Case Report

Juvenile trabecular ossifying fibroma associated with central giant cell granuloma and aneurysmal bone cyst like changes – A triple hybrid tumour? Or a pathologic sequelae?

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Abstract

Hybrid tumours encompass lesions containing two or more pathologic entities. The pathogenesis of these lesions is barely understood and described. Juvenile trabecular ossifying fibroma (JTOF) is a benign but locally aggressive fibro-osseous neoplasm commonly affecting the maxilla of the adolescent age group. Hybrid lesions of JTOF have been reported along with central giant cell granuloma (CGCG), aneurysmal bone cyst (ABC) and traumatic bone cyst, respectively. However, the co-occurrence of JTOF with CGCG and ABC in a single patient has not yet been reported in the literature, hence, making ours the first case report of this kind. Theories describing the pathogenesis of this rare phenomenon have also been proposed and elaborated.

Keywords: Aneurysmal bone cyst, central giant cell granuloma, hybrid, juvenile trabecular ossifying fibroma, pathogenesis

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INTRODUCTION

Juvenile trabecular ossifying fibroma (JTOF) is a benign fibro-osseous lesion of the craniofacial skeleton, histologically characterised by the presence of bony trabeculae in a hypercellular stroma. It was initially included among ossifying fibroma (OF) in the fibro-osseous and osteochondromatous category in WHO 2017.[1] It has now been separated as a distinct entity in the latest 2022 WHO classification of bone and cartilaginous tumours.[2]

Central giant cell granuloma (CGCG), earlier known as reparative giant cell granuloma, is a localised, aggressive, benign lesion of the jaw bones characterised by the presence of a vascularised stroma with osteoclast-type giant cells.

An aneurysmal bone cyst (ABC) is an expansile osteolytic lesion composed of large blood-filled cystic spaces separated by fibrous septa containing osteoclast-type giant cells. It may present as a primary neoplasm in 69% (WHO 2017)[1] of the cases associated with rearrangements in *CDH11* and *USP6* genes. Secondary ABCs' are present along with other primary lesions – the most common being with giant cell tumour.[3] In the WHO Classification

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of bone tumours (2020), the terms "ABC" and "ABC like changes" were suggested for Primary ABC and Secondary ABC respectively.[4]

Hybrid lesions are an amalgamation of different pathologic entities. Literature shows 39 hybrid lesions involving CGCG, among which 35.8% were associated with Central Odontogenic fibroma, 28.2% with central OF, 17.9% with fibrous dysplasia and 17.9% with other bone conditions.[5]

In this study, we present a rare case report with the co-occurrence of 3 pathologic entities.

CASE REPORT

A 14-year-old male patient came with the complaint of swelling over the lower posterior back tooth region on the right side for 10 months. The lesion had a sudden onset. It gradually progressed to its present size. It was an irregular, firm to hard non-tender swelling of size 8 × 4 × 3 cm producing buccal and lingual cortical expansion, extending anteroposteriorly from 42 to the angle of the mandible, supero-inferiorly from the corner of the mouth to the lower border of the mandible. There was obliteration of the buccal and lingual vestibule with normal overlying mucosa [Figure 1]. Mandibular Occlusal radiograph showed a well-defined mixed radiolucent lesion in the region of 41 to 46 with expansion of the buccal and lingual cortical plates.

Based on these findings, a provisional diagnosis of OF was given. Differential diagnoses of benign odontogenic neoplasms and developmental odontogenic cysts were also considered. An incision biopsy was taken from the region. Hematoxylin and eosin-stained (H & E) sections of the soft tissue showed a hypercellular connective tissue stroma composed of plump to spindle-shaped fibroblasts having vesicular nuclei interspersed with globular to irregularly shaped basophilic areas of calcification. A histopathologic diagnosis of central OF was given [Figure 2].

