Original Article

Juvenile ossifying fibroma: an analysis of clinico-pathological features in a case series with a literature review

H.G. Ruwandi. N.Weerasinghe[1], Pubudu. C. Wijesuriya[1] and Primali. R. Jayasooriya[2]

[1]Mahiyangana Base Hospital, Mahiyangana, Sri Lanka; [2]Department of Oral Pathology, Faculty of Dental Sciences, University of Peradeniya, Sri Lanka

DOI: http://doi.org/10.4038/jdp.v11i2.7705

Submitted on 22.04.2016 Accepted for publication on 22.07.2016

Summary

Juvenile Aggressive Ossifying Fibroma (JAOF) is divided into two entities namely Juvenile Psammomatoid Ossifying Fibroma (JPOF) and Juvenile Trabecular Ossifying Fibroma (JTOF). JAOFs are aggressive but benign tumours that require clinico-pathological correlation to arrive at the definitive diagnosis. We report nine new cases of JPOF and 6 cases of JTOF with a brief review of the literature to aid correct diagnosis of these two different entities. According to the clinico-pathological analysis both JPOF and JTOF had occurred in children and adults, with a mean age of 28.6 years and 21 years at presentation respectively. JPOF showed a male predilection while equal gender distribution was observed in JTOF. Both tumours occurred most often in the mandible. Regarding the histopathological features all tumours were unencapsulated. All cases of JPOF showed presence of psammoma bodies which can be considered as a main diagnostic feature. JTOF showed osteoid and immature woven bone trabeculae. Osteoblastic rimming was commonly observed among JTOF but absent in JPOF. Other histopathological features did not show any striking difference between the two lesions. In conclusion, the term "Juvenile aggressive ossifying fibroma" is a misnomer as it can occur in adults as well. Therefore, the word "Juvenile" should be excluded when renaming the tumour which is a "need of the hour". Further, the study demonstrates the use of demographic, radiological and histopathological features with clinico-pathological correlation to diagnose and exclude mimics of JPOF and JTOF.

Keywords: Juvenile psammomatoid ossifying fibroma, Juvenile trabecular ossifying fibroma, Fibro osseous lesions

Introduction

The term Juvenile Aggressive Ossifying Fibroma (JAOF) describes two distinct histopathological entities of ossifying fibromas known as Juvenile Psammomatoid Ossifying Fibroma (JPOF) and Juvenile Trabecular Ossifying Fibroma (JTOF).

JPOF was first reported by Benjamins, in 1938, under the term "osteoid fibroma with

Author for correspondence: P. R. Jayasooriya (BDS, PhD, MD(Oral Path) Department of Oral Pathology, Faculty of Dental Sciences, University of Peradeniya. E mail: primalij@yahoo.com

atypical ossification" of the frontal sinus (1). Next Gogl described it in 1949 as psammomatoid fibroma of the nose and paranasal sinuses. Since then, JPOF has been reported under many names, including juvenile active ossifying fibroma by Johnson et al in 1952, psammomatous desmo-osteoblastoma by Makek and juvenile psammomatoid cemento ossifying fibroma which was used in the 2005 World Health Organization classification of odontogenic tumors (2). JPOF is commonly seen in children and young adults with predilection for paranasal sinuses, orbit and fronto-ethmoidal complex (1 – 16). Histopathology shows dense cellular fibrous stroma with characteristic spheroid calcifications called psammoma bodies (2,15,17).

The JTOF was previously alluded to by Reed and Hagy, in 1965, also under the designation of JAOF (4), Makek, in 1983 (7), published the largest series and he named these tumours as trabecular desmo-osteoblastoma. Subsequently, the tumour was named as juvenile trabecular ossifying fibroma in the 2005 WHO classification of odontogenic tumors. JTOF commonly affects maxilla (2) and it is usually confused with osteosarcoma due to rapid enlargement and with fibrous dysplasia due to similar demographical and histopathological features. It is commonly seen in young individuals with a slight male predilection (1 – 16). Histopathologically the lesion shows cell rich fibrous tissue containing trabeculae of immature bone (2,15,17).

Diagnosis of JAOF is a challenge because they clinically and histopathologically resemble other fibro-osseous lesions, as well as benign tumours such as extra-cranial meningioma (JPOF) and malignancies such as osteosarcoma (JTOF). Therefore, the final diagnosis of JAOF is achieved by clinical, radiological and histopathological correlation. As JPOF and JTOF mimic reactive lesions as well as malignancies, accurate diagnosis is essential to avoid over or under treatment. Therefore, the purpose of this study was to present clinico-pathological features of 15 cases of JAOF and to describe its histopathological differential diagnoses in order to avoid misdiagnosis of JAOFs which occur exclusively in the craniofacial bones and sino- nasal locations.

