Benign Fibro-Osseous Lesions of the Craniofacial Area in Children and Adolescents: A Review

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Доброкачественные фиброзно-костные поражения краниофациальной зоны у детей и подростков: обзор

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Benign fibro-osseous lesions (BFOLs) of the craniofacial area are represented by a variety of morphologic processes that are characterized by pathologic ossifications and calcifications in association with a hypercellular fibroblastic marrow element. The current classification includes neoplasms, developmental dysplastic lesions and inflammatory/reactive processes [5]. The final diagnosis depends on clinical, radiological and pathological features. The clinicopathologic features of this heterogeneous group of diseases are presented in this article.

Keywords: Benign fibro-osseous lesions, Fibrous dysplasia, Cemento-osseous dysplasia, Ossifying fibroma.

BFOLs represent a dispersed group of intraosseous diseases that share common histologic features. Reactive, developmental, neoplastic and dysplastic pathologic processes are subsumed under the entity of BFOLs. Modern treatment varies for each disease and from case to case [5]. The concept of BFOL has evolved over the last several decades and now includes two major entities: fibrous dysplasia (FD) and ossifying fibroma (OF) [9]. Sudeendra Prabhu et al. [12] retrospectively described 80 cases of fibro-osseous lesions of the oral and maxilla-facial region, 75% were considered to be OF and 25% were classified as FD.

Radiographically, BFOL vary considerably from a simple radiolucent lesion to mixed radiolucent/radiopaque or totally radiopaque lesion. The lesion could be well defined or ill-defined blending imperceptibly into the surrounding bone. There may or may not be expansion of bone, with or without displacement of the teeth. Histologically, the BFOL consists of two components: «hard» tissue (osseous component in the form of woven or lamellar bone or cement) and «soft» tissue component (fibrous connective tissue) [6, 15].

Over the years various classification models have been put forward. The Waldron’s classification has gained considerable recognition. The classification system of Waldron has suggested that the BFOL originate from the periodontal ligament, which contains stem cells, which are known to differentiate into fibroblasts, cement and bone [7].

Waldron’s Modified Classification of BFOL (1993):
1. Fibrous Dysplasia
2. Cemento-Osseous Dysplasia (periapical cement-osseous dysplasia, focal cement-osseous dysplasia, florid cement-osseous dysplasia)
3. Fibro-Osseous Neoplasm (cementifying fibroma, ossifying fibroma, cemento-ossifying fibroma)

Some classification schemes include reactive reparative lesions such as traumatic periostitis, osseous keloid, sclerosing osteomyelitis, osteitis deformans, periostitis ossificans (Working Classification of Fibro-Osseous Lesions By Mico M. Malek, 1987; Eversole 2008 Classification). Another one includes central giant cell granuloma, aneurismal bone cyst and cherubism (WHO Classification, 1992; Brannon & Fowler Classification, 2001; WHO Classification Of Fibro-Osseous Lesion Of Jaws, 2005). Some authors have described primary malignant bone tumors (osteosarcoma and Ewing’s sarcoma) as fibrous-osseous lesion of the jaws as well as BFOLs [10].

BFOLs are characterized by the common histologic features: the substitution of normal bone by collagenous or fibrous stroma with variable amounts of mineralized substance that may be bone, cement or both [21]. Microscopic similarities and differences among BFOLs are shown in Table 1 [5].

The stromal element can be quite homogeneous and hyper cellular with monomorphic appearing fibroblasts. In other cases, the stroma is more mature or collagenous with a storiform fibroblastic pattern. The ossification in BFOL can be quite heterogeneous even within a specific disease entity. Newly formed bone shows a woven pattern, mature bone exhibits of a lamellar pattern. A lot of BFOLs have both: irregular trabeculae as well as spheroidal cementicle calcifications, so-called «cement-ossifying» lesions. The ossification patterns seen in BFOL often represent the «age» of the lesion. Formative processes in the early stages are more cellular. Osteoblastic rimming of trabeculae at that stage is more prominent than in «older» lesion [5].

