

Received: 2015.08.20
Accepted: 2015.05.06
Published: 2015.08.18

ISSN 1941-5923
© Am J Case Rep, 2015; 16: 548-553
DOI: 10.12659/AJCR.892284

Epithelial Dysplasia in Ameloblastic Fibrosarcoma Arising from Recurrent Ameloblastic Fibroma in a 26-Year-Old Iranian Man

Authors' Contribution:
Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
Funds Collection G

A 1 **Zhaleh Mohsenifar**
AE 2 **Samira Behrad**
E 2 **Fatemeh Mashhadi Abbas**

1 Department of Pathology, Taleghani Hospital, Shahid Beheshti University of Medical Sciences, Tehran, Iran
2 Department of Oral and Maxillofacial Pathology, Shahid Beheshti, Dental School, Tehran, Iran

Corresponding Author: Samira Behrad, e-mail: samirabehrad@yahoo.com
Conflict of interest: None declared

Patient: Male, 26
Final Diagnosis: Ameloblastic fibrosarcoma
Symptoms: Swelling
Medication: —
Clinical Procedure: Hemimandibulectomy
Specialty: Dentistry





Objective: Rare disease
Background: Ameloblastic fibrosarcoma (AFS) is a rare malignant odontogenic tumor with a mesenchymal component, showing sarcomatous features and epithelial nests resembling ameloblastic fibroma (AF).

Case Report: We report a case of AFS showing epithelial dysplasia arising in a recurrent AF in the left mandible after 3 years in a 26-year-old man, which is regarded as an uncommon histopathologic finding in AFS. We also emphasize the comprehensive clinical, radiographic, and histopathologic evaluation, and immunohistochemical staining of this patient.

Conclusions: We conclude that it is important to consider malignancy alternations in the epithelial component of AFS, along with that of the mesenchymal component, to provide a proper diagnosis and treatment of recurrent AF.

MeSH Keywords: Ameloblastoma • Odontoma

Full-text PDF: <http://www.amjcaserep.com/abstract/index/idArt/892284>

 1905   9  21



Background

Ameloblastic fibrosarcoma (AFS) or ameloblastic sarcoma is a rare odontogenic neoplasm with preponderance for the pre-molar and molar regions of the mandible [1,2]. Ameloblastic fibrosarcoma is regarded as the malignant counterpart of ameloblastic fibroma (AF). According to the 2005 World Health Organization (WHO) classification, it belongs to the group of odontogenic sarcomas, along with ameloblastic fibrodentinosarcoma (which demonstrates focal evidence of dentinoid deposits) and ameloblastic fibroodontosarcoma (with dentinoid and enameloid deposits) [3,4]. Ameloblastic fibrosarcoma has been reported to either arise as a *de-novo* lesion of the jaws or from malignant transformation of a pre-existing ameloblastic fibroma [5,6]. Histopathological features of AFS are benign epithelial nests resembling that of ameloblastic fibroma and a malignant ectomesenchymal component that shows the feature of a sarcoma [7,8]. Ameloblastic fibrosarcoma is usually regarded as a low-to-intermediate-grade malignancy. It has locally aggressive behavior and a high recurrence rate, but rarely metastasizes [9,10].

In this report, we describe a rare case of AFS with epithelial dysplasia, along with a brief review of its clinicopathological features. It is an uncommon finding because features of malignancy in AFS are restricted to the mesenchymal component, while the epithelial component remains rather subdued in most patients with AFS [11].

Case Report

In the winter of 2013, a 26-year-old man was referred to the Department of Oral and Maxillofacial Surgery (OMFS) of Thaleghani Hospital of Shahid Beheshti University of Medical Sciences for the evaluation of a continuous pain and paresthesia on the left side of his face. It was of 2-month duration, but did not interfere with chewing or cause difficulty with opening his mouth.

He was referred to this center with similar complaints 3 years ago. The patient had an enucleation done via an intra-oral approach with the preservation of the inferior dental nerve along with the inferior and posterior mandibular borders, and the biopsy revealed ameloblastic fibroma (Figure 1).

