Vascularized ameloblastoma: A case report and clinicopathologic review of 18 cases from the literature

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The notable features of ameloblastoma do not typically include prominent vascularity. However, on rare occasions, vascular ameloblastoma has been described under a variety of names. We present a case of vascularized ameloblastoma that had a bloody return on fine-needle aspiration. The English language literature contains a total of 16 reports (18 cases) of vascular or hemangioma-like ameloblastoma. We reviewed the clinical, pathologic, and radiographic features of the 19 cases, but further study and more cases are needed. The recognition of this variation of ameloblastoma is important for clinicians to note that fine-needle aspiration with a bloody return does not exclude ameloblastoma from diagnostic consideration. We suggest the term *vascularized ameloblastoma* to avoid any suggestion of a vascular neoplasm. (Oral Surg Oral Med Oral Pathol Oral Radiol 2020;129:e264−e268)

Ameloblastoma is widely considered the most common and most clinically significant odontogenic tumor.[1] The mandible is the most common site. The basic histology is composed of solid and cystic areas that resemble the enamel organ and that occur primarily in 6 histologic subtypes. The follicular and plexiform subtypes are the most common, followed by the acanthomatous, granular cell, desmoplastic, and basal cell types.[1] Histologic subtypes are not believed to reflect prognosis or biologic behavior and more than one histologic type may be seen in the same tumor.[2] Notable vascularity of the stroma is not commonly considered a feature of ameloblastoma.[3]

Vascularized ameloblastoma has been described in the English language literature under various names (Table I) in 16 reports (18 cases) of "vascular," "hemangiomatous," or "hemangioma-like" ameloblastoma. Early reports described a combination of adamantinoma, ameloblastoma, and hemangioma, noting the relationship between the vascularity of the developing enamel organ and the wide range of vascularity typically seen in ameloblastoma.[4-10] The next 9 case reports began 30 years later.[11-19] We describe here vascularized ameloblastoma, a rarely reported and less recognized histologic subtype, for the purpose of familiarizing clinicians with its features. We present a case of vascularized ameloblastoma and review previously reported lesions, with a focus on the clinical presentation, radiographic features, and microscopic findings to explore the possibility that this represents a distinct subset, with unique clinical and pathologic features that warrant recognition and further study.

CASE REPORT

A 64-year-old female was referred to the oral surgery department by an outside dentist for evaluation and treatment of a large, well-circumscribed, unilocular, radiolucent lesion in the right mandible, extending from the midline to the first molar and showing facial expansion (Figure 1). The lesion had been steadily growing for the previous $1\frac{1}{2}$ years, accompanied by swelling. Incisional biopsy was deferred after aspiration with frank blood return; 10 cc on the first draw and 5 cc on the second draw. The aspiration specimen was sent for cytology, which revealed hemorrhagic fluid with hemosiderin-laden macrophages and marked acute and chronic inflammation. Maxillofacial computed tomography (CT) with contrast was performed, and was interpreted by the radiologist as a $2.7 \times 4.8 \times 2.3$ cm, expansile, low-density mass involving the body of the mandible, with 39.08 Hounsfield units (HU) of blood (within normal range of expected blood), and several floating teeth. Ameloblastoma, dentigerous cyst, and odontogenic carcinoma were therefore considered in the radiographic differential diagnosis. The patient was then taken to the operating room, after being screened for blood type, in case of need for intraoperative transfusion. Before starting the procedure, a 10-cc syringe and an 18-gauge needle were used to aspirate the lesion. The aspiration resulted in frank blood return and a nonpulsatile lesion, and the lesion was noted to shrink in size. Careful dissection encompassing the soft tissue lesion as well as the expanded cortical bone margins was completed. There

Statement of Clinical Relevance

Vascularized ameloblastoma is a rarely reported variation of conventional ameloblastoma. Clinical, radiographic and histologic features of the 18 reported cases showed previous surgery in some cases. FNA could show a bloody return and clinicians should note that this result does not exclude ameloblastoma.

