Primary Ameloblastoma of the Sinonasal Tract
A Clinicopathologic Study of 24 Cases

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BACKGROUND. Ameloblastomas are locally aggressive jaw tumors with a high propensity for recurrence and are believed to arise from the remnants of odontogenic epithelium. Extraglandular ameloblastomas are unusual and primary sinonasal tract origin is extraordinarily uncommon.

METHODS. Twenty-four cases of ameloblastoma confined to the sinonasal tract were retrieved from the Otorhinolaryngic-Head & Neck Pathology and Oral-Maxillofacial Pathology Tumor Registries of the Armed Forces Institute of Pathology between 1956 and 1996.

RESULTS. The patients included 5 females and 19 males with an age range of 43–81 years, with a mean age at presentation of 59.7 years. The patients presented with an enlarging mass in the maxillary sinus or nasal cavity (n = 24), sinusitis (n = 9), or epistaxis (n = 8). Unilateral opacification of the maxillary sinus (n = 12) was the most common radiographic finding. Histologically, the tumors exhibited the characteristic features of ameloblastoma, including peripherally palisaded columnar cells with reverse polarity. The majority of the tumors showed a plexiform growth pattern. Fifteen tumors demonstrated surface epithelial derivation. Surgical excision is the treatment of choice, ranging from conservative surgery (polypectomy) to more aggressive surgery (radical maxillectomy). Five patients experienced at least 1 recurrence, usually within 1 year of initial surgery. With follow-up intervals of up to 44 years (mean, 9.5 years), all 24 patients were alive without evidence of disease or had died of unrelated causes, without evidence of disease.

CONCLUSIONS. Primary ameloblastoma of the sinonasal tract is rare. In contrast to their gnathic counterparts, sinonasal tract tumors have a predilection for older age men. Therapy should be directed toward complete surgical resection to prevent local tumor recurrence. Cancer 1998;82:667–74. © 1998 American Cancer Society.

KEYWORDS: ameloblastoma, nasal cavity, paranasal sinuses, treatment, prognosis.

Ameloblastomas are locally aggressive jaw tumors with a high propensity for recurrence that are believed to arise from remnants of odontogenic epithelium, lining of odontogenic cysts, and the basal layer of the overlying oral mucosa. Suggested sources for the odontogenic epithelium include cell rests of the dental lamina, an enamel organ, the lining of an odontogenic cyst, basal cells of the oral mucosa, or heterotopic embryonic organ epithelium. Ameloblastomas can occur in either the maxilla or mandible at nearly any age, but most frequently are discovered as a painless expansion in the mandible of patients in their 20s–40s. The age range is broad and the mean age of occurrence has varied from 35–45 years. Gender or race predilection in gnathic ameloblastomas has not been demonstrated.

Approximately 15–20% of ameloblastomas have been reported to originate in the maxilla with just 2% arising anterior to the premolars. There are numerous studies documenting the presence of
ameloblastomas within the sinonasal cavity. In the majority of these reports, the tumor was found to have originated from the maxilla. However, rare case reports document true primary sinonasal ameloblastomas without connection to gnathic sites. It is due to the rarity of primary sinonasal tract ameloblastoma that this study was undertaken. Our goal was to better characterize the clinicopathologic features of sinonasal tract ameloblastomas and to determine the probable histogenesis of this tumor. To the best of our knowledge, this represents the single largest report of primary sinonasal tract ameloblastomas.