He is a carpenter by profession and his medical history was uneventful. General examination was normal. On extra-oral examination, the face was asymmetrical because of a medium-sized swelling extending from the left angle of the mandible to the first molar area of the mandible (Figure 2). Palpation revealed a tender, bony, hard tumor without a fistula, in the left region of the mandible. Intraorally, a 5×5-cm swelling extending

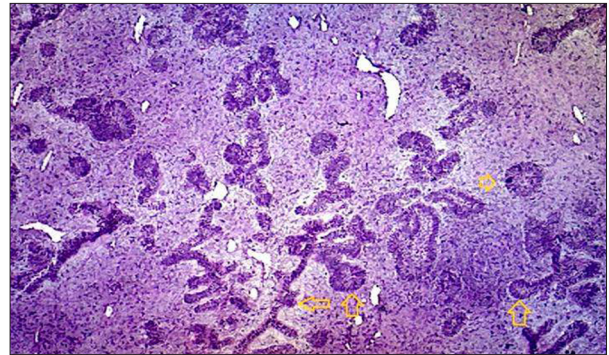


Figure 1. Small nests, islands, and thin cords of odontogenic epithelium and condensation of mesenchymal tissue were demonstrated by ameloblastic fibroma.

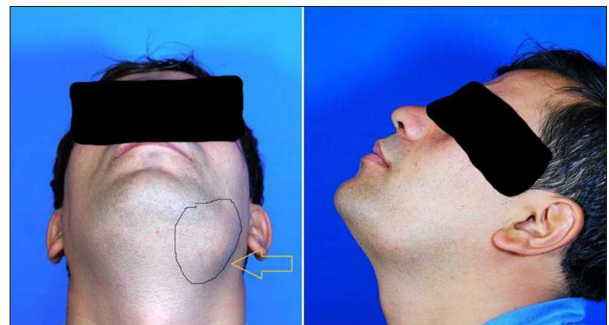


Figure 2. Swelling in lower left mandible.



Figure 3. Intraoral view shows swelling without ulceration on the left side of the mandible.

from the retromolar pad to the first molar area was seen. The mucosal surface was intact. No other intra- or extra-oral signs were observed (Figure 3).

The submandibular lymph node on the same side was enlarged, firm, tender, and mobile, measuring 1×1 cm. Hypoesthesia along the distribution of the alveolar nerve was observed. No other significant findings were seen, and laboratory values were in normal ranges. No evidence of regional or distant metastasis was observed.

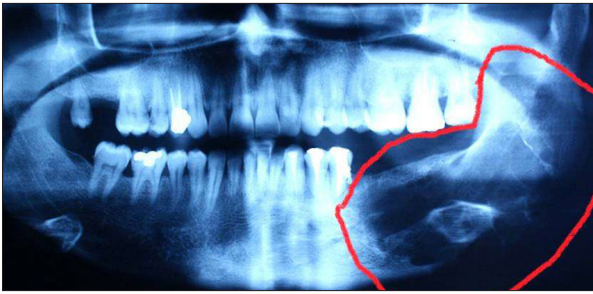


Figure 4. The panoramic radiographic view of the mandible showing a multilocular radiolucent lesion.

On radiographic examination, a well-defined multilocular radiolucency was seen extending from the second premolar to near the coronoid process of the mandible. The outline of the

mandibular canal in anterior region was poorly defined. Also, root resorption of first and second premolar was seen (Figure 4). Computerized tomography revealed an expansive and homogeneously radiolucent mass occupying the posterior part of the left mandible, with perforation of the lingual cortical plate. Calcifications were not observed within the lesion (Figure 5).

A primary pre-operative differential diagnosis of recurrent ameloblastic fibroma, aggressive central giant cell granuloma, ameloblastic fibrosarcoma, and ameloblastic carcinoma was made.

