CLINICOPATHOLOGIC STUDY OF 30 FIBROUS DYSPLASIA OF THE JAWS IN ENUGU, NIGERIA

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ABSTRACT

BACKGROUND: Fibrous dysplasia (FD) is a genetic-based benign fibro-osseous lesion known to affect the jaws and craniofacial bones. Reports of this entity in Eastern Nigeria are scarce.

OBJECTIVE: To determine the prevalence and clinicopathologic features of fibrous dysplasia.

MATERIALS AND METHODS: A total of 643 clinicopathological records (radiographs, clinical records, and histopathological records) collected between January 2012 and December 2019 were available. The demographic and clinicopathologic records of bone and maxillofacial pathologies were examined and correlated with histological findings to determine the prevalence of FD.

RESULTS: A total of 643 orofacial lesions of bone lesions were reviewed. In these, 86 benign fibro-osseous lesions (BFOLs) were identified, of which 30 (34.9%) were FDs. The majority of the BFOLs was ossifying fibromas (OFs). The patients with FD were in the 2nd to 3rd decades of life with a mean age of 19.4 ± 7.9 years.
The male to female ratio was 1: 2.8, while the mandible to maxilla ratio was 1: 4.3. There was a statistically significant prevalence of FD on the right-sided jaw, P = 0.000.

CONCLUSION: This study observed a low prevalence of FD of the jaws, mostly observed in young patients, affecting the right side.

KEYWORDS: craniofacial bones, Fibrous dysplasia, fibro-osseous lesion.

INTRODUCTION

Fibrous dysplasia (FD) is a Benign Fibroosseous Lesion (BFOL) with a mutation involving the GNAS 1 gene.[1] It may affect either single (monostotic) or multiple (polyostotic) bones. It is regarded as craniofacial fibrous dysplasia in contiguous craniofacial bones.[2] When FD affects multiple bones (polyostotic), they could form components of syndromes, such as McCune-Albright syndrome, Jaffe-Lichtenstein syndrome, and Mazabraud's syndrome.[2,3] Jaffe-Lichtenstein syndrome is characterized by polyostotic fibrous dysplasia and café-au-lait pigmentations.[2] Numerous endocrinopathies with café-au-lait pigmentations accompany polyostotic FD in McCune-Albright syndrome, while Mazabraud's syndrome is typified by polyostotic FD and multiple soft tissue myxomas.[2] BFOL are characterized by the replacement of normal bone and marrow with a benign cellular fibrous tissue which may contain varying degrees of mineralization in the form of woven/lamellar bone.[3] Von Recklinghausen was the first to describe the lesion in 1891,[4] which Lichtenstein and Jaffe termed fibrous dysplasia in 1938.[5] BFOLs include FD, ossifying fibroma, cemento osseous dysplasia, and familial gigantiform cementoma.[3]

FD is a fibro-osseous lesion with a poorly defined heterogeneous intraosseous disease processes similar clinically and histologically to ossifying fibroma and poses diagnostic difficulties,[6] and in classification and management.[7]
Fibrous dysplasia occurs with a global prevalence of 2.5% of all bone tumours and 7.5% of all benign bone neoplasms.[8] African data on the prevalence of fibro-osseous lesions are scarce; however, a study reported FD to account for 74.0% of fibro-osseous lesions.[9] while Lasisi et al.[10] reported FD (37.2%) as the second most common fibro-osseous lesion in Ibadan, with a mean age of 24.0 ± 10.2 years and a predilection for the maxilla. Both studies reported female gender predilection, with predominant occurrence in 2nd and 3rd decade age groups.

Although there are publications of FD in other parts of Nigeria,[10,11] there is a paucity of studies on fibrous dysplasia of the craniomaxillofacial region among the population of Southeast Nigeria. This study was carried out to bridge the knowledge gap, provide baseline data and add to the literature on fibrous dysplasia.

Materials and Methods:

This was a retrospective review of archival materials, including histology slides and reports, radiographs, and clinical records of histologically diagnosed fibro-osseous lesions and fibrous dysplasia from January 2012 to December 2019. These were among 643 clinicopathological records of specimens, histopathology blocks, and slides of patients with oral and maxillofacial lesions accessed for the study. Clinico-pathological data of lesion sites, histology, and demography of patients were retrieved from the Departments of Oral Pathology and Oral

Medicine records of the University of Nigeria Teaching Hospital, Enugu. Patients' radiographs, slides, and histopathology reports of histologically diagnosed fibro-osseous lesions and FD were reviewed again to confirm the diagnosis.

