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Maxillary Ameloblastoma with Orbital Involvement: An Institutional Experience and Literature Review

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Abstract

Purpose—To describe 8 patients with orbital involvement by ameloblastoma and to review the literature on this topic.

Methods—The electronic medical records and pathology databases of the Hospital of the University of Pennsylvania were searched to identify all patients with histopathologically confirmed ameloblastoma diagnosed between 1990 and 2015. PubMed database was searched for all well-documented cases of maxillary ameloblastoma and ameloblastic carcinoma exameloblastoma with orbital involvement published in the English literature. The information collected on the compiled 23 patients included age, sex, clinical presentation, imaging findings, management, tumor histopathologic features, and follow up.

Results—Review of medical records identified 8 patients with orbital involvement by ameloblastoma. Literature search yielded 15 patients with well-documented orbital involvement by ameloblastoma. Most tumors occurred in men (19 of 23, M:F = 4–5:1) with an average age of 56 years. The overall rates of recurrence, visual compromise, death, and confirmed disease-related mortality were 70% (16/23), 26% (6/23), 39% (9/23), and 22% (5/23), respectively. The initial surgical approach correlated with prognosis. The rates of recurrence, orbital exenteration, and mortality in the cohort managed with conservative surgery or partial maxillectomy were 57% (8/14), 29% (4/14), and 50% (7/14), respectively. In contrast, the patients initially managed with a radical resection had substantially lower frequencies of tumor recurrence (2/7, 29%), exenteration (1/7, 14%), and death (1/7, 14%). Malignant transformation to ameloblastic carcinoma occurred in the setting of recurrent disease in 3 patients and in 1 patient with prolonged duration of symptoms, suggestive of a long-standing tumor.

Conclusions—Maxillary ameloblastoma can rarely involve the orbit, leading to significant ocular morbidity and occasional mortality. Prompt radical resection of the tumor has the potential to decrease the likelihood of recurrence and visual compromise, and can improve survival.

Introduction

Ameloblastoma is an uncommon odontogenic epithelial neoplasm, comprising approximately 1% of all cysts and tumors of the jaws.¹ Eighty percentage of ameloblastomas arise in the mandible, but involvement of the maxilla is rare.² While histologically benign, ameloblastoma is characterized by locally malignant behavior with high propensity for

recurrence, local invasiveness, and the potential for direct involvement of vital structures, leading to local morbidity and mortality.^{1,3–11} Prolonged tumor duration and multiple recurrences following surgical intervention have been associated with a rare phenomenon of metastases of the histologically benign-appearing ameloblastoma, so called metastasizing ameloblastoma, which is frequently lethal.^{2,12} In addition, long-standing and recurrent ameloblastoma has been shown to rarely transform into aggressive ameloblastic carcinoma.^{3,5,13}

The current gold standard of care for ameloblastoma is prompt surgical excision with margin clearance.² Compared with its mandibular counterpart, maxillary ameloblastoma is inherently more difficult to treat due to extensive disease at the time of diagnosis and proximity to vital structures.^{8–10} Thus, collaborative surgical care is frequently required, which includes the oral and maxillofacial surgeons, otolaryngologists, plastic surgeons, and ophthalmologists.^{7,9,11} Understanding of the biologic behavior of this tumor, the signs and symptoms which herald orbital involvement, and the recommended current approach to care, are necessary to appropriately manage patients with this potentially lethal neoplasm. To the best of our knowledge, only 3 patients with orbital involvement by maxillary ameloblastoma have been described in detail in ophthalmic literature.^{7,11} Herein, the authors describe the 25-year experience with this rare neoplasm at a single institution and review the literature on this topic.