Later, the patient reported after 1 year for excision and showed marked enlargement of the lesion. Cone beam computed tomography showed a well-defined multilocular radiolucency with a peripheral sclerotic border extending from 33 to 47 producing buccal and lingual cortical expansion in the mandibular body region, crossing the midline [Figure 3]. The patient underwent excision of the entire lesion. The specimen macroscopy and specimen radiograph higlights the marked expansion of the lesion in the body of the mandible producing a multilocular pattern with fine bony septa [Figure 4 a-c]. Segmental mandibulectomy and reconstruction with a 2.5 mm reconstruction plate were planned. The lesion was approached extra orally with a submandibular incision on the right side extending to the submental area and crossing the midline. Segmental mandibulectomy was performed from distal aspect of 47 to distal aspect of 33 maintaining 5 mm of surgical margin. The mandibular continuity defect was reconstructed with a 2.5 mm titanium reconstruction plate and a 10 mm titanium screw and the occlusion was maintained with

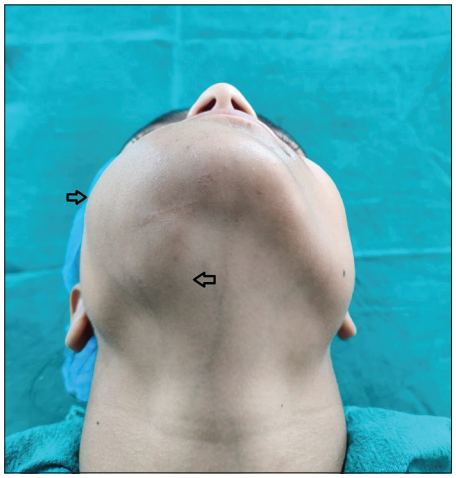

Figure 1: Extra-oral clinical photograph. Arrows point to the lesion on the right mandibular body producing buccal and lingual cortical expansion

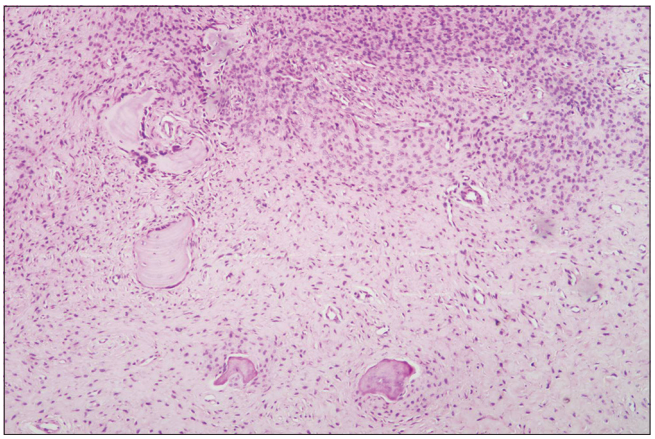

Figure 2: H & E stained section [10x] of incision biopsy shows a cellular connective tissue with bony trabeculae showing osteoblastic riming

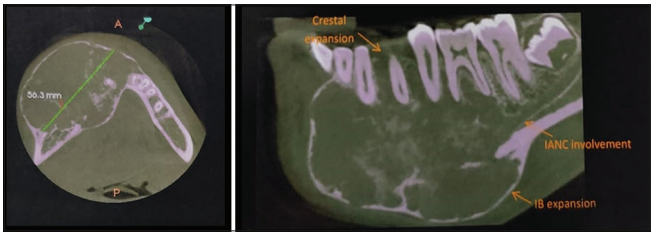

Figure 3: Cone beam computed tomography of the lesion

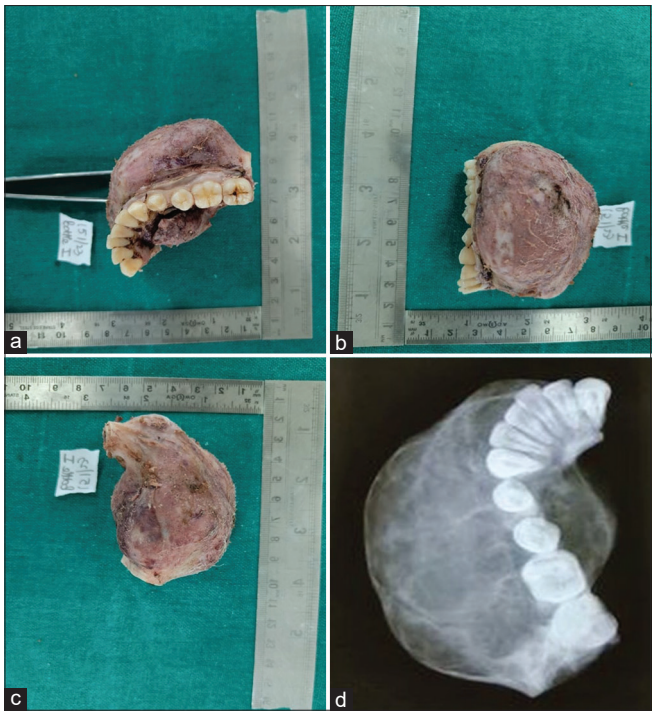

Figure 4: Gross and radiograph of resected specimen. (a): Occlusal aspect. (b): Buccal aspect. (c): Lingual aspect. (d): Radiograph

