% of FD. Patients with this form of disease are often younger at the time of diagnosis with median age for onset of symptoms being 8 years, and two thirds of the patients had symptoms before the age of ten.[11]

Polyostotic lesions often continue to enlarge after skeletal maturity. Diffuse polyostotic lesions in large weight-bearing bones are lead to bowing deformities that may account for pathologic fracture. The classic deformity of polyostotic FD is the so-called shepherd’s crook deformity of the proximal part of the femur. The oral manifestations may be expansion and deformity of the jaws and altered eruption pattern of the teeth due to loss of normal bony support during development. The endocrine disturbance may also account for the latter.[11]

McCune-Albright syndrome is a sporadic disorder that is characterized by the clinical triad of polyostotic FD, skin hyperpigmentation (cafe au lait spots), and multiple endocrinopathies, including gonadal hyper function leading to sexual precocity (especially in females).[12] Mazabraud syndrome is another rare, sporadic disease that is characterized primarily by polyostotic FD and intramuscular myxomas.[13]

Radiographically, the normal bone is replaced by tissue that is more radiolucent, with a grayish “ground-glass” pattern. The lesion characteristically is bounded by a distinct rim or shell of reactive bone. The lucent lesion with a thick sclerotic border is called the rind sign. FD commonly displays an abnormal opacification, which ranges from very numerous, small and diffusely distributed opacities (“ground glass” and “peau-d’orange”) to sclerosis, classically described as “cotton wool.”[14]

Serum alkaline phosphatase levels are often elevated during active phases of this disease. Patients with the polyostotic form, particularly McCune-Albright syndrome, must be evaluated to exclude hyperthyroidism, pituitary gigantism, or hypercortisolism (possible autonomous endocrine hyperfunction). Molecular diagnosis using the techniques of polymerase chain reaction analysis with peptide nucleic acid has shown that FD patients have blood cells with the G protein gene (GNAS) mutation.[5]

The histologic appearance of FD usually exhibits a moderately cellular, fibrous stroma containing haphazardly arranged, uniform, benign-appearing, spindle-shaped to ovoid fibroblasts which are well differentiated and mature.[15] The trabeculae tend to be delicate and curvilinear and have been linked to Chinese script-writing.[8]

Surgical procedures may be required for correction of the deformity, prevention of pathologic fracture, and/or eradication of symptomatic lesions. Malignant transformation of FD occurs very infrequently, with reported prevalence ranging from 0.4% to 4%.[16] Osteosarcoma makes up more than half of all the malignant diagnoses, followed by fibrosarcoma and chondrosarcoma.

II. Osseous dysplasia

Osseous dysplasias are the most common form of benign fibro-osseous lesion in the jawbones, yet they are probably the least recognized by surgical pathologists. There are three nonhereditary subtypes of osseous dysplasia: Periapical osseous dysplasia, focal osseous dysplasia, and florid osseous dysplasia. The distinction is based solely on the clinical and radiographic manifestations of the lesions. The histologic appearance of osseous dysplasia varies depending on the stage of the lesion.

(a) Periapical osseous dysplasia (osseous dysplasia; cemental dysplasia; periapical cementoma; periapical FD; periapical ossifying fibroma)

Periapical osseous dysplasia is a reactive fibro-osseous lesion and is thought to arise from elements in the versatile periodontal ligament, where mature osteoblasts, cementoblasts, and precursor cells reside.[17]

This disease entity has a distinct predilection for black females and develops almost exclusively after the age of 30 years. It is almost always asymptomatic and detected during a routine radiographic examination. Periapical osseous dysplasia is usually found in intimate association with the root apices of the mandibular anterior teeth.[3]

Although each individual lesion exhibits little tendency to enlarge, often adjacent lesions coalesce to form a larger, irregularly shaped, mixed radiolucent-radiopaque mass. Serial radiographs have demonstrated that periapical osseous dysplasia initially manifests as multiple, well-circumscribed, non-corticated radiolucent area at the apex of the tooth.[18]

The early area shows proliferating fibrous connective tissue with no evidence of an inflammatory infiltrate. Small foci of cementum, osteoid or bone are almost invariably present. Advanced lesions show a greater proportion of mineralized, cementum like material or thick, sclerotic bone trabeculae or an admixture of both.[5]
(b) **Focal osseous dysplasia**

Focal osseous dysplasia presents as a solitary lesion in the posterior jaws, most often the mandible. Waldron suggested that focal osseous dysplasia likely represents the most common benign fibro-osseous lesion of the jawbones. [5]

This condition is invariably asymptomatic, manifesting most commonly as a small, solitary, relatively well-demarcated lesion in the posterior mandible, either in close association with the apices of teeth or in areas where a tooth has been extracted previously. Focal osseous dysplasia is much more common in black females than males, and most lesions are recognized during the fourth and fifth decades of life. [19]

Radiographically focal osseous dysplasia tends to manifest as an irregularly shaped, mixed radiolucent-radiopaque lesion, occasionally with well-defined borders. [20]

(c) **Florid osseous dysplasia (florid cemento-osseous dysplasia; gigantiform cementoma; familial multiple cementomas)**

These types of dysplasia termed florid because of their widespread, extensive manifestation. In florid osseous dysplasia normal cancellous bone is replaced with dense, acellular cemento-osseous tissue in a background of fibrous connective tissue. However, if periapical cemental dysplasia is defined in three or four quadrants or is extensive throughout one jaw, it usually is considered to be florid osseous dysplasia. [17]