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Table I. Various terms for vascularized ameloblastoma

Case	*Author, year*	*Terminology*
1	Aisenberg, 1950	Adamantinohemangioma
2	Villa, 1953/1960	Ameloblastic hemangioma
3	Lucas et al., 1957	Vascular ameloblastoma
4	Oliver et al., 1961	Hemangioameloblastoma
5	Shklar et al., 1965	Vascular ameloblastoma
6	Gardner, 1966	Ameloblastoma with vascular component
7	Grover et al., 1971	Hemangioblastoma
8	Van Rensberg et al., 2001	Hemangiomatous ameloblastoma
9	Tamgadge et al., 2010	Hemangiomatous ameloblastoma
10	Jois et al., 2012	Hemangioma; ameloblastoma collision tumor
11	Sharma et al., 2012	Hemangiomatous ameloblastoma
12	Sarode et al., 2013	Hemangioameloblastomatous proliferation
13/14	Maheshwari et al., 2013	Vascularized ameloblastoma
15	Kansagari et al., 2015	Hemangiomatous ameloblastoma
16/17	Hegde et al., 2015	Hemangioameloblastoma
18	Venigalla et al., 2018	Hemangiomatous ameloblastoma
19	Current case, 2019	Vascularized ameloblastoma

was no excessive intraoperative bleeding. The lesion was removed by gently separating the thick capsule, which was easily cleaved from bony margins, and the specimen was submitted along with bony fragments for histopathologic examination. The surgical defect was reconstructed with allogenic cancellous bone infused with platelet-rich plasma, and a titanium mesh was adapted and secured with screws to span the buccal defect. The histopathologic results confirmed ameloblastoma with prominent vascularization (Figures 2 and 3). The patient returned 2 years later for follow-up with no evidence of disease.

DISCUSSION

The earliest case report we found in the literature was by Aisenberg in 1950, although this report included a reference to Thoma, who, in 1944, had described adamantinohemangioma as a rare variant of adamantinoma in his classification of odontogenic tumors.[4] Subsequent case reports from 1957 to 1971 used varying terminology.[5,7-10,20,21] Thereafter, the next case was reported 30 years later in 2001.[11] We found a total of 18 cases in 16 articles published to date. Including our case, the average patient age was 34.8 years (range 13−76 years; age not given in 1 case); only 1 case gave the maxilla as the location (location not given in 1 case report); and the female/male ratio was 1:1 (sex not given in 1 case).

The varying terminology seems to reveal the authors' divergent opinions as to the pathologic basis of the vascularity of the lesion: reactive or neoplastic. Aisenberg thought that vascularity was a reflection of the natural vascularity of the enamel organ, although Smith believed that the vascularity of ameloblastoma was variable.[22,23] Others believed that the vascular component represented a neoplastic process and favored the use of a nomenclature reflective of such.[6,7] Some authors did not consider hemangioma to be a neoplastic process.[8] Still others favored the idea that the vascularity represented a degenerative process.[5] We favor the term "vascularized"[16] because it does not imply a separate, vascular neoplasm.

The microscopic features of vascularized ameloblastoma are summarized in Table II. As with conventional ameloblastoma, the plexiform pattern was the most common microscopic pattern. One author noted giant cells in conjunction with new bone formation and hemorrhage.[16] In most cases, the vascular component appears as both dilated channels and extravasated serum and red blood cells seen in cyst-like spaces. Angiogenesis has been the subject of studies of conventional ameloblastoma.[24-26] For example, the microenvironment has been examined and found to show a correlation between macrophage density and microvessel density in ameloblastoma, with different densities seen in the solid/multicystic, unicystic, and desmoplastic types.[26] Seifi et al. looked at the intratumoral and cystic vessels in ameloblastoma and found that a difference in the vessel size and distribution may be a factor in clinical differences in the behaviors of ameloblastoma and keratocyst.[25] In another study, intraepithelial blood vessels in ameloblastoma were evaluated for potential vascular assessment usefulness in predicting clinical behavior.[24] These types of studies in the future may shed light on the nature of vascularized ameloblastoma.