Data collection: Age, sex, site of lesion, clinical features, radiologic presentation, type of FD, histological diagnosis of lesions, and recurrence status.

Data analysis
Data collected were analyzed using the IBM SPSS Statistics, version 24 software. Categorical (Non-continuous) variables such as gender and site of the lesion were summarized as frequencies and percentages. Quantitative (Continuous) data like age was expressed as means ± standard deviations. The prevalence of FD was compared among gender and age groups using the chi-square χ^2 test and significance set at $p < 0.05$. Fisher's exact test analyzed age, site, and specific site distribution.

Though no significant ethical issues were encountered because it was a retrospective study with no patient interface, ethical approval was obtained as part of a larger study from the Health Research Ethics Committee (HREC) of the University of Nigeria Teaching Hospital Enugu, (NREC/05/01/20088-FWA00002458-IRB00002323).

RESULTS

A total of 643 samples (bone/ soft tissue or both) had diagnostic slides with confirmed diagnoses during the study period. Ninety-three cases of benign fibro-osseous lesions (BFOL) were identified and extracted. Due to deficiencies in the records of duration, radiographic features, and other clinical data, six cases of BFOL were excluded, leaving a total of 86.

Prevalence: Thirty (34.9%) cases of BFOL out of 86 were histologically confirmed as FD and satisfied the inclusion criteria for the study. Fibrous dysplasia was the second most common BFOLs to ossifying fibroma, 56 (65.1%). The prevalence of FD among orofacial lesions was 30 (4.7%),

Types: Only two cases of polyostotic FD, 2 (6.7%), were identified and involved bones of the mandible, maxilla, frontal and ethmoid. The monostotic FD was 28 and constituted 93.3% of cases. In 21 (70.0%) cases of monostotic FD, it involved only the facial bones without affecting cranial bones, while in 7(23.3%) cases of monostotic FD, multiple contiguous facial and cranial bones were involved in near equal frequencies: ethmoid bone (3), sphenoid bone (2), Zygoma (2), Frontal (2), orbital rim (2), and Nasal (2). A syndrome was not associated with either type of FD.
Age: The clinical characteristics of the patients are summarized in Table 1.

Table 1. The age distribution, location, and site-specificity of Fibrous Dysplasia

Variable	Frequency (%)
Age Groups (yrs)	
1-10	4(13.3)
11-20	14(46.7)
21-30	10(33.3)
31-40	1(3.3)
41-50	1(3.3)
Major facial bones involved	
Maxilla	24(80.0)
Mandible	4(13.3)
Maxilla+mandible	2(6.7)
Side of Jaw	
Left	9(30.0)
Right	18(60.0)
Anterior	1(3.3)
Bilateral	1(6.7)

The median age at presentation was 19.5 years, with an overall mean age of 19.4 ± 7.9 years (range, 8 years to 42 years). Most of the FD patients, 24 (80%), were in the 2nd to 3rd decades of life, Figure 1.

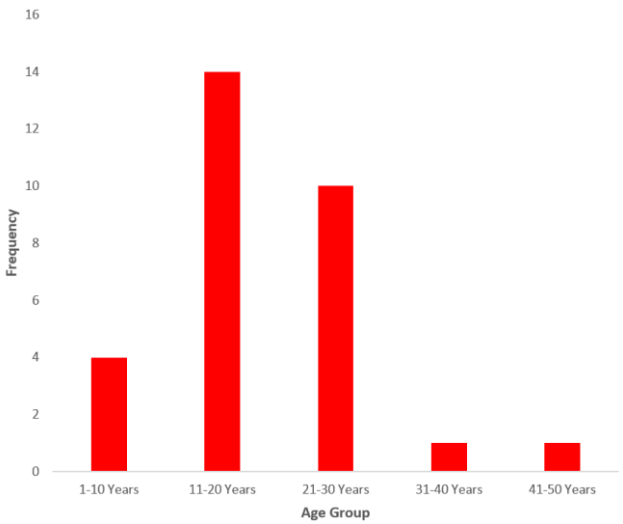

Figure 1. Histogram for Age Distribution of Patients

The mean age at tumour onset in female patients was 18.5 years ±7.9 years (range, 7years to 41 years), while in male patients it was 22.0 years ±8.7 years (8years to 31 years). The mean duration of lesions at diagnosis was 3.6 ± 4.2 years.
Gender: Fibrous dysplasia was more common in the female 22 (73.3%) than in the male 8 (26.7%), with a male to female ratio of 1: 2.8.
Craniofacial Site: The maxilla was the most affected site, 24 (80%) in monostotic type, while the mandible accounted for 4 (13.3%), Table 1. The mandible to maxilla ratio was 1 to 4.3. Regarding specific jaw site of occurrence, Table 1 shows that FD was observed most commonly in the right maxilla, 18 (60.0%).