This form predominantly involves black women with a marked predilection for middle-aged to the elderly. The lesions show a marked tendency for bilateral and often quite symmetric involvement, and it is not unusual to encounter extensive lesions in all four posterior quadrants. Both dentulous and edentulous areas may be affected. Thus in most cases, an innocuous, self-limiting disease and is found incidentally during a radiographic examination. [17]

The epicenter is apex of teeth, within the alveolar process and usually posterior to the cusp, in the mandible, lesions occur above the inferior alveolar canal. Initially, the lesions are predominately radiolucent but with time become mixed, then predominantly radiopaque with only a thin peripheral radiolucent rim. [3]

All three patterns of cemento-osseous dysplasia demonstrate similar histopathologic features. The tissue consists of fragments of cellular mesenchymal tissue composed of spindle-shaped fibroblasts and collagen fibers with numerous small blood vessels. Free hemorrhage is typically noted interspersed throughout the lesion. Within this fibrous connective tissue background dense, sclerotic masses which have been interpreted as cementum is seen. As the lesions mature and become more sclerotic, the ratio of fibrous connective tissue to mineralized material decreases.

(d) **FGC**

FGC or familial florid osseous dysplasia is an autosomal dominant disorder with variable phenotypic expressivity. It is a disorder of gnathic bone that ultimately leads to the formation of massive sclerotic masses of disorganized mineralized material. The number of affected families have been identified, including a large pedigree of 55 individuals spanning 3 generations. [21, 22]

III. **Ossifying fibroma (cementifying fibroma; cemento-ossifying fibroma)**

Ossifying fibroma is usually seen in second to fourth decades of life, with women being affected more often than men. Unlike FD, ossifying fibromas are characteristically monostotic. Less than 5% involve more than one bone and they are almost exclusively found in the cranial bones, with only a rare case reported in the long bones. Of the cranial bones, the mandible is the most common site (75% in some series), followed by rarer reports of the ethmoid, frontal, and sphenoid sinuses, as well as the orbit, occiput, and temporal bone. [10] Although ossifying fibroma is usually a benign, slow-growing, painless, and often asymptomatic tumor, a rapid growth pattern with a “malignant” or aggressive behavior is sometimes noted, particularly as stated earlier, when the tumor is located outside the mandible. With involvement of the mid-face and paranasal sinuses, patients commonly have a painless swelling of the cheek, unilateral proptosis with diplopia, persistent nasal obstruction, rhinorrhea and epiphora, and recurrent epistaxis and hemoptysis. [20]

Radiographically, it typically appears as unilocular lesions with sharply defined, smooth, corticated borders, a feature that is used to differentiate ossifying fibromas from FD. They are spherical, having expanded and thinned cortical outlines, which displaces adjacent structures. It is well delineated from the surrounding tissues. Early lesions are largely radiolucent with a cyst-like in appearance. As they enlarge and mature, they will become mixed radiolucent-radiopaque then completely radiopaque surrounded by a radiolucent rim. [20]

Ossifying fibromas usually consist of a moderately cellular, relatively avascular, dense fibrous stroma. Focally scattered multinucleated giant cells also may be seen. The calcified material may consist of thin, irregularly shaped trabeculae of woven bone; scattered trabeculae of lamellar bone; deposits of basophilic staining, round or ovoid, cellular or acellular calcified deposits that have been linked to cementum; or any combination. [10]

(a) **Juvenile ossifying fibroma**

Brannon RB and Fowler CB consider juvenile ossifying fibroma as a unique benign fibro-osseous neoplasm. [9] Zupi et al. reported two features that help in distinguishing juvenile active ossifying fibroma from ossifying fibroma. First, the juvenile active ossifying fibroma occurs at a far lower mean age than the ossifying fibroma. Second, the histological pattern of the juvenile active ossifying fibroma seems to be unique in being highly cellular with entrapped osteoblasts. Unlike the ossifying fibroma, juvenile active ossifying fibroma grow massively with extensive cortical expansion. [20]

There are 2 variants of juvenile ossifying fibroma commonly reported in the literature: A TJOF and a PJOF. The latter is reported more frequently in the literature. [22]

Juvenile active ossifying fibroma is a rare lesion that affects the craniofacial skeleton. The clinical signs and symptoms are
related to the anatomic site of involvement. The tumor probably originates in early childhood, but enlarges slowly, resulting in its delayed detection in adults. In most patients (85%), the tumors are located in the facial bones, but they also involve the calvaria (12%) and extracranial sites (4%). Among facial lesions, 90% arise from paranasal sinuses and the remaining 10% arise from the mandible, perhaps from maldevelopment of the tissue generating the bony septa between the roots of molar teeth.[22]

The tumor may manifest as well-demarcated, unilocular or multilocular radiolucencies with a variable amount of radiopacity, usually manifesting as fine specks or as scattered, irregularly shaped bony trabeculae and calcified spherules amid a background of relatively avascular, cellular fibrous tissue. Conservative surgical excision is the treatment of choice for juvenile ossifying fibroma; however, recurrences are seen in 30% to 50% of cases.[23]

Conclusion

Nomenclatures of fibro-osseous lesions have been historically been consistent and confusing so far. In recent years significant progress has been achieved in understanding the histopathogenic similarities and differences of various fibro-osseous lesions, thereby enhancing one’s ability to diagnose accurately and to manage them. When a differential diagnosis is not possible on the basis of clinical and radiographic features, a molecular analysis can be helpful. However, the need for further research into these lesions remains paramount to understand their deviant behavior.

References