Methods

After the institutional review board approval was obtained for this study, the electronic medical records and pathology databases of the Hospital of the University of Pennsylvania were searched to identify all patients with histopathologically confirmed diagnosis of ameloblastoma between January 1, 1990 and July 1, 2015. PubMed database was searched for all cases of maxillary ameloblastoma and ameloblastic carcinoma ex-ameloblastoma with orbital involvement published in the English literature (keywords: ameloblastoma, adamantinoma, maxilla/maxillary, ameloblastic carcinoma, orbit, eye). The information collected included the patient age, sex, clinical presentation, imaging findings, management, tumor histopathologic findings, and follow up.

Results

Review of the Hospital of the University of Pennsylvania medical records identified 101 patients with histopathologically confirmed diagnosis of ameloblastoma. Of these, 26 (25.7%) involved the maxilla, and the remainder originated in the mandible. Orbital involvement was noted in 8 patients (31%) with maxillary ameloblastoma. PubMed literature search yielded 15 patients with well-documented orbital involvement by ameloblastoma.^{3–11} Clinical characteristics, histopathology, management, and follow-up data of the compiled 23 patients are summarized in Table. Most tumors occurred in men (19 of 23, M:F = 4–5:1). While the majority of ameloblastomas were diagnosed during the fifth and sixth decades (average 56 years, median 63 years), there was a wide age distribution (range: 15–81 years). The initial symptoms were most commonly related to the obstruction of the maxillary sinus by a mass (nasal congestion or discharge [8/17, 47%], facial swelling

over the maxilla [6/17, 35%], upper tooth pain [2/17, 12%], loose tooth [1/17, 6%], and upper gum ulcer [1/17, 6%]). Involvement of the orbit was manifested by proptosis (8/17, 47%), decreased vision (4/17, 24%), hypoesthesia in the distribution of ophthalmic and maxillary branches of trigeminal nerves (3/17, 18%), diplopia/blurred vision (3/17, 18%), and limitation of ocular motility (1/17, 6%). Approximately half of the patients had orbital involvement at the time of presentation [11/23 patients (48%)], while the remainder developed orbital involvement by a recurrent neoplasm. The diagnostic modalities at the time of initial evaluation and follow up included bone dental X-rays (pantomography) and plain films in earlier studies, and CT scans and MRI in later studies. In the current series, all 8 patients underwent the initial diagnostic testing and annual postsurgical follow-up monitoring with both CT scan and MRI. The classic radiographic appearance of ameloblastoma at the time of initial presentation was that of an expansile multiloculated maxillary mass with scalloped margins, associated with tooth resorption and extension into the adjacent maxillary sinus and nasal cavity (Fig. 1A).

The overall length of follow up was 9.9 years (range: 0.5–31 years). Patients managed initially with conservative surgery (curettage, enucleation, conservative excision, wide local excision) had the longest average follow up of 14.3 years. Those managed with initial maxillectomy were followed on average for 6.5 years. The average time to recurrence was 3.8 years. Patients managed initially by conservative excision had on average shorter time to recurrence (3.4 years) when compared with those managed with maxillectomy (4.5 years). The overall rates of recurrence, visual compromise, death, and confirmed disease-related mortality were 70% (16/23), 26% (6/23), 39% (9/23), and 22% (5/23), respectively.

Initial surgical approach correlated with risk of recurrence, local disease aggressiveness, and mortality. Eleven patients (48%) were initially managed with a conservative surgery, with subsequent tumor recurrence in all patients, orbital soft tissue invasion in approximately half of the patients (5/11, 45%), optic canal and chiasm infiltration in 2 patients (2/11, 18%) and nasolacrimal duct involvement in 1 patient, (1/11, 9%), leading to visual compromise in 4 patients (4/11, 36%), orbital exenteration in 2 patients (2/11, 18%), and death in more than half of the patients (6/11, 55%). Three patients (13%) were initially managed with partial maxillectomy, with subsequent tumor recurrence in the orbital soft tissues of all patients, leading to orbital exenteration in 2 patients (2/3, 67%) and death in 1 patient (1/3, 33%). The overall frequencies of recurrence, orbital exenteration, and mortality in the cohort managed with conservative surgery or partial resection were 57% (8/14), 29% (4/14), and 50% (7/14), respectively. In contrast, 7 patients (30%) initially managed with a radical resection (total or radical maxillectomy) had substantially lower frequencies of tumor recurrence (2/7, 29%), exenteration (1/7, 14%), and death (1/7, 14%). Two patients received external beam radiotherapy as a sole treatment modality due to unresectable disease at presentation; one of these patients died with disease. Five patients received adjuvant external beam radiotherapy as an initial or subsequent intervention. Of these, 2 patients died of disease, and 1 is presumably dead of disease. Two patients were managed with adjuvant chemotherapy for recurrent advanced tumors. One succumbed to disease, and another is presumably dead of disease.