The association between right-sided jaw occurrence and FD is significant, with P= 0.000.
There were recurrent lesions in 10 (33.3%) FD cases, and all were observed only in the female, with a significance value of P= 0.02.

Radiographic Presentation: Various patterns of radiographic presentations were observed. The classic ground-glass appearance was observed in 4 (13.3%), the mixed lucent-opacity pattern occurred in 7 (23.3%), while other radio-opacity pattern was observed in 9 (30.0%). Other irregular radiographic patterns constituted 10 (33.3%).

Histologic Features: The diagnosis of fibrous dysplasia requires a correlation of clinical, radiologic, histopathologic, and surgical findings.

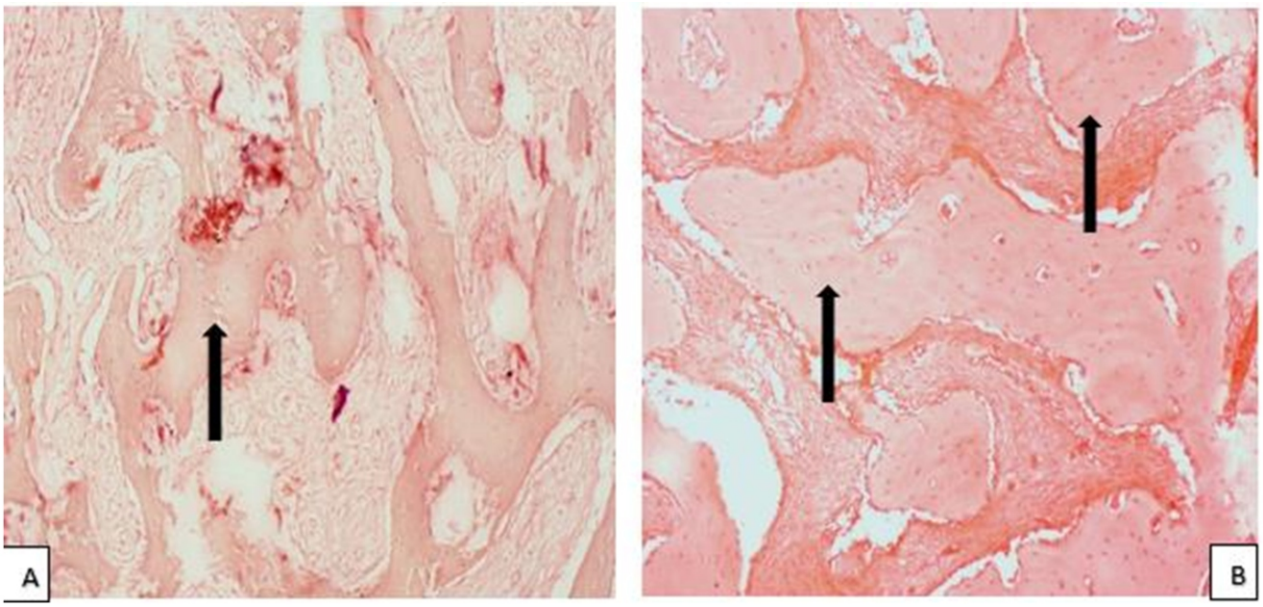

Figure 2. Photomicrographs of fibrous dysplasia A and B [H & E (A) x100 (B) x400 magnifications] Curvilinear woven bone trabeculae (black arrows) in a fibrous tissue stroma.

Figure 2 shows the histology of the cases that exhibited irregular, curvilinear, and discontinuous trabeculae of woven bone in a fibrous connective tissue stroma with variable cellularity. The presence of peri-trabecular clefting and absence of osteoblastic rimming further differentiated FD from OF under the hematoxylin and eosin (H&E) staining method, Figure 3.