Materials and Methods

Fifteen cases of JAOF of the craniofacial skeleton were retrieved from the archives of the Department of Oral Pathology, University of Peradeniya, Sri Lanka. These cases were accessioned during the period from 2000 to 2014. Out of the total number of cases, 6 were of trabecular type and 9 were of psammomatoid type. Clinical and demographic data of these cases were recorded.

Microscopic slides of each case were reexamined under the light microscope using histopathological parameters described in 2005 WHO classification (2) to confirm the diagnosis and to identify histopathological features that could be used to exclude mimics of JAOFs. To minimize the subjectivity, the procedure was conducted independently without knowledge of the final diagnosis in the following manner. Initially all relevant clinical and radiological features were entered in to excel sheets (without the final diagnosis) by investigator HGRW. Thereafter, the slides were assessed by PRJ with clinicopathological correlation to obtain the current diagnosis. When the current and initial diagnoses were compared a single case with the current diagnosis of conventional cemento-ossifying fibroma was excluded from the study, resulting in a study sample of 15 cases of JAOF.

Results

The demographic features of JAOF are presented in Table 1. Accordingly, 55.5% of JPOF occurred in adults, and showed male predilection with a male: female ratio of 3.5:1. Majority of the lesions (77.8%) occurred in the mandible. Radiographic examination showed

expansion of the affected bone. Most of the lesions (66.7%) showed a mixed radio dense appearance and had well defined margins (77.8%) (Fig 1). In contrast to JPOF, 66.7% of JTOF occurred in children and young adults and showed equal gender distribution. Fifty percent of JTOF occurred in the mandible while equal number of cases showed mixed radio dense and radiolucent presentations. In addition, 83.4% of JTOFs showed well defined radiological margins.

Table 1. Demographic and radiological characteristics of juvenile ossifying fibroma

Patient characteristics	**JPOF (n= 9)**	**JTOF (n=6)**
Age distribution		
>10 years	01	02
11-20 years	03	02
21-30 years	01	02
>30 years	04	00
Age range (years)	9- 45	9-29
Gender distribution		
Males	07	03
Females	02	03
Males: Female ratio	3.5:1	1:1
Site distribution		
Maxilla	01	02
Mandible	07	03
Sino-nasal location	01	00
Other carnio-facial bones	00	01
Radiological presentation		
Mixed radiodense lesion	06	03
Radiolucent lesion	03	03
Radiological interpretation of margins		
Well defined	07	05
Ill defined	02	01

Histopathological features of JAOFs are presented in Table 2. All JPOFs were unencapsulated and showed numerous small rounded mineralized collagenous bodies (psammomatoid ossicles) uniformly distributed within a cellular fibroblastic stroma which is classical to JPOF (Figs 2, 3). In addition, 44.5% of the cases showed irregular cementoid masses. The cellularity of the fibroblastic stroma varied in different tumours and at different sites within the same lesion. Approximately, 33.3% of JPOFs showed storiform arrangement of spindle shaped cells (Fig 2). In the stroma loose collagen was a common feature (33.3%) than dense collagen (11.1%). In contrast to JPOF, JTOF showed immature cellular osteoid and or woven bone with osteoblastic rimming in all cases (Fig 4, 5). Myxoid change with aneurysmal bone cyst formation was infrequently observed in both lesions (Fig 6).

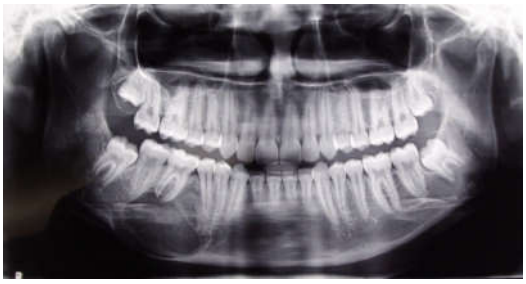

Figure 1. Radiological presentation of JAOF-Note the well defined margins, which is a useful clue to differentiate from malignancies such as osteosarcoma.

Discussion

JAOFs are classified under fibro-osseous lesions (FOLs), a group of disease entities that may pose diagnostic difficulties as they share common radiological and histopathological feature (6). However, correct identification of these distinct entities classified under FOLs is important for therapeutic management. Most comprehensive classification of FOLs proposed by Eversole in 2008 is given in Table 3 (17).