Information on adequacy of surgical excision was available on 11 patients, 3 from reports by Zwahlen and Grätz¹⁰ and Leibovitch et al.,¹¹ and 8 from this series. With the exception of patient 2 in this series (Table), all other tumors were excised with clear margins during initial or subsequent treatment. Recurrence despite pathologically confirmed margin clearance occurred in 2 of 11 (18%) patients, 1 reported by Zwahlen and Grätz¹⁰ and 1 from this series (patient 7, Table).

Histopathology data was available on 22 patients. Follicular and plexiform histologic patterns were most commonly encountered, each accounting for approximately half of cases (follicular: 10/22, 45%; plexiform: 9/22, 41%). Basal cell-like ameloblastoma (2/22, 9%) and mixed ameloblastoma (1/22, 4.5%) were the other 2 histologic patterns noted. All histologic patterns were comparable in aggressiveness. Visual compromise was noted in 4 patients with follicular ameloblastoma (40%), 3 patients with plexiform ameloblastoma (33%), and 1 patient with basal cell-like ameloblastoma (50%). Two patients with follicular ameloblastoma (20%) and 2 patients with plexiform ameloblastoma (22%) succumbed to disease. Progression to ameloblastic carcinoma occurred in 4 of 23 patients (17%), from pre-existing follicular ameloblastoma in 2 cases, plexiform ameloblastoma in 1 case (patient 2, Table, Fig. 1), and basal cell type ameloblastoma in 1 case (patient 7, Table, Fig. 2). Malignant transformation occurred in a setting of recurrent disease in 3 patients. One patient from the current series with a prolonged history of nasal congestion, suggestive of a long-standing tumor, presented initially with a focus of malignant transformation in an otherwise histologically benign neoplasm (patient 2, Table, Fig. 1).

Discussion

Ameloblastoma is an uncommon benign, slow-growing, but locally invasive neoplasm of odontogenic origin, which can infrequently involve the maxilla and, eventually, adjacent structures, such as the orbit.^{1–11} Male predilection has been reported in some series of maxillary ameloblastomas, and is prominent in patients with orbital involvement.¹⁰ Maxillary ameloblastoma has been shown to occur at an older age than its mandibular counterpart (4th–5th decade vs. 3rd–4th decade), potentially due to delay in diagnosis.^{2,10} The patients with orbital involvement are even older (5th–6th decade), likely reflecting the disease duration and the natural, locally aggressive course.

Maxillary ameloblastomas have been traditionally regarded as inherently more aggressive due to their origin in the thin and fragile bone of the maxilla, which lacks the thick confining cortical plates of the mandible, allowing unimpeded spread of the tumor to surrounding vital structures.^{8–10} Since the current gold standard of care for ameloblastoma is complete surgical excision, aggressive surgical resection is advocated in patients with maxillary ameloblastoma to ensure recurrence-free outcome.^{2,14} For tumors involving the orbital floor only, total maxillectomy has been recommended. When orbital soft tissues are involved, total maxillectomy with orbital exenteration are advocated. Total maxillectomy with anterior skull base resection and orbital exenteration have been suggested for tumors involving the skull base.¹⁴ Incorporation of these guidelines is seen in the more recent approach to care of patients in this series, with a substantially decreased risk of tumor recurrence, local morbidity, and mortality.