MATERIALS AND METHODS
Twenty-four cases of ameloblastoma with primary involvement of the sinonasal tract were retrieved from the files of the Otolaryngologic-Head & Neck Pathology and Oral-Maxillofacial Pathology Departments of the Armed Forces Institute of Pathology (AFIP). These cases represent consultative material submitted between 1956 and 1996 from military, Veterans Administration, and civilian hospitals. Of 19,658 sinonasal tract tumors seen in consultation between 1970 and 1996, 21 (0.11%) were diagnosed as ameloblastomas. In contrast, ameloblastomas comprised 43.1% of all oral cavity, mandibular, and maxillary odontogenic cysts or tumors accessioned to the AFIP over the same time period. Hematoxylin and eosin stained histologic slides were reviewed with characteristic histologic features, precluding the necessity for histochemical, immunohistochemical, or electron microscopic studies. Clinical and demographic data were summarized from the admitting history, physical examination, radiographic study reports, and pathology requisitions provided by the contributing facilities. Follow-up data regarding patient outcome was obtained wherever possible. This included 1) a description of the treatment rendered (both initial and subsequent, whether surgery, radiation, or chemotherapy); 2) radiographic or clinical evidence to verify the site of origin; 3) recurrence data; and 4) morbidity for all cases. Attention was centered on the review of available imaging studies and/or radiology reports to determine the exact anatomic location and extension of the tumor.

RESULTS
Clinical
The clinical features are detailed in Table 1. In brief, the patients included 19 males and 5 females, demonstrating a male predilection of 3.8:1. The age at presentation ranged from 43–81 years, with an overall mean age at presentation of 59.7 years. This average age was approximately about 15–25 years later than in patients with ameloblastoma occurring within the jaws. The patient’s race was documented in 21 of the 24 cases. There were 19 whites and 2 African-Americans.

The patients usually presented with a mass lesion and nasal obstruction (n = 15). Additional signs and symptoms included sinusitis (n = 9), epistaxis (n = 8), facial swelling, dizziness, and headaches. The duration of symptoms ranged from 1 month to several years. Nine of the 24 ameloblastomas involved only the nasal cavity (including the nasal septum, lateral wall, middle or superior turbinate), 6 tumors were confined to the paranasal sinuses (maxillary, frontal, ethmoid, or sphenoid) and 9 involved both the nasal cavity and the paranasal sinuses at presentation.

In contrast to the characteristic multilocular and radiolucent presentation of ameloblastomas within the jaws, the sinonasal lesions most often were described radiographically as solid masses or opacifications filling the nasal cavity, maxillary sinus, or both (Fig. 1A) Bone destruction, erosion, and remodeling (remnant of bony shell delimiting the lesion as it grew) was noted in a minority of cases (Fig. 1B). Primary origin in, or continuity with, the maxillary alveolar process could not be demonstrated in any of the cases examined.

Pathologic Features
On gross examination, the tissue specimens ranged in size from several millimeters to 9.0 cm in greatest aggregate dimension. Although several of the lesions confined to the nasal cavity had retained a polyoid appearance (Fig. 2), most of the tissue had been fragmented during surgical harvest. The tissue most frequently was described as predominantly solid in appearance with glistening gray-white, pink, or yellow-tan color and a consistency varying from rubbery to granular. The lesions were not described as cystic. Residual bone of the sinonasal cavity was present in a number of the specimens.

By light microscopic examination, the plexiform pattern, comprised of a network of long anastomosing cords of odontogenic epithelium, was the sole or predominant histologic pattern in 22 of 24 cases (92%) (Fig. 3A). The epithelial strands are bounded at the periphery by a layer of columnar cells exhibiting hypochromatic, palisaded, and reverse polarized nuclei, along with subnuclear cytoplasmic vacuolization (Fig. 3B). The stellate reticulum-like component associated with the other patterns of ameloblastoma often is less conspicuous in association with the plexiform histologic type. The acanthomatous pattern, characterized by squamous metaplasia and keratin formation of the central portions of the epithelial islands, was the next most common histologic pattern observed, but was limited to a secondary or focal component (Fig. 3C). In two patients, the tumor presented with a predomi-
nantly follicular histologic pattern characterized by islands of epithelium resembling enamel organ epithelium. In 15 cases, the ameloblastomatous proliferation could be observed arising in direct continuity with the intact sinonasal surface mucosal epithelium (Fig. 4). In the remaining nine cases, the surface epithelium was not identifiable due to ulceration or sampling, precluding the identification of an association between the ameloblastomatous proliferation and the sinonasal surface epithelium.