The two FOLs considered in the differential diagnosis of JPOF were conventional cemento ossifying fibroma (COF) and focal cemento-osseous dysplasia (FCOD). The conventional COFs are generally encapsulated lesions that may be surgically shelled out from the surrounding bone with ease. It occurs predominately in women in their third and forth decades of life, and affects the tooth bearing areas of jaws, particularly the mandible. Microscopically, it is composed of immature bone trabeculae or cementum- like tissue, or both, in a fibrous stroma (1). The hard and soft tissue distribution in conventional COF is unequal with some areas composed predominantly of soft tissue and other areas containing hard tissues. In contrast, JPOF is unencapsulated and show psammomatoid calcification which is distributed equally among the fibrous tissue

Table 2. Histopathological data of juvenile ossifying fibroma

Histopathological feature	JPOF (n= 9)	JTOF (n=6)
Capsule		
Present	00	00
Absent	09	06
Hard tissue		
Psammomatoid calcifications	09	03
Separate curvilinear bony trabeculae	03	03
Osteoid	00	04
Osteoblastic rimming	00	06
Cementoid masses	04	03
Stroma		
Storiform arrangement	03	00
Dense collagen	01	01
Loose collagen	03	05
Myxoid change with cystic degeneration	01	03
Other features		
Giant cells	00	03
Aneurysmal cyst formation	01	02

stroma. FCOD, presents as an unencapsulated lesion in young adult females. As it is distributed equally among the fibrous tissue unencapsulated, excision, results in multiple fragments which under the microscope reveals a rich vascular stroma. In contrast, JPOF though unencapsulated can be removed without fragmentation, and it does not show a rich vascular stroma. These features were used to differentiate JPOF from FCOD. Another lesion that was considered in the differential diagnosis of JPOF was primary extracranial psammomatoid meningioma (PEPM) which constitutes 2% of all psammomatoid meningiomas, and many of them involve paranasal sinuses. Immunoreactivity for EMA and Vimentin has been considered as characteristic of PEPM and useful to differentiate PEPM from JPOF in the past. However, Granados et al. showed that JPOF have an immunophenotype characterized by the expression of Vimentin, EMA, SMA, and CD10 with lack of expression of CD34, S100 and cytokeratins. As the immunoprofile is identical in both entities diagnosis of PEPM solely based on EMA and vimentin expression should be avoided (10).

With reference to differential diagnosis of JTOF the two main lesions that should be excluded are osteosarcoma and fibrous dysplasia (FD). In contrast to JTOF which occur in children, osteosarcomas of the jaw bones predominantly occur in adults in 3rd - 4th decade of life. JTOF can be differentiated from osteogenic osteosarcoma, by less aggressive growth pattern, presence of partial capsule or circumscribed nature of the lesion, radiologically showing well defined margins and lack of cellular anaplasia, abnormal mitosis and necrosis. FD is a genetically based disease with a characteristic mutation -GNAS leading to increased c-AMP production affecting proliferation and differentiation of pre-osteoblasts (1, 17). FD is generally considered as a self-limiting condition, where the growth ceases with skeletal maturation (2). FD presents as a mixed radiodense lesion with ill-defined margins and lack of osteoid.

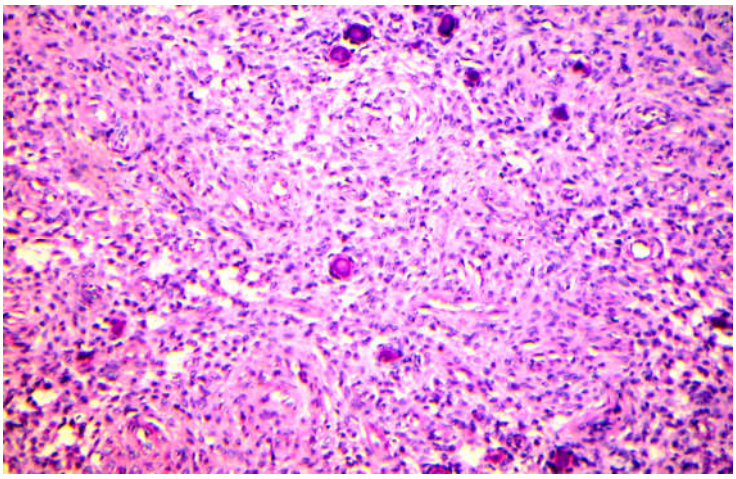

Figure 2. Histopathological appearance of immature JPOF showing small psammomatous calcifications in a fibrocellular stroma showing storiform arrangement reminiscent of PEPM (H&E x10)