Various approaches have been advocated to ensure completeness of surgical resection. Traditionally, preoperative imaging has been utilized to guide surgical excision. In the maxilla, preoperative MRI in addition to the standard CT scan have been recommended to highlight the extent of soft tissue involvement.^{2,15} Intraoperative imaging has been advocated by some experts as a superior modality to assess surgical margins.¹⁵ Although preoperative and intraoperative imaging greatly aids in ensuring completeness of resection, ameloblastoma specimens generally demonstrate 2mm to 8mm microscopic extension beyond the boundaries of radiographic margins. Thus, the recommended surgical margins are 1 cm to 2 cm beyond the radiographic tumor margins.² Finally, intraoperative frozen section consultation has been advocated for immediate assessment of tumor margins, although the accuracy in diagnosis of ameloblastoma has been limited by sampling and by the technical difficulties encountered in performing frozen sections on bone.^{2,15} This series highlight the trend for more frequent use of intraoperative frozen section in recent years, but are limited by the relatively short patient follow-up in prediction of its utility.

The data on radiotherapy and chemotherapy is controversial due to absence of prospective randomized studies, although most experts believe that these treatment modalities are not effective in management of ameloblastoma.^{2,16} Some studies advocate for adjuvant radiotherapy in ameloblastic carcinoma, although the data are mixed.²

Several microscopic patterns of ameloblastoma are recognized, which include follicular, plexiform, acanthomatous, basal cell-like, desmoplastic, and granular cell. The patterns can coexist in a tumor, which is defined by the most predominant pattern present.^{2,17,18} Follicular and plexiform ameloblastomas are the most commonly encountered histologic patterns, which is also the case in the tumors with orbital involvement.^{17,18} Several studies noted increased risk of recurrence in follicular ameloblastoma when compared with the plexiform variant.^{17,18} This was not observed in this series, potentially due to a relatively small patient number.

Ameloblastoma is, in essence, a lifelong disease. In approximately half of the patients with recurrent tumors, the recurrences have been observed more than 5 years after the initial diagnosis, and have been described as late as 33 years.¹⁷ Thus, the patients with ameloblastoma require continued monitoring with clinical exams and imaging studies.^{17,18} This is particularly vital in patients with maxillary ameloblastoma and orbital involvement. In addition to the higher risk of visual loss and mortality from local recurrence of ameloblastoma, the patients with orbital ameloblastoma appear to have higher risk of developing ameloblastic carcinoma ex-ameloblastoma (17% vs. traditionally reported risk of 2%).²

While the dire outcomes of patients with orbital involvement by ameloblastoma are most likely related to the more advanced disease at presentation and inadequacy of surgical excision, the recent data suggest that maxillary ameloblastomas may have a different mutation profile when compared with the mandibular counterparts, which may also account for their intrinsically more aggressive biologic behavior.²

In summary, maxillary ameloblastoma is a locally aggressive neoplasm with a potential to involve the orbit and the cranium, leading to significant ocular morbidity and mortality. A collaborative approach is advocated in management of patients with maxillary ameloblastoma. Thus, orbital surgeons should be aware of the biologic behavior of this tumor and current management recommendations.

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FIG. 1.

Patient 2. Ameloblastic carcinoma ex-ameloblastoma. A, Coronal CT scan demonstrates a heterogeneous soft tissue mass, originating from the maxilla, involving the right maxillary sinus and the orbital roof, and extending into the right nasal cavity. B, Histopathology of the biopsied mass demonstrates both benign appearing interweaving bands of plexiform ameloblastoma (arrow) and the adjacent solid growth of pleomorphic, poorly differentiated, mitotically active cells, consistent with ameloblastic carcinoma ex-ameloblastoma (asterisk; stain, hematoxylin-eosin; original magnification $\times 25$). C, Ki-67 immunostain highlights the increased nuclear proliferative activity in a malignant focus (antibody, ki-67; original magnification $\times 25$).

FIG. 2.