Fibrous Dysplasia
FD is the most common fibro-osseous lesion of childhood. In a majority of biopsy series of bone tumors in children, approximately 6% of cases were FDs, some series show 10% incidence of FD in children [18].

By definition FD is a benign medullary, genetically-based, sporadic fibro-osseous lesion, which may involve one or more bones (monostotic FD or polyostotic FD) [2]. FD of multiple adjacent craniofacial bones is considered a monostotic (craniofacial FD) [8].

In Mayo Clinic the patients with FD were divided into four distinct groups:
1. With involvement of the jaws,
2. With involvement of the skull bones,
3. With involvement of the ribs,
4. With involvement of all other bones.

The largest single group was the last one. The jawbones accounted for the second largest group, and of these, the maxilla was involved much more commonly than the mandible [3].

The monostotic FD is equally distributed in both genders and ethnic groups and is six times more common than the polyostotic FD. The monostotic form is not a precursor of the polyostotic form and accounts for 80—85% of FD cases [11].

Cytogenetic abnormalities have been described supporting neoplastic nature of FD. All forms of FD are associated with a non-germ cell acquired mutation at codon 201 within exon 8 of the GNAS1 gene located on chromosome 20q [4]. Mutations in the GNAS1 encoding for the alpha-subunit of a signal transducing G-protein lead to increased c-AMP production affecting proliferation and differentiation of preosteoblasts. Mutation analysis of the alpha-subunit of the G protein by pyrosequenc-
ing has significant potential for improving distinction between FD and other BFOLs in problematic cases [20].

In the jaws, FD occurs more often in the maxilla than in the mandible, and may involve adjacent bones (zygoma or the sphenoid).

Complaints usually consists of painless swelling often leading to facial asymmetry, occasionally accompanied by irregular café-au-lait spots. Maxillary and mandibular involvement may lead to displacement of teeth and/or malocclusion. In FD affecting the paranasal sinuses nasal obstruction may occur.

Sometimes facial pain, headaches or facial numbness can develop. Children presenting with FD and irregular café-au-lait spots should be carefully examined for McCune-Albright syndrome. FD associated with single or multiple soft tissue myxomas is known as Mazabraud syndrome [4].

Three different radiographic patterns of FD involving the maxillofacial skeleton have been described: cystic (radiolucent or lytic; early lesions), sclerotic (mid-phase lesions), and mixed radiolucent/radiopaque (pagetoid; late lesions) comprising 21%, 23% and 56%, respectively. Margins are well defined, sometimes marked by a ring of bone sclerosis, no periosteal reaction [1] (Picture 1, 2). Asymmetric homogeneously radiodense opacities with «ground glass» appearance that bland into normal bone, thin cortices and bone expansion are highly characteristic for FD and best seen on CT scans on bone windows.

**Picture 1.** FD of the mandible. Expanded Heterogeneous partially ossified lesion with thin continuous calcified border.

**Picture 2.** FD of the maxilla. Expanded Heterogeneous partially ossified lesion, thin calcified border partially interrupted.

**Picture 3.** Fibrous displasia. Well-defined margin. Irregular curvilinear trabeculae of woven bone, surrounded by a fibrous-appearing stroma. Scan, low-power view, H&E.

**Picture 4.** JOF, psammomatous variant. Well limited expanded homogeneous ground glass lesion. Rim a little thick and a little interrupted.
with relative increase in collagen component. The reason for decrease in cellularity can be attributed to the decrease in frequency of mutated cells, which have a higher proliferation rate, compared to normal cells [17]. Occasionally, lesions of FD show calcified spherules similar to those seen in OF [19]. Benign giant cells and foam cells are commonly found. No mitotic activity, no atypia. May have ABC-like areas [1]. Cartilaginous foci in FD of the jaws or skull have not been documented.

The treatment is frequently not needed. In most cases of FD, the lesions seem to stabilize with skeletal maturation. Surgical interventions may be necessary for functional reasons or severe disfigurement [8].