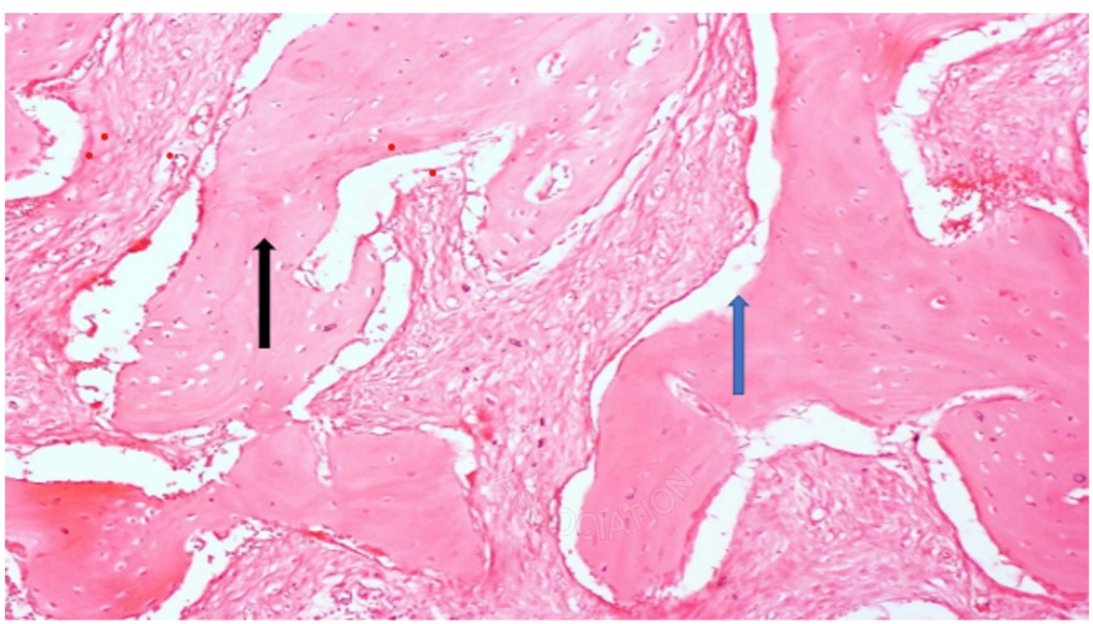

Figure 3. Photomicrograph of fibrous dysplasia [H & E x100 magnification] Woven bone trabeculae (black arrow) in an irregular pattern with marked peri-trabecular clefting (blue arrow) within a sparsely cellular stroma.

DISCUSSION

The prevalence of FD (34.9%) was second to that of ossifying fibroma in this study and corresponds to reports from some studies in Nigeria,[10,12] and Ghana,[13] The most common fibro-osseous lesion fluctuates between fibrous dysplasia and ossifying fibroma. In Uganda, fibrous dysplasia was reported as the most prevalent lesion (56.1%)[14] in agreement with an earlier report from Nigeria by Ajagbe et al.[9]

Two cases of polyostotic type FD were identified in this series and involved both the maxilla and the mandible and frontal and ethmoidal bones. The polyostotic form is less common, occurring in about 25%-30% of FD cases,[3] and shows female predilection, with a male: female ratio of 1 : 3. Only about 3% of polyostotic FD cases are associated with syndromic states.[3] There were no syndromes associated with any of the lesions in this series. When FD affects multiple bones (polyostotic), they could form components of syndromes, such as McCune-Albright syndrome, Jaffe-Lichtenstein syndrome, and Mazabraud's syndrome.[2,3] Jaffe-Lichtenstein syndrome is characterized by polyostotic fibrous dysplasia and café-au-lait pigmentations.[2] Numerous endocrinopathies with

café-au-lait pigmentations accompany polyostotic FD in McCune-Albright syndrome, while Mazabraud's syndrome is typified by polyostotic FD and multiple soft tissue myxomas.[2,6]

Similar to findings by Moshy et al.,[15] and others,[9] this study observed 80% of FD in the 2nd and 3rd decades of life and a lower mean age of FD onset in the female gender. However, Langdon et al.[16] reported a second-decade occurrence. The overall mean age of patients at the onset of FD in this study was 19.4 ± 7.9 years. This is lower than the range of 21-26 years reported by some authors.[9,10] The relatively low mean age from this study could be because the more representative age at onset of FD was used in place of the age at clinic presentation. The low value also could reflect the early development in these patients. This study also observed that as age increased, there was a decrease in the occurrence of these lesions. This observation suggests that aging decreases the development of FD. Moreover, this discrepancy in the mean age of patients in different studies may be due to variations in race and the sample size employed in respective studies.

