Ameloblastic fibroma: a stage in the development of a hamartomatous odontoma or a true neoplasm? Critical analysis of 162 previously reported cases plus 10 new cases

Amos Buchner, DMD, MSD,[a] and Marilena Vered, DMD[b]
School of Dental Medicine, Tel Aviv University, Tel Aviv; and Institute of Pathology, Chaim Sheba Medical Center, Tel Hashomer, Ramat Gan, Israel

Objective. To analyze neoplastic and hamartomatous variants of ameloblastic fibromas (AFs).
Study Design. Analysis of 172 cases (162 previously reported, 10 new).
Results. AF emerged as a lesion primarily of children and adolescents (mean age, 14.9 years), with about 80% diagnosed when odontogenesis is completed (age, < 22 years). Around 28% of all AFs were small and asymptomatic, and 72% exhibited moderate-to-severe bone expansion.
Conclusions. There are 2 variants of AF: neoplastic and hamartomatous. Lesions in patients aged >22 years are considered true neoplasms, while those in younger patients may be either true neoplasms or odontomas in early stages of development. Although the histopathology of hamartomatous and neoplastic variants of AF are indistinguishable, clinical and radiologic features can be of some help to distinguish between them. Asymptomatic small unilocular lesions with no or minimal bone expansion in young individuals are likely to be developing odontomas, and large, expansile lesions with extensive bone destruction are neoplasms. (Oral Surg Oral Med Oral Pathol Oral Radiol 2013;116:598-606)

Ameloblastic fibroma (AF) is a rare benign odontogenic tumor that is characterized by proliferation of both odontogenic epithelium and odontogenic mesenchyme. Most tumors occur in children and young adults (mean age, 14.8 years), although AFs are occasionally diagnosed in older patients.[1] AFs belong to the group of mixed odontogenic tumors that also includes ameloblastic fibrodentinoma (AFD), ameloblastic fibroodontoma (AFO), and the fully mineralized odontoma (complex and compound).[2] The histopathology of this group of lesions resembles various stages of tooth development.

There is no consensus among investigators whether these tumors represent separate entities or different stages in maturation of the same lesions.[3] Some authors claim that AF is a separate specific neoplastic entity that does not develop into a more differentiated odontogenic tumor,[4] while others suggest that if an AF is left undisturbed, it will ultimately mature into an AFO and then continue to mature into a completely differentiated odontoma, which is considered to be a hamartoma.[5] According to this latter theory, an AF is not a neoplasm but rather the early stage of a developing odontoma.

AF is a rare tumor, and its relative frequency within the group of odontogenic tumors, as seen in oral pathology biopsy services in various parts of the world, ranges from 0.6% to 3.1%.[6] Because of its rarity, there are sparse details in the literature regarding its clinical and radiologic features, and some of the data in the existing reports are conflicting. There are also conflicting reports regarding the recurrence and malignant transformation rates of AF.

Except for one comprehensive review that was published in 1997,[7] most of the papers on AF describe single cases, and there are few reports on small series of cases.

The purposes of this study were to critically analyze the clinical and radiologic features of AF based on case reports and case series published in the literature from 1961 to 2011, and to add 10 new cases from our files. Furthermore, based on the information yielded by that analysis, this study addresses the question of whether AF is a true neoplastic lesion or an early stage in the development of a hamartomatous odontoma.

Statement of Clinical Relevance

There are 2 variants of ameloblastic fibroma: neoplastic and hamartomatous (the early state of a developing odontoma). Since the histopathology of these 2 variants is indistinguishable, only clinical and radiologic features can be of potential help to distinguish between them.

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[a]Professor of Oral Pathology, Department of Oral Pathology and Oral Medicine, School of Dental Medicine, Tel Aviv University, Tel Aviv, Israel.
[b]Associate Professor of Oral Pathology and Chairman, Department of Oral Pathology and Oral Medicine, School of Dental Medicine, Tel Aviv University, Tel Aviv; Senior Pathologist, Institute of Pathology, Chaim Sheba Medical Center, Tel Hashomer, Ramat Gan, Israel.
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METHODS