Pre-operative aspiration biopsy of this swelling containing some blood was free of malignant cells. The patient underwent left hemimandibulectomy after 1 week of presentation at this center. The mandibular condyle was preserved and the position

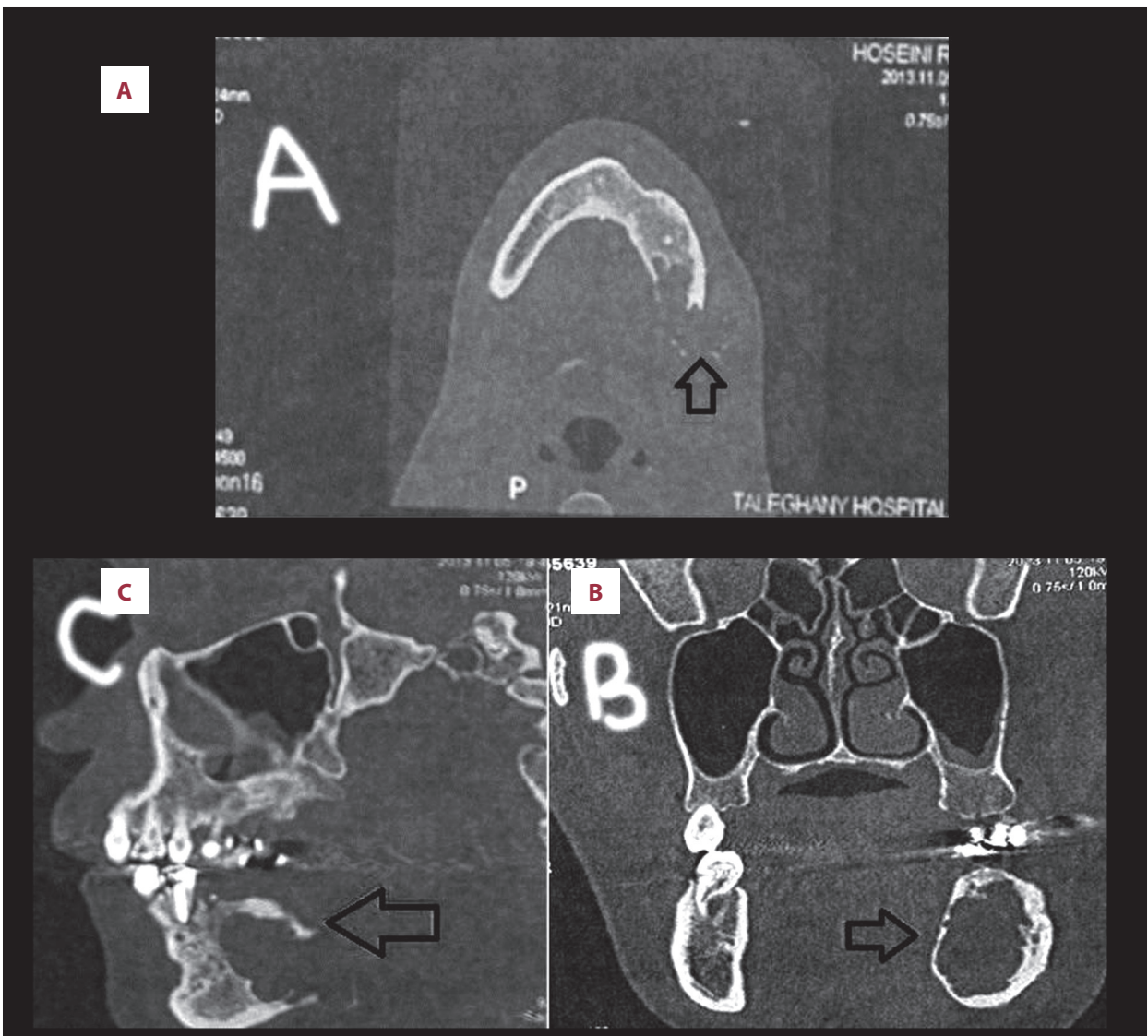


Figure 5. Computerized tomography shows an expansile radiolucent lesion of the left mandible with perforation and thinning of adjacent bones. (A) Axial, (B) frontal, (C) coronal.