The clinical and radiographic features of vascularized ameloblastoma are summarized in Table III. Only 1 case occurred in the maxilla.[14] Radiographic features varied, but most mirrored the descriptions generally accepted for conventional ameloblastoma. The history of previous surgery was remarkable, in that 7 cases had history of previous extraction or minor surgery or both. Only 2 of 19 cases were specifically described as recurrences in the published reports, and we take this to mean that those cases were diagnosed as conventional ameloblastoma at the initial surgical intervention and that vascularization was subsequently found in the recurrence. The follow-up period in all of the published reports was too short (ranging from 0 to 2 years) to be of value in determining the relationship between vascularization and recurrence. Perhaps further studies may shed light on this question.

Most authors agreed that the vascular component did not seem to have a measurable effect on recurrence. We noted that the total number of cases was small and, therefore, not statistically significant, but future studies

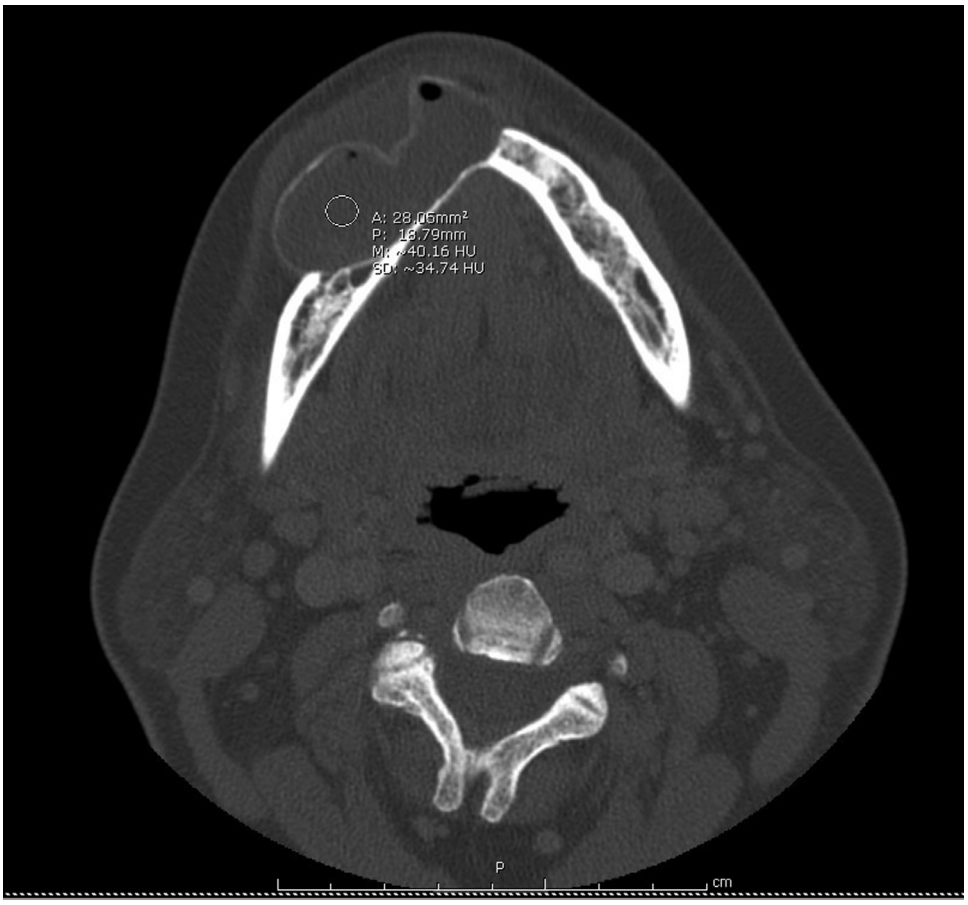

Fig. 1. Computed tomography (CT) image showing expansile lesion of the mandible.