### Table 1. Microscopic similarities and differences among BFOLs

<table>
<thead>
<tr>
<th>Fibrous element variant</th>
<th>Ossifying (trabecular) variant</th>
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<tbody>
<tr>
<td>Homogeneous plump monomorphic fibroblast, hypercellularity, thin collagen fibers</td>
<td>Metaplastic woven bone</td>
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<tr>
<td>Mature, hypo cellular</td>
<td>«Chinese/Hebrew» figure trabeculae</td>
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<tr>
<td>Fasciculated, storiform</td>
<td>Lamellar bone trabeculae</td>
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<td></td>
<td>Osteoblastic rimming</td>
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<tr>
<td></td>
<td>Mosaic resting/reversal lines</td>
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<td></td>
<td>Trabecular paralleling</td>
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<tr>
<td></td>
<td>Cemental woven</td>
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<td></td>
<td>Cemental microlamellar</td>
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<tr>
<td></td>
<td>Sharpey fiber fringe</td>
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<td></td>
<td>Droplet (psammomatoid)</td>
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<td></td>
<td>Curvilinear conglomerates («Ginger root»)</td>
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</tbody>
</table>

**Picture 5.** JOF, psammomatous variant. Expanded partially ossified and partially liquid heterogeneous lesion with thin calcified border, partially interrupted.

**Picture 6.** JOF, trabecular variant. Scan, low-power view, H&E.

Grossly, the tissue cuts with a gritty consistency and is grayish white. The cortical bone often is thinned and expanded [19].

Classically, FD consists of cellular fibrous tissue with spindle shaped cells and immature, isolated trabeculae of woven bone generally without rimming of osteoblasts (Picture 3). The transition of normal to abnormal bone is often abrupt [19]. The bony trabeculae are arranged in a «Chinese letters» fashion. Characteristically, bundles of collagen fibers oriented perpendicular to the bone surface, compatible with Sharpey fibers. Osteoid seams to be present and best visualized on undecalcified sections [8]. In the early phase of maturation, pronounced osteogenesis is seen with thin osteoid anastomosing trabeculae that are rimmed by osteoblasts. The stromal fibroblastic component is proliferative and hypercellular although no pleomorphism can be seen. With ensuing weeks, the trabeculae thicken, yet the osseous collagen pattern remains woven and the trabeculae assume the classic «Chinese figure» characteristic. The fibrous element continues to be hypercellular. In later stages of the disease woven bone is replaced by lamellar bone trabeculae [5]. The cellularity of the stroma decreases in «old» FD cases with relative increase in collagen component. The reason for decrease in cellularity can be attributed to the decrease in frequency of mutated cells, which have a higher proliferation rate, compared to normal cells [17]. Occasionally, lesions of FD show calcified spherules similar to those seen in OF [19]. Benign giant cells and foam cells are commonly found. No mitotic activity, no atypia. May have ABC-like areas [1]. Cartilaginous foci in FD of the jaws or skull have not been documented.

The treatment is frequently not needed. In most cases of FD, the lesions seem to stabilize with skeletal maturation. Surgical interventions may be necessary for functional reasons or severe disfigurement [8].

### Cemento-Osseous Dysplasia

Cemento-Osseous Dysplasias, or osseous dysplasias (OD) according to the WHO classification (2005) are idiopathic pro-
OD has a predilection for middle-aged black females, so without much experience, we will described it briefly.

The condition occurs in various clinical forms that bear different names. When occurring in the anterior mandible and involving only a few adjacent teeth, it is called periapical osseous dysplasia. A similar limited lesion occurring in a posterior jaw quadrant is known as focal osseous dysplasia, formerly called focal cemento-osseous dysplasia. Two other types of OD are more extensive, occurring bilaterally in the mandible or even involving all 4 jaw quadrants. The first is known as florid osseous dysplasia. The second occurs at young age and causes considerable jaw expansion. This OD type is called familial gi-
giantiform cementoma; it shows an autosomal dominant inheritance with variable expression but sporadic cases without a history of familial involvement have been reported.