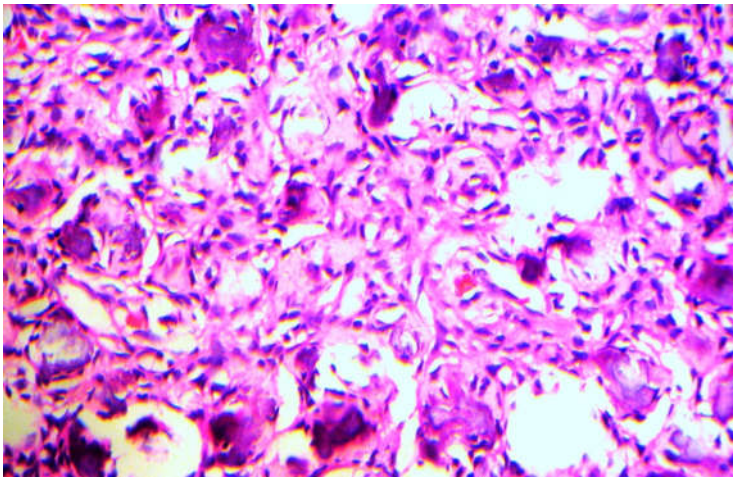

Figure 3. Mature JPOF showing numerous psammomatous calcifications (H&E x10)

In contrast to FD, JTOF requires surgical intervention which makes the correct diagnosis essential for proper management.

According to literature, JPOF shows a slight male predominance with mean age range of 16 years to 33years (7). In the present study, ages ranged from 9 to 45 years with a mean age of 28.6 years and showed a male predilection with male to female ratio of 3.5:1. These findings are compatible with the cases reported in the literature (1,3,5,9). With reference to the site of occurrence, current study demonstrates quite different results from the reported cases in the literature by showing more occurrences in the mandible (77%). One reason for this discrepancy could be the fact that the center where the study was conducted deals with oral biopsies, contributing to lower number of cases from nose and sinuses. With reference to JTOF, literature reveals a mean age of 12 years at presentation with slight male predilection and male to female ratio of 1.3:1(1,10). In the present study, mean age at presentation for JTOF was 21 years and showed equal prevalence in both males and females. Results from the current study for JTOF deviates from the finding in the literature which demonstrates disease in patients in their second decade of life (1,8,12). In the current study mandible was the commonest site of involvement accounting for 50% of the cases, in contrast to international literature, where majority of cases had developed in the maxilla (1,8,12).

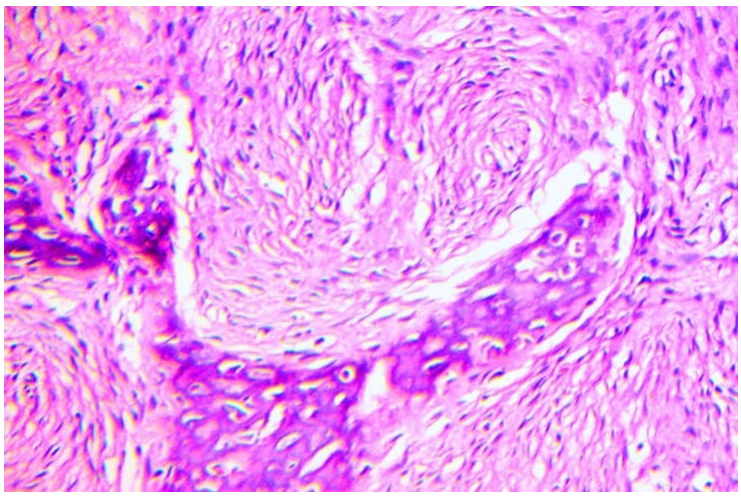

Figure 4. Histopathological appearance of JTOF showing woven bone and osteoid in a myxoid stroma (H&E x10)