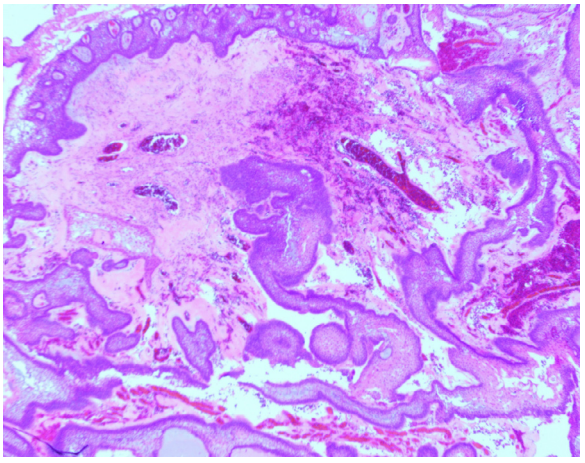

Fig. 2. Low-power view of ameloblastoma epithelium closely associated with vascularized areas (hematoxylin and eosin [H&E] stain; magnification × 40).

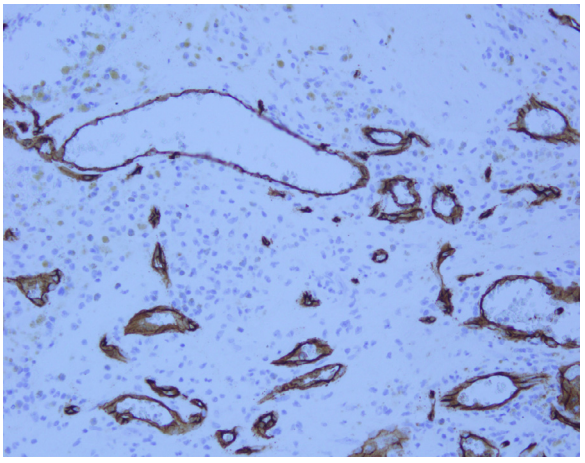

Fig. 3. CD31 immunohistochemical antibody highlighting vascular channels in the same case as Fig. 2 (magnification × 200).

may shed additional information on prognosis. Standardized terminology and recognition in the literature may aid future studies.

None of the previous reports included a description of fine-needle aspiration (FNA) findings, which we considered important in our case. The FNA of the right mandibular cyst in our case revealed hemorrhagic fluid, hemosiderin-laden macrophages, and inflammation (not available for photomicrograph). Because the initial FNA was "bloody" rather than serous, the result indicated the

Table II. Microscopic features of vascularized ameloblastoma

Author, year	*Epithelial component*	*Vascular component*
Lucas et al., 1952	Plexiform and follicular	Dilated capillaries and blood in cysts
Aisenberg, 1950	Adamantinoma	Endothelial lined capillaries and blood in cystic spaces
Villa, 1953	Plexiform ameloblastoma	Coalescing capillaries and blood-filled cavities
Oliver et al., 1961	Simple ameloblastoma	Dilated vascular channels
Shklar et al., 1965	Plexiform ameloblastoma	Endothelial lined and unlined vascular channels
Gardner, 1966	Plexiform ameloblastoma	Dilated capillaries, blood-filled cavities
Grover et al., 1971	Ameloblastoma without stellate reticulum	Endothelial lined lumens, formed blood elements
Van Rensberg et al., 2001	Plexiform ameloblastoma	Endothelial-lined channels, blood-filled spaces, thrombus formation
Tamgadge et al., 2010	Plexiform ameloblastoma	Endothelial-lined channels and blood-filled spaces
Jois et al., 2012	Plexiform ameloblastoma	Cavernous endothelial-lined channels
Sharma et al., 2012	Follicular type ameloblastoma	Endothelial-lined channels and blood-filled spaces
Sarode et al., 2013	Unicystic ameloblastoma	Endothelial-lined vascular spaces and hemangiomatous spaces
Maheshwari et al., 2013	Unicystic ameloblastoma	Giant cells, new bone formation, vascular spaces, hemorrhage
Hegde et al., 2015	Plexiform ameloblastoma and unicystic ameloblastoma	Dilated endothelial-lined blood vessels and extravasated red blood cells
Venigalla et al., 2018	Desmoplastic and plexiform ameloblastoma	Endothelial-lined channels, blood filled spaces and vascularity
Current case	Conventional solid and microcystic ameloblastoma	Endothelial-lined channels and extravasated red blood cells

possibility of a vascular lesion, such as a hemangioma, aneurysmal bone cyst, or arteriovenous malformation. This possibility influenced the differential diagnosis. We believe that clinicians should recognize that a "bloody" return on FNA does not exclude the possibility of ameloblastoma.