Patient 7. Ameloblastic carcinoma ex-ameloblastoma. A, Histopathology of the original tumor excision demonstrates basaloid nests of cells with peripheral reversely polarized, palisaded nuclei and central stellate reticulum, consistent with basal cell-like ameloblastoma. Central focus of squamous differentiation is present (*), consistent with acanthomatous pattern (stain, hematoxylin-eosin; original magnification $\times 50$). B, Recurrent neoplasm 5 years later is composed of poorly differentiated nests of epithelial cells with pleomorphic nuclei and mitotic activity (stain, hematoxylin-eosin; original magnification $\times 25$). C, Orbital invasion is characterized by bands of cells with hyperchromatic nuclei within a markedly desmoplastic stroma (stain, hematoxylin-eosin; original magnification $\times 25$).

Table

Author (year), patient number	Age,* Sex	Symptoms/signs, [†]	Histopathology	Sites of invasion outside of maxilla [‡]	Management [§]	Disease duration (years)
Kyriazis et al. (1971) ³	73 F	N/A	Ameloblastic CA, ex-follicular ameloblastoma	Orbital soft tissue (5); MCF, BOS, petrous apex (8)	Partial maxillectomy (0); WLE (3, 5)	657 pt
Shaw and Katsikas (1973) ⁴	81 M	Facial swelling, discharge, proptosis (0)	Plexiform ameloblastoma	Orbital floor (0)	XRT	Died with disease, 4
	77 F	Facial swelling, proptosis (0)	Follicular ameloblastoma	Orbital floor (0)	XRT, conservative resection (0); partial maxillectomy (2)	No recurrence, 3½
	37 M	Nasal congestion (0)	N/A	Orbital floor (0)	Conservative resections (0–8); total maxillectomy (7)	No recurrence, 12
Daramola et al. (1980) ⁵	20 M	N/A	Ameloblastic CA, ex-follicular ameloblastoma	Orbital floor (2); frontal sinus, pulmonary metastases (5)	WLE (0); total maxillectomy (3); XRT, chemotherapy (5)	Presumed dead, 5
Komisar (1984) ⁶	63 M	N/A	Plexiform ameloblastoma	Orbital floor and BOS (2)	Curettage (0); total maxillectomy (2)	Presumed dead, 3
Weiss et al. (1985) ⁷	72 M	Loose tooth (0), blurred vision, proptosis, LOM (5)	Plexiform ameloblastoma	Orbital soft tissue (5); MCF (6)	WLE (1); partial maxillectomy (2); XRT (5); radical maxillectomy, ethmoidectomy, sphenoidectomy, orbital exenteration (5½); craniotomy and debulking (6)	Died of disease, 7
Bredenkamp et al. (1989) ⁸	53 M	Nasal congestion, decreased VA, proptosis, hypoesthesia (0)	Mixed	Orbital soft tissue, MCF, BOS (0)	XRT	Alive with disease, 1
	15 M	Facial swelling (0)	Plexiform ameloblastoma	Orbital soft tissue (2); BOS (5); MCF (14)	Maxillary tumor enucleation (0); radical maxillectomy, orbital exenteration (2); XRT (4); chemotherapy (8); debulking (8– 14)	Died of disease, 15
	37 F	Facial swelling (0), loss of vision (8)	Follicular ameloblastoma	Palate, nasopharynx, orbital floor and apex, BOS, internal carotid artery (8)	Curettage (0); partial maxillectomy (1); XRT (2); completion maxillectomy (7); multiple WLE (8)	Died of disease, 8
	43 M	Tooth ache (0)	Follicular ameloblastoma	Orbital floor (3); nasopharynx (4); palate, sphenoid, BOS (7)	Total maxillectomy (0); WLE (3); repeated cryotherapy (4–11)	Presumed dead, >11
Sato et al. (1994) ⁹	68 M	Facial swelling (0) Maxillary ulcer (0), proptosis, diplopia, hypoesthesia (9), decreased VA (13)	Follicular ameloblastoma	Orbital floor (0), orbital soft tissue (9); optic canal, MCF, ACF (11)	Radical maxillectomy (0); debulking (9); orbital exenteration (10); craniotomy and debulking (11)	Alive with disease, 12
Zwahlen and Grätz (2002) ¹⁰	44 M		Follicular ameloblastoma	Orbital floor, BOS (6); orbital soft tissue, mandible, extensive BOS infiltration	En block resection (0); partial maxillectomy, ethmoidectomy (6); radical maxillectomy,	Died of disease, 13