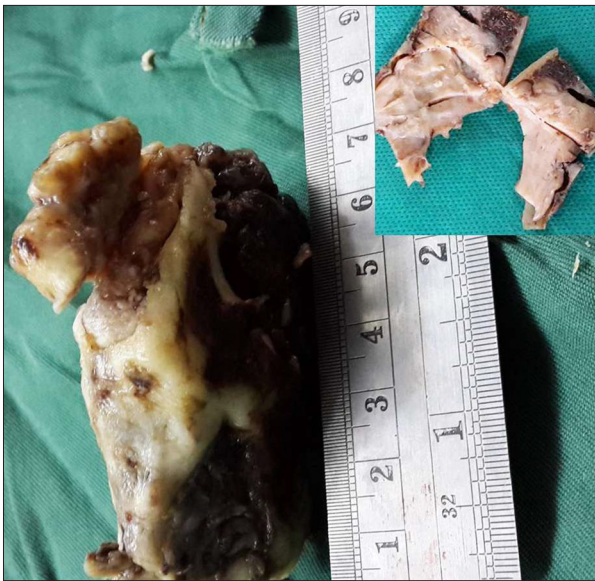


Figure 6. Cross-section of the resected specimen shows a 7.0×5.0×5.0 cm multinodular mass of the posterior left side of the mandible.

of the mandible was stabilized by a reconstruction plate. All surgical resection margins were tumor-free. Finally, a surgical specimen was submitted for histopathological examination.

The excised specimen consisted of the left half of the body and ramus of the mandible, with the tumor mass measuring 7.0×5.0×5.0 cm, which perforated the inferior mandibular border and lingual cortical bone. The tumor was firm, tan-brown, and had a fleshy appearance (Figure 6).

Microscopic examination of the hematoxylin-eosin stained slides revealed a neoplastic tissue with cords and nests of epithelial cuboidal or columnar ameloblast-like cells with peripheral palisading. In some areas, epithelial components show pleomorphism, hyperchromatism, and increased nuclear-to-cytoplasmic ratio. The mesenchymal background was mostly composed of plump stellate-shaped and ovoid-to-spindle-shaped cells. Nuclear hyperchromatism, pleomorphism, and scattered mitotic figures were identified in some areas, as well as giant and bizarre cells. There were also wide areas of necrosis (Figure 7).

Immunohistochemistry was done using the proliferation marker Ki-67, and pan-cytokeratin and vimentin was also used to confirm the epithelial component of the islands and the mesenchymal stroma (Figure 8). Ameloblastic epithelium showed positive immunoreactivity for pan-cytokeratin and the spindle cell component was positive for vimentin. Furthermore, Ki-67 labeling index of the spindle cell component and epithelial component increased to 13.2% and 6.6%, respectively. This

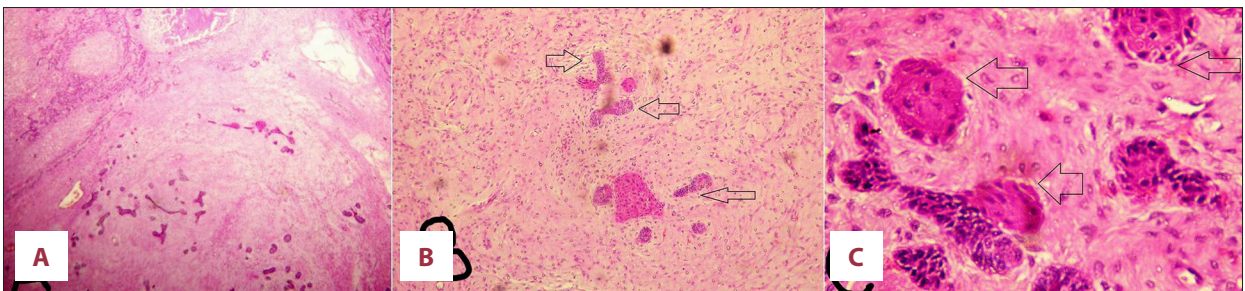


Figure 7. Islands and cords of odontogenic epithelial nest in a sarcomatous background (H and E, magnification ×4), (A). Epithelial dysplasia in islands of odontogenic epithelium in a sarcomatous background with frequent mitoses (H and E, magnification ×10), (B). Dysplastic epithelial component with pleomorphism, increased nuclei to cytoplasm ratio and nuclear hyperchromatism (H and E, magnification ×40), (C).