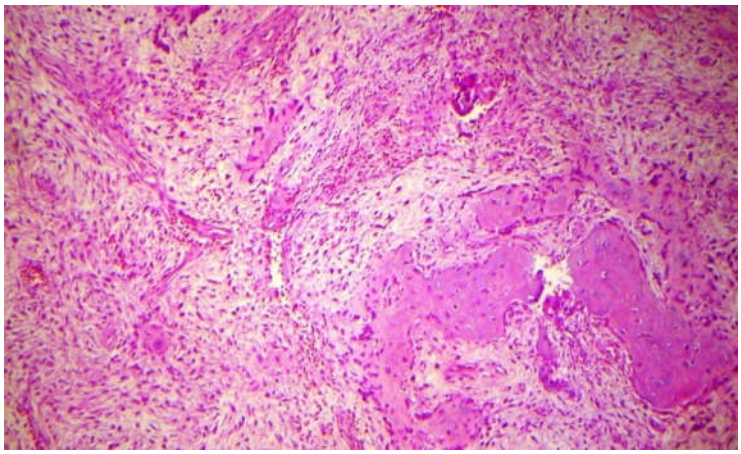

Figure 5. Mineralization of immature bone observed in JTOF (H&E x20)

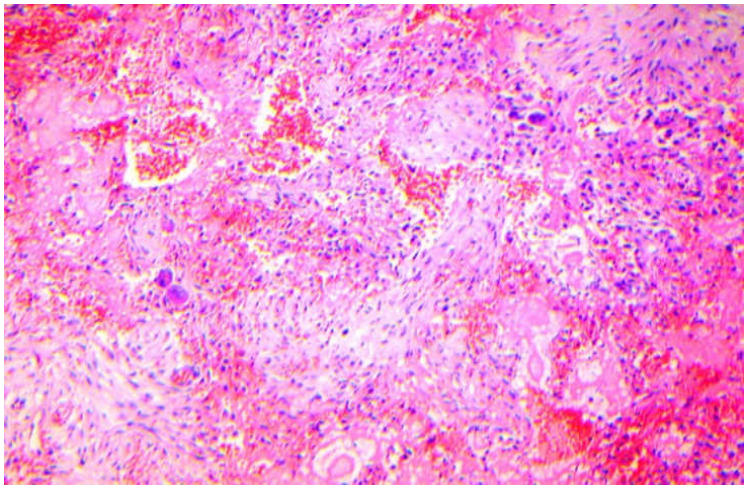

Figure 6. Early aneurysmal bone cyst formation in a JTOF (H&E x10)

Table 3. Classification of Fibro-osseous lesions

Category	Disease entity
Bone dysplasias	Fibrous dysplasia (Monostotic, polyostotic, polyostotic with endocrinopathy-*McCune –Albrights syndrome* and craniofacial fibrous dysplasia) Osteitis deformans Pagetoid heritable bone diseases of childhood Segmental odonto-maxillary dysplasia
Reactive dysplastic lesions	Periapical cemento-osseous dysplasia Focal cemento-osseous dysplasia Florid cemento-osseous dysplasia
Inflammatory lesions	Focal sclerosing osteomyelitis Diffuse sclerosing osteomyelitis Proliferative periostitis
Metabolic bone disease	Hyperparathyroidism
Neoplasms	Ossifying fibroma (conventional) Juvenile ossifying fibroma – Trabecular and psammomatoid types Gigantiform cementoma

According to the literature plane radiography, computed tomography (CT), magnetic resonant imaging (MRI) can be used, but they are neither specific to JAOF nor diagnostic. The radiological features are variable depending on the site and the extent of the ossification. It can be radiolucent, mixed, or radiopaque, depending on the degree of calcification and extent of the cystic changes. Root displacement is common and resorption, though rare, can occur (7). On CT JAOF appears as an expansive but circumscribed lesion surrounded by a thick shell of bone and internal content of varying density.

Histopathologically JPOF is characterized by presence of psammoma bodies identified in all cases analyzed in the present study as well. In contrast, JTOF shows fibrillary osteoid matrix incorporating plump eosinophilic osteoblastic cells. Progressive calcification of the osteoid results in anastomosing trabeculae of immature woven bone (1). The stroma of JPOF contains fibroblastic spindle cells occasionally showing storiform growth pattern. This was seen among 33% of cases of JPOFs of the present study, while none of the JTOFs showed storiform pattern. Similar to literature findings occasional cases showed mitotic figures in cellular stroma without atypical mitosis, cellular pleormorphism, anaplasia or necrosis (9).

Concurrent occurrence of aneurysmal bone cyst (ABC) in JAOF is a commonly reported finding in the literature that was occasionally observed in our cases as well. It is suggested that ABC develops initially as focal myxoid change in the stroma with haemorrhage and aggregation of osteoclastic giant cells, with gradual expansion and formation of cysts with thin fibrous walls. Cystic changes were seen in 53% of the cases reviewed by Johnson et al. (2). These cystic changes are commonly seen in young individuals and large in aggressive maxillary lesions.