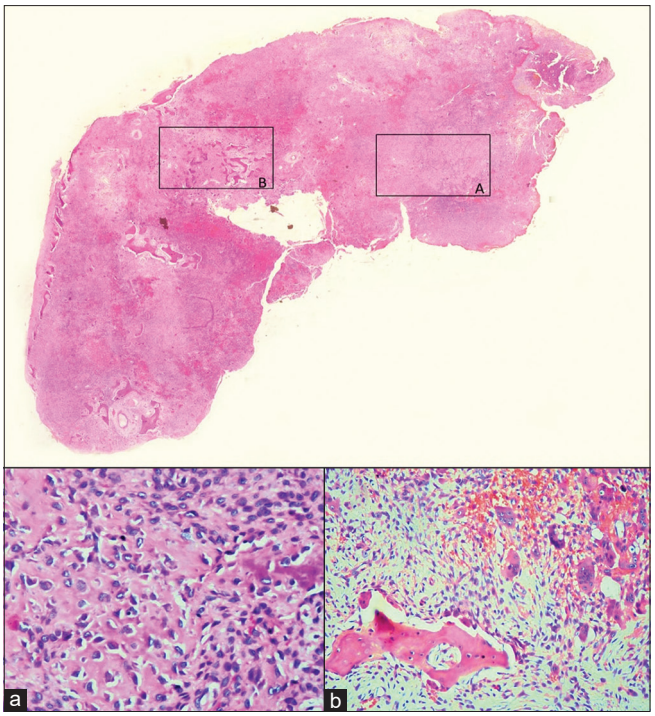

Figure 5: Manual Whole slide image of excision biopsy [10x]. (a): Fine seams of osteoid within a hypercellular stroma [20x]. (b): CGCG like area with osteoclast like giant cells in the upper portion and reactive bone formation and focal areas of resorption in the lower area [20x]

upper–lower arch bar. The resected specimen [Figure 4] contained a portion of the mandible extending from the left para symphysis region to the right body of the mandible corresponding to 33–47. The buccal aspect showed expansion of cortex measuring 5 × 4 × 2.5 cm in size and the lingual cortical expansion measured 3.5 × 4.5 × 2 cm. The inferior border of the mandible was bowed. The specimen radiograph demonstrated well-defined soap bubble radiolucency with a ground glass appearance within the fine bony trabeculations [Figure 4d].

H & E stained sections of the lesional tissue taken from the lingual aspect showed a hypercellular connective tissue stroma interspersed by giant cells and calcifications. The connective tissue was composed of spindled to stellate fibroblasts arranged in short interlacing fascicles and short parallel bundles. Numerous scattered mineralised masses in the form of trabeculae of woven bone, mature bone showing osteocytes within lacunae and osteoblastic rimming and extensive areas showing seams of osteoid surrounded by plump osteoblasts were noted. At foci, small, rounded ossicles with basophilic centre and eosinophilic osteoid-like areas at the periphery were seen. Foreign body type multinucleated giant cells having 4–20 hyperchromatic nuclei were seen scattered within the stroma, especially in areas of hemorrhage [Figure 5]. A large cystic cavity filled with pools of RBCs lined by compressed connective tissue walls showing giant cells was also present [Figure 6].

Correlating the clinical, radiographic and histopathologic features, a diagnosis of JTOF associated with CGCG and ABC-like changes was given.

The patient had an uneventful postoperative healing period with no signs of recurrence in the 1 year follow-up period.

DISCUSSION

The present case report highlights the presence of three pathologic entities within the same lesion –JTOF, CGCG and ABC. Verma *et al.* (2022)[6] reported a triple hybrid tumour involving CGCG, OF and ABC in a 17-year-old male patient. This mandibular lesion was the only available literature comparable to the present case.

The pathogenesis of hybrid tumours is barely discussed in the literature. We would like to propose 3 theories to explain this phenomenon based on evidence from previous literature [Figure 7].