Author (year), patient number	Age,* Sex	Symptoms/signs [†]	Histopathology	Sites of invasion outside of maxilla [‡]	Management [§]	Disease duration (years)
Leibovitch et al. (2006) ¹¹	57 M	Diplopia, globe displacement, decreased VA (3)	Follicular ameloblastoma	(9–11); optic chiasm, lung and heart metastases (13)	sphenoidectomy (8); XRT (9), palliative debulking (11–13)	No recurrence, 4½
	43 M	Diplopia, globe displacement, decreased VA (30)	Plexiform ameloblastoma	Orbital soft tissue (3) MCF, temporal area, orbital soft tissue (30)	Partial maxillectomy, XRT (0); orbital exenteration, partial zygomatic bone resection (3); Multiple resections (0–30); skull base and orbital tumor resection (30)	No recurrence, 30½
Milman (2015)						
Patient 1	67 M	Nasal congestion (0)	Plexiform ameloblastoma	Orbital floor, nasopharynx (0)	Radical maxillectomy, skull base resection, FESS (0)	No recurrence, 6
Patient 2	73 M	Nasal congestion (0)	Ameloblastic CA, ex-plexiform ameloblastoma	Orbital floor, nasopharynx (0)	Total maxillectomy, skull base resection, XRT (0)	No recurrence, 2
Patient 3	71 M	Nasal congestion (20)	Follicular ameloblastoma	Orbital floor (20), nasolacrimal duct (27)	Conservative resection (0, 9, 14), partial maxillectomy (20), FESS (27)	No recurrence, 30
Patient 4	73 M	Nasal congestion (0)	Plexiform ameloblastoma	Orbital floor, nasopharynx (0)	Total maxillectomy, skull base resection (0)	No recurrence, 1
Patient 5	63 M	Facial swelling (0)	Basal cell-like ameloblastoma	Orbital floor, nasopharynx (0)	Total maxillectomy, skull base resection, turbinectomy (0)	No recurrence, ½
Patient 6	61 M	Tooth ache (0)	Plexiform ameloblastoma	Orbital floor (0)	Total maxillectomy, skull base resection (0)	No recurrence, ½
Patient 7	63 F	N/A	Ameloblastic CA, ex-basal cell-like ameloblastoma	Orbital floor (0); zygoma (4); orbital soft tissue, temporal dura (5); mandible (7)	Partial maxillectomy (0); wide resection (4); skull base resection, orbital exenteration (5); total mandibulectomy, neck dissection (7)	No recurrence, 9
Patient 8	38 M	Nasal congestion (0), hyposesthesia (8), proptosis (24)	Follicular ameloblastoma	Orbital floor (8); orbital soft tissue (24)	Conservative resection (0), partial maxillectomy (1), ethmoidectomy (2), orbital floor resections (8, 10, 18); orbital soft tissue resection (24)	No recurrence, 31

* Age and symptoms at the time of diagnosis.

[†]Number in parenthesis indicates number of years after diagnosis the symptoms/signs of disease developed.

[‡]Number in parenthesis indicates number of years after presentation that anatomic site became involved.

[§]Number in parenthesis indicates number of years after presentation the treatment was undertaken.

BOS, base of skull; CA, carcinoma; FESS, functional endoscopic sinus surgery; F, female; LOM, limitation of ocular motility; M, male; MCF, middle cranial fossa; N/A, not available; VA, visual acuity; WLE, wide local excision; XRT, external beam radiotherapy.