Figure 8. Immunostaining for pan-cytokeratin showing positive cells in the epithelial component, (A). Immunostaining for vimentin highlighting mesenchymal components, (B). (magnification ×10). Immunostaining for Ki67 showing positive cells in the epithelial and mesenchymal components (original magnification×100), (C).

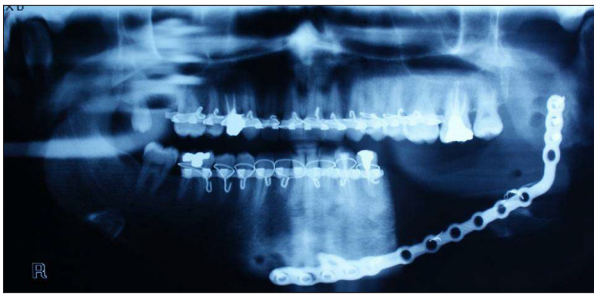


Figure 9. Panoramic radiographic after two weeks of surgery.

indicates a moderately low proliferative activity of AFS, unlike in a carcinosarcoma (because in ameloblastic carcinosarcoma both components are malignant and the Ki-67 marker for both components is above 10%). Finally, the tumor was diagnosed as “ameloblastic fibrosarcoma” according to clinicopathologic findings. The patient was regularly followed up. He did not have radiotherapy and remains disease-free 20 months after surgical intervention. The radiograph of this patient did not show radiolucent lesion after 2 weeks (Figure 9).

Discussion

Ameloblastic fibrosarcoma (AFS) was first described by Heath in 1887 as a spindle cell sarcoma with epithelial cells resembling those of the enamel organ; it is a rare, malignant, odontogenic tumor [7]. However, 71 cases have been reported in the English literature so far. Most have occurred in the mandible and in the third decade of life [12].

Ameloblastic fibrosarcoma occurs in a wide age range, from 3 to 83 years (mean, 27.3 years). Patients with AFS are typically 10 years older than those with AF [13]. Ameloblastic fibrosarcomas occur about 1.5 times as often in males as in females. Bregni et al. reported a male-to-female ratio of 1.6:1 [8]. Our patient was 26 years old at presentation, similar to the mean age reported. According to cases reported, no significant difference was observed in age and sex distribution between our case and those in the literature [12]. Although either the maxilla or the mandible may be involved, AFS more frequently occurs in the mandible (79%) than the maxilla (21%) and most that were similar to our case were found in the posterior region of the mandible [10]. Clinical appearance and symptoms vary among the reported cases, but swelling and pain are the most common clinical findings, as in our patient. Involvement of the cervical or submandibular lymph node and hypoesthesia are uncommon findings [7–10,12–14]. The tumor usually shows a destructive radiolucent pattern with ill-defined borders suggestive of malignancy in panoramic radiographic and computerized tomography images in AFS [15]. In our case, destructive behavior of the lesion was obvious in both conventional radiographs and computerized tomography images.

In approximately half of known cases, the most commonly proposed pathogenesis of AFS is transformation of an existing AF after surgical procedures. The mechanism of this transformation is not completely understood [8,16,17]. Muller et al. reported that 44% of AFS patients had a previous diagnosis of AF [14]. Thus, serial sampling of the surgical specimen of AF is helpful for early diagnosis of AFS.

Definitive diagnosis of AFS is established based on histopathological evaluation of the mesenchymal components, which usually demonstrates various features of malignancy, including cellular atypia, hyperchromatic nuclei, bizarre pleomorphic cells, and mitotic figures. The epithelial component appears histopathologically benign, like ameloblastic fibroma, and does not demonstrate any cytologic atypia [7,8].

Khalili and Amini Shakib reported a case of AFS in the left posterior region of the maxilla with benign-appearing epithelial islands and highly cellular mesenchymal tissue with pleomorphism and scattered bizarre giant cells [12]. The histological study of the present case revealed epithelial dysplasia in islands of odontogenic epithelium with pleomorphism, nuclear hyperchromatism, increased N/C ratio, and atypical mitoses in highly cellular mesenchymal tissue with spindle-shaped cells showing marked pleomorphism and infrequent mitoses. Strands of odontogenic epithelium were composed of 2 layers of cells that are columnar or cuboidal in shape, like AF.