ODs may be predominantly radiolucent, predominantly radiodense or mixed. Radio density tends to increase with time. All types of OD consist of cellular fibrous tissue, woven as well as lamellar bone and masses of cementum-like material. There is no capsule. OD resembles OF histologically. Secondary inflammatory changes may occur, especially with the florid OD and the familial gigantiform cementoma.

The various forms of OD do not require treatment unless complications occur such as infection of sclerotic bone masses as may be encountered in florid OD or facial deformity, that could be seen in familial gigantiform cementoma [8].

**Ossifying Fibroma**

OF is well-demarcated lesion composed of fibrocellular tissue and mineralized material of varying appearances. According to the WHO Classification (2005) most OFs commonly occurs in the 2nd to 4th decades and shows a predilection for females [8].

The most common form of OF is located in the maxilla and mandible and represents a neoplastic process that is typically painless, presenting with expansion of the buccal and lingual cortices and in larger lesion may expand towards the inferior aspect of the mandible. Radiographically, early stage lesions in their formative phase, are typically radiolucent since the osseous element is noncalcified osteoid. Over time, the tumors become progressively radiopaque as more matrix calcifies [5] (Picture 4, 5).

Very few molecular and chromosomal abnormalities have been reported for the OF group of lesion [8].

Subsumed under this diagnostic category is the ossifying/cementifying fibroma not otherwise specified (NOS), implying that the clinico-pathologic features do not conform to the other types of OFs. OF NOS shows three histologic patterns and some demonstrate a mixture of these patterns:

1. Common «ossifying» variant,
2. The «cementifying» variant,
3. The «storiform» variant.

The common «ossifying» variant of OF shows a pattern that can be indistinguishable from FD, with small irregular osteoid trabeculae, that are typically rimmed by osteoblasts. The stromal element is hypercellular and the fibroblastic cells are plump. The immature cellular osteoid is not always easily distinguished from the cellular stroma (Picture 6, 7). Irregular mineralization takes place at the center of the strands. Maturation to lamellar bone is not observed. Local aggregates of osteoclastic giant cells are invariably present in the stroma [5]. Mitoses are present, especially in the cell-rich areas.

**JPOF** is the tumor that affects predominantly the extragnathic craniofacial bones, especially centered on the periorbita, frontal, end ethmoid bones. This lesion was initially described by Gogol in 1949 as psammomatoid fibroma of the nose and paranasal sinuses. Patients tend to be young, although the average age of incidence has varied in different studies from 16 to 33 years with an age range of 3 months to 72 years. In general, the patients with JPOF are a few years older than those with JTOF. The greatest majority of the reported cases of JPOF originated in the paranasal sinuses, particularly frontal and ethmoid. About 10% have been reported in the calvarium.

**JPOF** is manifested as a bone expansion that may involve the orbital or the nasal bones and sinuses. Orbital extension of sinu-nasal tumors may result in proptosis, and visual complaints including blindness, nasal obstruction, ptosis, papillodema, and disturbances in ocular mobility. Radiographic examination shows a round, well-defined, sometimes corticated osteolytic lesion with a cystic appearance. Sclerotic changes are evident in the lesion, that show a ground-glass appearance. In CT scans set on bone window, the lesion appear less dense than normal bone and can vary in size from 2 to 8 cm in diameter. Areas of low CT density may be noted due to cystic changes. It is stated that in the facial skeleton a well-circumscribed expansive mass with a thick wall of bone density on CT scan and enhancement of this area on post contrast MRI image is strongly suggestive of JPOF.