Theory 1: Theory of disrupted vascularity

The patient initially developed JTOF. Owing to its

rapid growth, a major vascular supply of the lesion was disrupted/traumatised, which in turn led to extravasation of RBCs into the connective tissue stroma–producing ABC-like areas. With continued tumour growth, the connection between the disrupted vessel and stroma was severed, leading to the development of CGCG-like areas. This theory is inline with the pathogenesis of ABC given by Hillerup and Hjørting-Hansen (1978).[7]

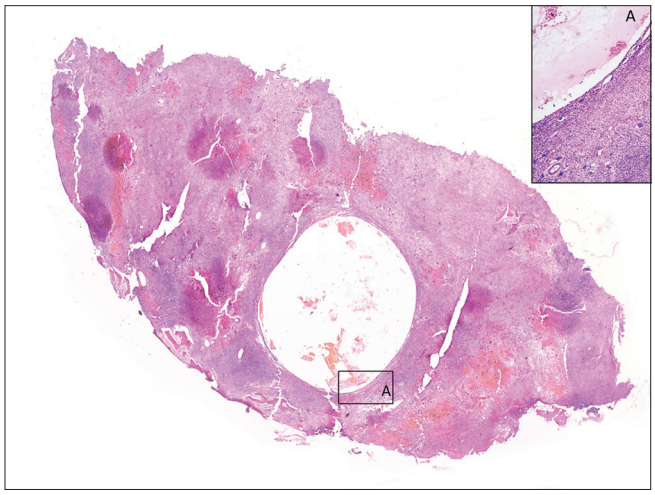

Figure 6: Manual Whole slide image [4x] of excision biopsy showing ABC like area lined by compressed osteoclast containing cyst wall. Inset (a) shows the low power [10x] magnification of the area

Theory 2: Theory of paracrine stimulation

As the patient developed JTOF, the osteoblasts within the lesion stimulated and recruited multinucleated osteoclasts into the area through paracrine stimulation.[8,9] This led to the formation of CGCG-like areas. Later on, disrupted vascularity paved the way for the development of ABC-like changes.

Theory 3: Theory of co-occurrence (hybrid lesion)

JTOF and CGCG are two independent lesions that happened to develop and co-exist in the same site at the same point in time to form a hybrid lesion. The rapid growth and aggressive behaviour of the tumour produced alterations in the lesional hemodynamics, leading to the development of ABC-like changes.

When all three hypotheses are considered, the theory of disrupted vascularity best explains the pathogenesis of the present case. Evidence of this is the following points:

1. The initial radiographic finding was a mixed radiolucency with well-defined borders on the mandibular body, which when correlated with age suggests to the presence of OF, which is JTOF in the present case (the primary lesion).
2. Because of the rapid growth rate of JTOF, the disrupted vascularity led to the formation of ABC-like changes, which is even evident in the gross specimen, showing a bowed mandibular border.