In another study, by Yamamoto et al., the presence of keratin in the columnar and polyhedral cells of the epithelial component and vimentin in the ectomesenchymal component was demonstrated, verifying the biphasic nature of this tumor [18]. Williams et al. demonstrated a case of anaplastic ameloblastic fibrosarcoma arising in an ameloblastic fibroma with histopathological findings including benign, interlacing and uniform, and epithelial islands within a bland spindle-cell background characteristic of AF [9].

Sometimes it may be difficult to differentiate AFS because it can be similar to low-grade tumors from ameloblastic fibroma to a carcinosarcoma that is a malignant mixed-type tumor similar in pattern to an AFS, but in which both the epithelial and the ectomesenchymal components show cytological features of malignancy [1–10,12–14].

Several studies have suggested biomarkers associated with cell proliferation (Ki67, PCNA, and c-KIT) and apoptosis (BCL2) to overcome difficulties in the diagnosis of the tumor with low malignant potential in the mesenchymal component without considering clinical and radiographic findings [9–11,12–19]. A high Ki-67 labeling index indicates a high proportion of proliferating cells in the malignant epithelial and the mesenchymal components; therefore, it may be useful in differentiating the

malignancy of the epithelial portion of carcinosarcoma from that of AFS [20]. In our case, Ki-67 labeling index rate showed $x < 10\%$ in epithelial portion and $x > 10\%$ in mesenchymal portion and the rate of Ki-67 marker for ameloblastic carcinoma was 48.7% (Figure 8C) [20]. We submit that our case is that of ameloblastic fibrosarcoma with epithelial dysplasia. This may explain the more aggressive behavior of the carcinosarcoma as opposed to the less aggressive fibrosarcoma in which the epithelial component is benign [1–9].

Once the diagnosis of ameloblastic fibrosarcoma has been confirmed, radical surgical excision with a margin of normal tissue appears to be the treatment of choice. Curettage or local excision is usually followed by rapid local recurrence. Some investigators recommend adjuvant chemo- and/or radiotherapy, but others are uncertain about their benefits [15–21].

Ameloblastic fibrosarcoma is locally aggressive and infiltrates adjacent bone and soft tissues, but regional lymph node involvement or distant metastasis has been reported in a few cases [14]. Documented metastasis has been reported only once in the literature [8–10,12,13]. Recurrence rate is high in AFS; 25 (35%) of the 71 reported cases have had at least 1 recurrence during the follow-up period [12–16]. Furthermore, it has caused death in 14 (19.7%) reported cases at between 3 months and 19 years, usually because of uncontrollable locally

invasive recurrences [12–15], therefore, long-term follow-up would provide more information on survival and recurrence rates of this tumor.

Our patient underwent radical surgical resection with free margins. He had no chemotherapy or radiotherapy. There is no evidence of recurrence or metastasis after 20 months.

Conclusions

We report a rare example of ameloblastic fibrosarcoma development in an ameloblastic fibroma patient 3 years after the primary excision, which manifested a different histological feature showing epithelial dysplasia. This histopathologic feature in our case is distinctly different from those previously reported, and suggests that the benign odontogenic epithelium in AFS may progress to malignant transformation such as carcinosarcoma. We conclude that epithelial dysplasia in ameloblastic fibrosarcoma needs more attention and evaluation of both the epithelial and mesenchymal components in all odontogenic tumors.

Conflict of interests

The authors declare that they have no conflict of interests.

References:

1. Kunkel M, Ghalibafian M, Radner H et al: Ameloblastic fibrosarcoma or odontogenic carcinosarcoma: a matter of classification? *Oral Onc*, 2004; 40: 444–49
2. DeLair D, Bejarano PA, Peleg M, El-Mofty SK: Ameloblastic carcinosarcoma of the mandible arising in ameloblastic fibroma: a case report and review of the literature. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod*, 2007; 103(4): 516–20
3. Carlos R, Altini M, Takeda Y: Odontogenic sarcomas. In: Barnes L, Eveson JW, Reichart P, Sidransky P (eds.), *World Health Organization Classification of Tumours Pathology and Genetics of Head and Neck Tumours*. Lyon: IARC Press; 2005; 294–95
4. Lee JS: Odontogenic sarcoma and carcinosarcoma. *Semin Diagn Pathol*, 1999; 16(4): 325–32
5. Dallera P, Bertoni F, Marchetti C et al: Ameloblastic fibrosarcoma of the jaw: report of five cases. *J Cranio Maxillofac Surg*, 1994; 22: 349–54
6. Howell RM, Burkes EJ: Malignant transformation of ameloblastic fibro-odontoma to ameloblastic fibrosarcoma. *Oral Surg*, 1977; 43: 391–401
7. Reichart PA, Philipsen HP (eds.), *Odontogenictumours and allied lesions*. 1(st ed. London: Quintessence Publishing; 2004
8. Bregni RC, Taylor AM, Garcia AM: Ameloblastic fibrosarcoma of the mandible: Report of two cases and review of the literature. *J Oral Pathol Med*, 2001; 30: 316–20
9. Williams MD, Hanna EY, El-Naggar AK: Anaplastic ameloblastic fibrosarcoma arising from recurrent ameloblastic fibroma: Restricted molecular abnormalities of certain genes to the malignant transformation. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod*, 2007; 104: 72–75
10. Demoor-Goldschmidt C, Minard-Colin V, Cassagneau E et al: Ameloblastic fibrosarcoma of the mandible: Report of 2 chemosensitive pediatric cases. *J Pediatr Hematol Oncol*, 2011; 34: e72–76
11. Neville BW, Damm DD, Allen CR, Bouquot JE: *Oral and Maxillofacial Pathology*, 3rd ed. Philadelphia: WB Saunders, 2009; P722–23
12. Khalili M, Amini Shakib P: Ameloblastic fibrosarcoma of the upper jaw: Report of a rare case with long-term follow-up. *Dent Res J (Isfahan)*, 2013; 10(1): 112–15
13. Zabolinejad N, Hiraifar M, Anvari K, Razavi AS: Ameloblastic fibrosarcoma of the maxillary sinus in an infant: A case report with long-term follow-up. *J Pediatr Surg*, 2008; 43: e5–8
14. Muller S, Parker DC, Kapadia SB et al: Ameloblastic fibrosarcoma of the jaws. A clinicopathologic and DNA analysis of five cases and review of the literature with discussion of its relationship to ameloblastic fibroma. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod*, 1995; 79: 469–77
15. Kousar A, Hosein MM, Ahmed Z, Minhas K: Rapid sarcomatous transformation of an ameloblastic fibroma of the mandible: Case report and literature review. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod*, 2009; 108: e80–85
16. Howell R, Burkes D: Malignant transformation of ameloblastic fibro-odontoma to ameloblastic fibrosarcoma. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod*, 1977; 43: 391–401
17. Kobayashi K, Murakami R, Fujii T et al: Malignant transformation of ameloblastic fibroma to ameloblastic fibrosarcoma: case report and review of the literature. *J Craniomaxillofac Surg*, 2005; 33(5): 352–55
18. Yamamoto H, Caselitz J, Kozawa Y: Ameloblastic fibrosarcoma of the right mandible: Immunohistochemical and electron microscopical investigations on one case, and a review of the literature. *J Oral Pathol*, 1987; 16: 450–55
19. Pontes HA, Pontes FS, Silva BS et al: Immunoeexpression of Ki67, proliferative cell nuclear antigen, and Bcl-2 proteins in a case of ameloblastic fibrosarcoma. *Ann Diagn Pathol*, 2010; 14: 447–52
20. Bologna-Molina R, Mosqueda-Taylor A, Molina-Frecherro N et al: Comparison of the value of PCNA and Ki-67 as markers of cell proliferation in ameloblastic tumors. *Med Oral Patol Oral Cir Bucal*, 2013; 18(2): e174–79
21. Demoor-Goldschmidt C, Minard-Colin V, Cassagneau E et al: Ameloblastic fibrosarcoma of the mandible: Report of 2 chemosensitive pediatric cases. *J Pediatr Hematol Oncol*, 2011; 34: e72–76