This study observed a female predilection for fibrous dysplasia, similar to other reports in the literature,[9,17] but contrasts those of Mcdonald-Jankowski and Li,[8] who reported male predilection in their respective reports.

The maxilla was more commonly involved than the mandible in this study, similar to the report by Waldron.[18] The reason for this distribution is unclear and requires further evaluation. In contrast, Langdon et al.[17] reported a mandibular predilection in their study. Most of the FD in this study occurred on the right side of the jaws and craniofacial bones. This is similar to the report by Mcdonald-Jankowski and Li.[8] This study, in addition, found the right-sided occurrence to be statistically significant, P= 0.000. The clinical relevance of this right-sided observation is not known to the authors. Lasisi et al.[10] reported a predilection for the maxilla, particularly the left quadrant, which agrees with the study by Waldron.[18] Maxillary lesions often involve adjacent or contiguous bones, including zygoma and sphenoid.[18] Depending on location, maxillary lesions affecting the paranasal sinuses, orbits, and cranial foramina present varieties of features ranging from headache, visual impairment, proptosis, diplopia, hearing impairment, anosmia, nasal obstruction, epistaxis, epiphora and sinusitis.[3,18]

The seven cases of craniofacial FD in this series were observed to involve the following bones in near equal frequencies: zygoma, frontal bone, orbital rim, nasal bones, sphenoid bone, ethmoid bone, and the skull base. Monostotic FD was the majority of cases in this study. Other authors reported that monostotic FD accounts for 70%-75% of all cases of FD, are diagnosed during the second decade, and show equal sex predilection.[2,3]

The radiographic features observed in these cases presented a variety of radiographic patterns that included the classic ground glass appearance and other patterns of radio-opacity, as well as the mixed lucent-opacity pattern. Radiographic features depend on the stage of the disease and extent of mineralization, ranging from cyst-like radiolucencies through mixed types to dense, sclerotic lesions.[3,6,15] Radiopacity is often in the form of 'ground-glass,' 'orange peel,' or 'fingerprint' appearance, notably showing indistinct borders that blend imperceptibly with the normal surrounding bone.[2,6,15]

The histology of the cases in this series exhibited irregular, curvilinear, and discontinuous trabeculae of woven bone in a fibrous tissue stroma with variable cellularity. The histologic features of blending into the surrounding normal bone, per trabecular clefting, and the absence of osteoblastic rimming were indispensable in differentiating FD from OF under the H&E staining method. The shared clinical, histopathological, and radiographic similarities make a definitive diagnosis of FD difficult by routine histopathology alone. Adjunctive immunological tests could aid in differentiating fibro-osseous lesions by showing that stromal cells and bony matrix in FD express more osteocalcin immunopositivity in FD than in OF.[1] Osteoblastic rimming is rarely seen in FD,[5,19] The bone in craniofacial FD has been suggested to undergo maturation to lamellar bone. These mature bony trabeculae tend to be parallel to one another.[3,6]

There is no specific treatment modality for FD, but the existing guidelines for treatment are not globally accepted,[6] and the management may present significant challenges.[2] However, recent efforts by an international consortium of clinicians and researchers have developed consensus guidelines for the management.[20] Spontaneous remission of FD can occur, requiring no intervention. Asymptomatic non-progressive lesions that do not cause deformities or functional impairment are often monitored.[3,6] Surgical intervention is indicated when vital structures are prone to compression, functional impairment, patient age, psychosocial concerns, and aesthetics ranging from osseous re-contouring to resection.[2,3,6] In some cases of polyostotic FD, intravenous bisphosphonate therapy has been applied, achieving relief of bone pain and reduction of osteoclastic activity with partial filling of osteolytic lesions.[2,6]

Sarcomatous transformation has been reported in a few cases of FD, most of which were osteosarcoma,[2,3] or rarely, fibrosarcoma and chondrosarcoma.[5] The majority of these cases were associated with post-radiation therapy for FD.[2] The rate of malignant transformation in untreated FD is 0.5%; however, it increases considerably in patients who received radiation therapy.[3]

In conclusion, this study observed a low prevalence and mean age of onset for fibrous dysplasia in Enugu compared to other regions of Nigeria, and right-sided occurrence was significantly associated. The cases shared similar features of frequency in the second and third decades, more female predilection, and more maxillary occurrence.

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