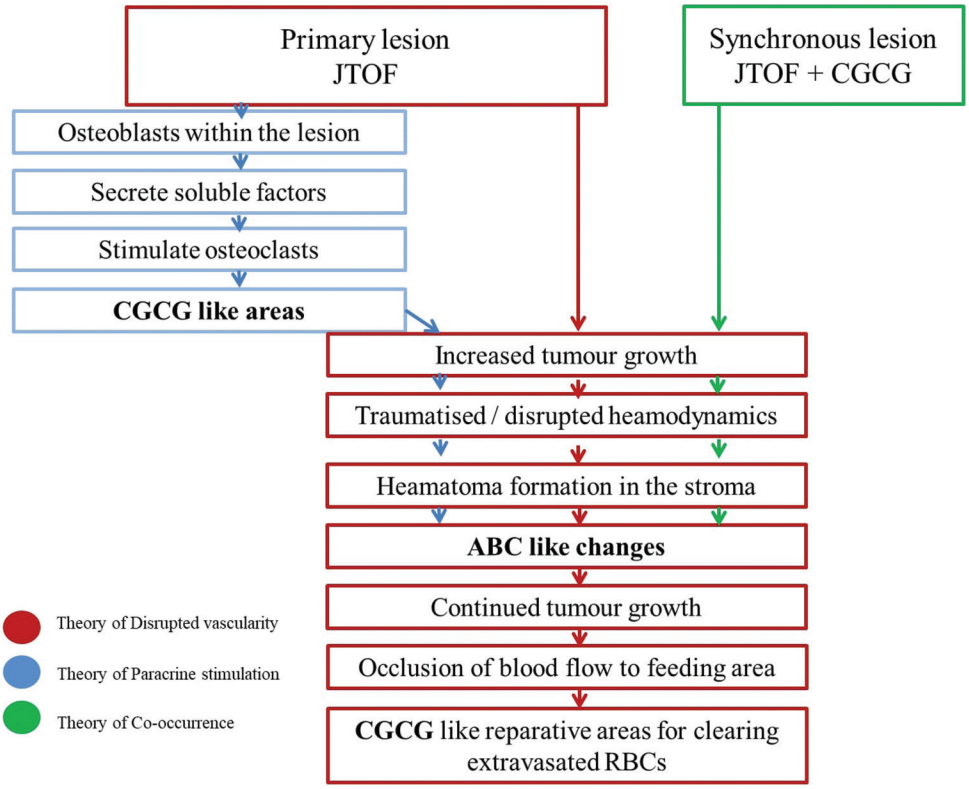

Figure 7: Flowchart – Pathogenesis of the lesion

Table 1: Literature review of Hybrid JTOF with CGCG

Author, year	Age/sex	Site	Radiographic finding	Final diagnosis
Geetha *et al*., 2011[10]	9/M	Mandible, angle	Well-defined unilocular radiolucency with scattered radio-opacities	JTOF with secondary CGCG undergoing degeneration to solitary bone cyst
Saad *et al*. 2019[11]	9/F	Mandible, anterior	Well-defined multilocular radiolucency with diffuse flecks of radio-opacities	Hybrid lesion of CGCG with JTOF

Table 2: Literature review of JTOF with ABC like changes

Author, year	Age/sex	Site
Noffke *et al*. 1998[12]	4/M	Mandible
Sankaranarayanan *et al*. 2011[13]	6/F	Maxilla
Silva *et al*. 2011[14]	9/F	Maxilla
Yazici *et al*. 2011[15]	28/M	Lateral orbital wall
Yang *et al*. 2012[16]	Data not available	Paranasal sinus
Urs A B *et al*. 2013[17]	10/F	Maxilla
	14/F	Mandible
Reddy *et al*. 2014[18]	16/F	Mandible
Abdalla *et al*. 2021[19]	12/F	Fronto-orbital region

3. The absence of giant cells in the incision biopsy rules out the presence of CGCG in the initial presentation.
4. CBCT image of multilocularity, which was absent in the incision biopsy, gives a clue to the development of CGCG later within the lesion

Hybrid lesions of JTOF and CGCG are rare with only two cases[10,11] reported in the literature [Table 1]. Both cases occurred in the mandibular body as well-defined lesions with mixed radiolucencies, one was unilocular, while the other presented with multilocularity mimicking the appearance of CGCG. Gutierrez *et al*.,[3] in their study on secondary ABC, reported most of the cases take the radiographic appearance of the primary lesion that was associated with ABC. In this study, among the 3 cases (present case included) of JTOF with CGCG, 2/3 predominated the radiographic appearance of CGCG - multilocular expansile lesion with ground glass appearance within the fine septations.

However, 9 cases of JTOF showing ABC-like changes[12-19] have been reported in the literature [Table 2]. Among them, 6/9 occurred in the maxillary complex and 6/8 cases occurred in females.

Ours is the first case report of JTOF being associated with both CGCG and ABC in a pediatric patient. Combined lesions show an overlap of multiple features, compromising their diagnosis. The incisional biopsy may hide the hybrid component of such lesions due to their limited depth, making an accurate diagnosis challenging until the entire excisional tissue is thoroughly examined. Hybrid lesions are managed based on these incomplete incisional biopsy reports, compromising the treatment plan. Owing to the paucity of studies, a detailed evaluation of the clinical and radiographic features of these hybrid lesions will prove beneficial in their better clinical identification.

The exact biologic behaviours of hybrid lesions are yet to be understood owing to the limited number of reported cases. The risk of recurrence or the possibility of malignant transformation cannot be negated without long-term follow-up. A complete diagnosis of such cases still relies on histopathology of excisional tissue, which unfortunately provides the final diagnosis after the completion of the planned treatment. This necessitates long-term follow-up of the patients to identify recurrence/signs of malignant transformation. The importance of early intervention in such cases must also be emphasised as it disrupts the pathologic sequelae involved in the growth and development of the controversial hybrid component within these lesions.