The prognosis of JAOF is considered to be good and no malignant transformations have been reported. There are some surgical complications and local complications of the tumour, such as significant blood loss and loss of vision. Meningitits secondary to invasion in to the cranial cavity has been also reported (15). JPOF is reported more frequently than JTOF (1,8). A comprehensive review of the literature done by Samir et al showed that the total number of reported cases of JPOF exceed that of the JTOF by a ratio of more than 4 to 1 (1). Similar results were found in the current case series also with more JPOF than JTOF (3:2).

In conclusion, as JPOF and JTOF shares similarities with benign and reactive fibro-osseous lesions as well as PEPM and osteosarcoma, definitive diagnosis should be achieved with clinico-pathological correlation.

References

1. Samir EM. Psammomatoid and trabecular juvenile ossifying fibroma of the craniofacial skeleton: Two distinct clinicopathologic entities. Oral Surgery Oral Medicine Oral Pathology Oral Radiology Endodontics 2002; 93:296-304.
2. Barnes L, Eveson JW, Reichart P, Sidransky D. World health organization, tumours of oral cavity and oropharynx: In Pathology and genetics of Head and Neck tumours. Slootweg PJ, El Mofty SK. Ossifying fibroma Lyon: IARC press 2005: 319-320
3. Johnson LC, Yousefi M, Vinh TN, Heffner DK, Hyams VJ, Hartman KS. Juvenile active ossifying fibroma: its nature, dynamic and origin. Acta Otolaryngology suppliment 1991:488,1-40.
4. Reed RJ, Hagy DM. Benign nonodontogenic fibro-osseous lesions of the skull. Report of two cases. Oral Surgery Oral Medicine Oral Pathololgy 1965;19:214-27.
5. Sachin C, Gargi S, Pushkar W, Anuprita P, Jashika M. Juvenile psammomatoid ossifying fibroma: A review. Oral Oncology 2007; 47:1110-116.
6. Zupi A, Ruggiero AM, Insabato L, Senghore N, Califano L. Aggressive cement-ossifying fibroma of the jaws. Oral Oncology 2000;36:129-133
7. Makek M. Clinical pathology of fibro- osteo-cemental lesions of the cranio-facial skeleton and jaw bones. Basel karger; 1983, 128-227. e-ISBN: 978-3-318-00167-9 DOI:10.1159/isbn.978-3-318-00167-9
8. Slootweg PJ, Muller H. Juvenile ossifying fibroma: report of 4 cases. Craniomaxillofacial Surgery 1990;18:125-9.
9. Wenig BM, Vinh TN, Smirniotopoulos JG, Fowler CB, Houston GD, Heffner DK. Aggressive psammomatoid ossifying fibroma of the sinonasal region: a clinicopathologic study of distinct group of fibro osseous lesions. Cancer 1995;76:1155-65.
10. Grandos R, Carrillo R, Najera L, Gracia-Villanueva M, Patro M. Psammomatoid ossifying fibromas: immunohistochemical analysis and differential diagnosis with psammomatous meningiomas of craniofacial bones. Oral Surgery Oral Medicine Oral Pathology Oral Radiology Endodontics 2006; 101:614-9.
11. Smith AG, Zavaleta A. Osteoma, ossifying fibroma and fibrous dysplasia of facial and cranial bones. Archives of Pathology 1952; 54:507-27.
12. William HK, Mangham C, Speight PM. Juvenile ossifying fibroma. An analysis of eight cases and a comparison with other fibro osseous lesions. Journal of Oral Pathology and Medicine 2000;29:13-8.
13. Sebastian A, Villanueva J, Hampel H, Reyes D. Spontaneous regeneration after juvenile ossifying fibroma resection: case report. Oral Surgery Oral Medicine Oral Pathoology Oral Radiology Endodontics 2006;102:32-35.
14. Malizos K. Papatheodorou L. The healing potential of periosteum, Molecular aspects. Injury 2005;36S:S13-9.
15. Brannon RB, Fowler CB. Benign fibro-osseous lesions: a review of current concepts. Advances in Anatomical Pathology 2001;8:126-43.
16. Warnakulasuriya S, Tilakaratne WM. Oral Medicine and Pathology, Jaypee brothers, 2014: 167-73.
17. Hall G. Fibro-osseous lesions of the Head and Neck. Diagnostic Histopathology 2012: 18: 149-158.