Macroscopically, the tumor is yellowish, white and gritty. Histologically, the lesion consists of multiple round uniform small ossicles (psammomatoid bodies) embedded in a relatively cellular stroma composed of uniform, stellate, and spindle shaped cells (Picture 8, 9, 10). Occasionally, shrunken cells become embedded in the calcified matrix of the ossicles. The psammomatoid bodies are basophilic and bear superficial re-

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**ОБЗОРЫ ЛИТЕРАТУРЫ**

1. **Ossifying Fibroma**
2. **Juvenile**
3. **Giantiform**
4. **Fibroma**
5. **Bone**
6. **Recurrences**
7. **Tumor**
8. **OD**
Clinical features

Expansile
- Expansion of bone
- Unilateral, painless
- Mono or Polyostotic

Non-expansile
- Painless

Radiologic findings

Focal circumscribed apical lesions
- Lucent or target lesions
- Root divergence

Circumscribed lucent or target lesions
- Root divergence

Cementifying
- Sclerotic
- Osseous
- Cementifying
- Storiform

Histology

Trabecular «Chinese/Hebrew» letter figure
- Cementifying
- Sclerotic
- Osteoid
- Storiform

Table 2. Some clinical, radiographic and histologic characteristics of BFOLs

<table>
<thead>
<tr>
<th>Disease</th>
<th>Clinical features</th>
<th>Radiologic findings</th>
<th>Histology</th>
</tr>
</thead>
<tbody>
<tr>
<td>FD</td>
<td>Expansion of bone</td>
<td>Diffuse radiolucent or ground-glass</td>
<td>Trabecular «Chinese/Hebrew» letter figure</td>
</tr>
<tr>
<td></td>
<td>Unilateral, painless</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>Mono or Polyostotic</td>
<td></td>
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<tr>
<td>OD</td>
<td>Non-expansile</td>
<td>Focal circumscribed apical lesions</td>
<td>Trabecular</td>
</tr>
<tr>
<td></td>
<td>Painless</td>
<td>Lucent or target lesions</td>
<td>Cementifying</td>
</tr>
<tr>
<td>OF NOS</td>
<td>Expansile</td>
<td>Circumscribed lucent or target lesion</td>
<td>Sclerotic</td>
</tr>
<tr>
<td></td>
<td>Painless</td>
<td>Root divergence</td>
<td>Osseous</td>
</tr>
<tr>
<td></td>
<td>Rarely multifocal</td>
<td></td>
<td>Cementifying</td>
</tr>
<tr>
<td></td>
<td>Jaws</td>
<td></td>
<td>Storiform</td>
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<tr>
<td>JTOF</td>
<td>Expansile</td>
<td>Circumscribed lucent or target lesion</td>
<td>Trabecular</td>
</tr>
<tr>
<td></td>
<td>Painless</td>
<td>Flocular opacities</td>
<td>Giant cell foci</td>
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<td></td>
<td>Aggressive</td>
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<tr>
<td>JPOF</td>
<td>Expansile</td>
<td>Circumscribed</td>
<td>Psammoma bodies</td>
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<tr>
<td></td>
<td>Facial bones</td>
<td>Dense flocular opacities</td>
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<td></td>
<td>Aggressive</td>
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</tbody>
</table>

Table 2. Some clinical, radiographic and histologic characteristics of BFOLs

- FD affecting the craniofacial area histologically confirmed not as FD, but only as a BFOL. The Charles Waldron wrote, «In absence of good clinical and radiologic information a pathologist can only state that a given biopsy is consistent with a BFOL. With adequate clinical and radiologic information most lesions can be assigned with reasonable certainty into one of several categories» [11, 13].

Discussion

The BFOLs are one of the commonest entities reported in the head and neck region. The BFOL of the jaws comprise a diverse, interesting, and challenging group of diseases that pose difficulties in classification, differential diagnosis and treatment [12].
tation in FD of the jaws while OFs are negative [5, 20]. Some investigators offer a scoring criterion, which may help in differentiating FD from juvenile ossifying fibroma. According to this criteria, a unique score was allotted to each category or histological presentation of the seven parameters (morphology of calcifications, structure of calcifications, osteoblastic rimming of calcifications, cellularity of stroma, vascularity of stroma, collagen pattern of the stroma and presence of oxta- 

lan fibres), and the total of all the scores for a particular case was calculated [17].

Conclusion

BFOLs have overlapping clinical, imaging and pathological features. The final diagnosis depends on multidisciplinary interactions (clinical, radiological and pathological features).

REFERENCES