The English-language literature was searched for adequately documented cases of AF published between 1961 and 2011. Medline's PubMed and Google Scholar were searched using the keyword *ameloblastic fibroma*. References of published papers were also searched for additional cases. The cases included in this study were restricted to those that exhibited the histopathologic features of AF, namely the presence of dental papilla–like tissue with epithelial strands and nests and no presence of dental hard tissues.[2] Additional inclusion criteria were information on the clinical features and an acceptable radiographic image or detailed radiologic description for each case. Not all data were available for all cases. Excluded from the study were cases that were reported as variants of AF (i.e., cystic AF, granular AF, peripheral AF) and cases that were reported as being AF but in which the histopathology revealed hard tissue formation of dentin or enamel. Cases that were reported multiple times were recorded once. Finally, the series of cases by Buchner et al.[6] and Carnelio and Vij[8] were not included because no individual clinical and radiologic information were available.

A total of 172 cases (162 from publications and 10 new cases from the authors' files) were analyzed.[9-88] The data on the new cases are summarized in Table I and Figure 1. The histopathologic features of those 10 new cases were similar: the lesions were composed of soft tissue that exhibited nests, strands, and cords of odontogenic epithelium that resembled dental lamina (Figure 2, *A* and *B*). In a few cases, the lesion also contained epithelial islands that consisted of a peripheral layer of columnar cells, which enclosed loosely arranged cells resembling an early stage of the enamel organ of a developing tooth (see Figure 2, *C* and *D*). Those epithelial elements were supported by loose primitive connective tissue that resembled the dental papilla of a developing tooth. All cases were treated by enucleation and curettage except for No. 8 (see Table I), which was treated by marginal resection. Follow-up ranged from 7 to 20 years, and there were no recurrences.

The clinical and radiologic data of the 172 lesions were evaluated according to the criteria proposed by White,[89] which include age, gender, location, symptoms, and expansion, as well as radiologic features of lesion size, content, borders, loculation, tooth relation, tooth impaction, tooth displacement, and root resorption. The size of the lesion was determined according to its greatest dimension. In the present study, the anterior region consisted of the incisors and canines, and the posterior region consisted of the premolars (or primary molars), molars and ramus (in the mandible), and molars and sinus (in the maxilla).

Odontogenesis occurs at various ages, depending on the site in the jaw, with the latest being around 22 years in the third molar area. Odontomas, being hamartomas, develop during the period of normal odontogenesis, and if specific AFs are to be considered hamartomas, they should therefore have developed by the age of 22 years.[90] Accordingly, we also divided all the cases into one group comprising patients younger than 22 years and another group of patients who were older.

Differences in the frequency of AF according to gender, age, jaw location (mandible or maxilla), and lesion size (mandible versus maxilla) were analyzed by the χ^2 test and crosstabs test using SPSS software (version 16; SPSS, Inc, Chicago, IL, USA). Significance was set at $P < .05$.

The study was approved by the Research and Ethics Committee of Tel Aviv University.

RESULTS

A total of 172 AF cases were analyzed, of which 10 were new and are now being reported for the first time. The age and gender distributions of the patients were known in all 172 cases (Figure 3). At the time of initial presentation, the patients' ages ranged from 1 month to 57 years (mean, 14.9 years; median, 11 years). Nearly 80% (N = 136) of the cases were diagnosed by the age of 22 years (younger group), and only 20% (N = 36) were diagnosed later than 22 years (older group). There were 99 (58%) male patients and 73 (42%) female patients, with a male-to-female ratio of 1.4:1. The differences in the distribution of gender in the entire group and separately in the younger and older groups were not significant.

AF was located in the mandible in 132 (77%) cases and in the maxilla in 40 (23%) cases, with a mandible-to-maxilla ratio of 3.3:1 ($P < .001$). Figure 4 shows the specific location of 167 cases within the mandible and maxilla. A total of 82% were in the posterior region of the jaws, 7.8% were in the anterior region, and 10.2% occupied both anterior and posterior regions. Most lesions in the anterior region were in the maxilla, and most lesions in the posterior region were in the mandible ($P = .02$). Interestingly, the posterior mandible was the most common site (74% of all cases).

Clinical presentation was reported in 141 cases. The lesion usually manifested as a painless swelling that grew slowly and with time expanded the cortical plates. Painless expansion of bone was reported in 65 (46%) cases and in an additional 25 (17.7%) cases the painless expansion was so severe that it caused facial asymmetry. Painful expansion of bone was reported in 12 (8.5%) cases. In contrast, the lesion was completely