When the features of vascularized ameloblastoma are compared with those of conventional ameloblastoma, in spite of the small number of cases, some trends emerge (Table IV). The histologic appearance of the epithelial component and the recurrence rate, based on the existing data, do not seem to be at variance with those of conventional ameloblastoma. It is difficult to directly compare radiographic appearances because of the variations in the descriptive terminology, but the differences do not seem

Table III. Clinical and radiographic features of vascularized ameloblastoma

Author, year	*Age/Gender*	*Location*	*Radiographic description*	*History of previous surgery*	*Follow-up period, finding*
Aisenberg, 1950	48/F	Mandible	Bone destruction	8 years s/P ext #29	2 years, NED
Lucas et al., 1952	45/F	Mandible	"typical ameloblastoma"	None	None
Villa, 1953		Mandible			
Oliver et al., 1961	33/F	Mandible	RL	None	2 years, NED
Shklar et al., 1965	13/M	Mandible	Well defined RL	None	None
Gardner, 1966	76/F	Mandible	RL	3 years s/P ext of mandibular teeth	None
Grover et al., 1971	46/M	Mandible	RL	6 months s/P tooth ext in region	4 weeks, no complications
Van Rensberg et al., 2001	26/F	Mandible	Moderately well-defined, mixed RL/RO	11 years s/P ext #18	None
Tamgadge et al., 2010	31/M	Mandible	Well defined RL	Minor surgery and ext #21	4 months, good healing
Jois et al., 2012	42/M	Mandible	Poorly defined mixed RL/RO	None	2 years, NED
Sharma et al., 2012	15/M	Maxilla	Well defined RL	None	None
Sarode et al., 2013	18/M	Mandible	ML/RL	RCT and Ext #31	None
Maheshwari et al., 2013	51/M	Mandible	RL	Recurrent ameloblastoma	None
	19/M	Mandible	ML/RL	Recurrent ameloblastoma	None
Hegde et al., 2015	18/F	Mandible	ML/RL	None	18 months, NED
	24/M	Mandible	ML/RL	None	1 year, NED
Kasangari et al., 2015	35/F	Mandible	Mixed RO/RL ML/RL	None	None
Venigalla et al., 2018	35/F	Mandible	Mixed RL/RO	Possible tooth extraction	15 months, NED
Present case	64/F	Mandible	UL/RL	none	2 years, NED

EXT, extraction; *F,* female; *M,* male; *ML,* multilocular; *NED,* no evidence of disease or recurrence; *RCT,* root canal therapy; *RL,* radiolucent; *RO,* radiopaque; *UL,* unilateral.

Table IV. Comparison of features of conventional and vascularized ameloblastoma

Feature	*Conventional ameloblastoma*	*Vascularized ameloblastoma*
Epithelial component	Follicular and plexiform	Follicular and plexiform
Prominent vascular component	No	Yes
Radiographic	Multilocular radiolucent or unilocular radiolucent except desmoplastic ameloblastoma	Varies from multilocular radiolucent to mixed radiopaque
Recurrence rate	Varies, but generally regarded as high	Most cases gave a history of previous surgery to the area
Fine-needle aspiration	Serous or serosanguinous	Bloody

clinically significant. However, as a result of the increase in vascularity, vascularized ameloblastoma may show a "bloody return" on FNA, as in our case. A previous history of surgery, which was distinctly present in 7 of the 19 cases reviewed here, may be a contributing factor to the vascularization process. More studies are needed to determine the significance of this theory.

CONCLUSIONS

We reported here a variant of ameloblastoma not often described in the literature. The clinical and pathologic features of the current case were examined together with the features of the 18 previously reported cases of vascularized ameloblastoma. Awareness of this variation is of importance to clinicians because FNA findings may influence operative planning. Additional studies are needed to further clarify the features of this rare variant of ameloblastoma.

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