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Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

REFERENCES

1. Wright JM, Vered M. Update from the 4th edition of the World Health Organization classification of head and neck tumours: odontogenic and maxillofacial bone tumors. Head Neck Pathol 2017;11:68-77.
2. Vered M, Wright JM. Update from the 5th edition of the World Health Organization classification of head and neck tumors: odontogenic and maxillofacial bone tumours. Head Neck Pathol. 2022;16:63-75.
3. Gutierrez LB, Link TM, Horvai AE, Joseph GB, Donnell RJO,

Motamedi D. Secondary aneurysmal bone cysts and associated primary lesions: Imaging features of 49 cases. Clin Imaging 2020;62:23-32.
4. Sbaraglia M, Bellan E, Dei Tos AP. The 2020 WHO classification of soft tissue tumours: News and perspectives. Pathologica 2021;113:70-84.
5. Alsufyani NA, Aldosary RM, Alrasheed RS, Alsaif RF. A systematic review of the clinical and radiographic features of hybrid central giant cell granuloma lesions of the jaws. Acta Odontol Scand 2021;79:124-31.
6. Verma A, Dabas J, Mohanty S, Urs AB. A hybrid lesion of the mandible with three co-existent pathologies: Report of a rare case with literature review. J Pierre Fauchard Acad (India Section) 2022;36:119-25.
7. Hillerup S and Hjørting-Hansen E. Aneurysmal bone cyst — simple bone cyst, two aspects of the same pathologic entity? Int J Oral Surg 1978;7:16-22.
8. Wong GL. Paracrine interactions in bone-secreted products of osteoblasts permit osteoclasts to respond to parathyroid hormone. J Biol Chem 1984;259:4019-22.
9. Penfold CN, McCullagh P, Eveson JW, Ramsay A. Giant cell lesions complicating fibro-osseous conditions of the jaws. Int J Oral Maxillofac Surg 1993;22:158-62.
10. Geetha N, Pattathan RK, Shivakumar H, Upasi A. Fibro-osseous lesions vs. central giant cell granuloma: A hybrid lesion. Ann Maxillofac Surg 2011;1:70.
11. Saad HR, Kamal NM, Amer HW. Case report: Rare hybrid lesion of a central giant cell granuloma within a juvenile ossifying fibroma. F1000Res 2019;8:1-10.
12. Noffke C. Juvenile ossifying fibroma of the mandible. An 8 year radiological follow-up. Dentomaxillofac Radiol 1998;27:363-6.
13. Sankaranarayanan S, Srinivas S, Sivakumar P, Sudhakar R, Elangovan S. "Hybrid" lesion of the maxilla. J Oral Maxillofac Pathol 2011;15:299-302.
14. Silva C, Silva A, Soares J, Furuse C, de Araujo N, de Araujo V. Trabecular juvenile ossifying fibroma with aneurysmal bone cyst: A rare presentation. Pediatr Dent 2011;33:388-91.
15. Yazici B, Yazici Z, Yalçinkaya U. Aneurysmal bone cyst secondary to ossifying fibroma in the orbit. Ophthal Plast Reconstr Surg 2011;27:e84-5.
16. Yang BT, Wang YZ, Wang XY, Wang ZC. Imaging study of ossifying fibroma with associated aneurysmal bone cyst in the paranasal sinus. Eur J Radiol 2012;81:3450-5.
17. Urs AB, Augustine J, Arora S, Kumar P. Rare pediatric presentation of aneurysmal bone cyst with trabecular juvenile ossifying fibroma and ossifying fibroma. Int J Pediatr Otorhinolaryngol 2013;77:576-80.
18. Reddy AVS, Rajeevkumar Reddy K, Reddy ARK, Rajinikanth, Vidhyadhari P. Juvenile ossifying fibroma with aneurysamal bone cyst: A case report. J Clin Diagnostic Res 2014;8:ZD01-3.
19. Abdalla I, Basalamah A, alwhaibi O, Alrikabi A, Al Boukai A, Elwatidy S. Juvenile trabecular ossifying fibroma (TrJOF) orginating from lateral fronto-orbital bone with secondary aneurysmal bone cyst (ABC) formation: Report of an unusual case and literature review. J Ophthalmol Res 2021;4:205-20.