Other histologic changes identified included the presence of squamous metaplasia of the surface respiratory epithelium in areas adjacent to the ameloblastomatous proliferation, and a mixed chronic inflammatory cell infiltrate with edematous changes within the lamina propria.

**Treatment and Prognosis**

Surgical excision was the treatment of choice in all cases. The type and extent of surgery varied per individual case and encompassed conservation surgery (i.e., polypectomy) and more aggressive surgical procedures, including Caldwell-Luc resection, lateral rhinotomy, and partial or radical maxillectomy. Radiation
was used in conjunction with maxillectomy in the treatment of one patient (Case 2) after the third recurrence. Five patients (21%) experienced at least 1 recurrence. Recurrence of the tumor generally occurred within 1 to 2 years of the initial procedure but 1 patient (Case 9) did not experience recurrence until 13 years after his initial surgery. The histologic appearance of all recurrent tumors was identical to that of the primary neoplasm. Overall treatment success correlated most positively with complete surgical eradication when performed in conjunction with thoroughly detailed radiographic imaging.

Follow-up was available for 23 of 24 patients (96%), all of whom were either alive without evidence of disease or had died of unrelated causes without evidence of recurrence. Follow-up periods ranged from 1–44 years (average, 9.5 years). One patient (Case 3) was lost to follow-up.
Our findings parallel those of the literature with the average age at presentation in the late 6th decade of life (59.7 years) and a clinical presentation of sinonasal-related symptoms, including obstruction and epistaxis. None of our patients presented prior to the fifth decade of life and almost all the patients were men. In contrast to sinonasal tumors, ameloblastomas of the oral cavity typically occur in younger age patients (15–25 years younger) without gender predilection. We are unsure why the sinonasal cavity ameloblastomas show a preference for older age men. The gender predilection most likely is a chance occurrence. An explanation for the older age at onset could be that the sinonasal ameloblastomas require a longer period of time before attaining sufficient size to present with symptoms. These tumors may have been present at an earlier age but remain clinically silent or produce nonspecific symptoms (e.g., sinusitis) until they are large enough to become clinically evident. This is entirely speculative but we do not have another explanation for the unusual demographics associated with sinonasal ameloblastomas.

DISCUSSION

Ameloblastomas are epithelial-derived odontogenic tumors that typically originate in jaw bones, primarily involving the mandible and less often the maxilla. Ameloblastomas originating separate from normally situated odontogenic epithelium represent a rare occurrence. Included among the extragnathic sites of origin of ameloblastomas is the sinonasal tract. Previous documentation of sinonasal tract ameloblastomas include those case reports in which the tumors were identified as a primary sinonasal tract lesion without extension from a gnathic ameloblastoma. In contrast, Tsaknis and Nelson reported 24 cases of maxillary ameloblastomas that included patients whose tumors were identified clinically extending into the sinonasal region from a primary gnathic origin.

Previous case reports of primary sinonasal tract ameloblastomas indicate that these tumors primarily affect individuals in the sixth to eighth decades of life presenting with nasal obstruction, sinusitis, and epistaxis. Our findings parallel those of the literature with the average age at presentation in the late 6th decade of life (59.7 years) and a clinical presentation of sinonasal-related symptoms, including obstruction and epistaxis. None of our patients presented prior to the fifth decade of life and almost all the patients were men. In contrast to sinonasal tumors, ameloblastomas of the oral cavity typically occur in younger age patients (15–25 years younger) without gender predilection. We are unsure why the sinonasal cavity ameloblastomas show a preference for older age men. The gender predilection most likely is a chance occurrence. An explanation for the older age at onset could be that the sinonasal ameloblastomas require a longer period of time before attaining sufficient size to present with symptoms. These tumors may have been present at an earlier age but remain clinically silent or produce nonspecific symptoms (e.g., sinusitis) until they are large enough to become clinically evident. This is entirely speculative but we do not have another explanation for the unusual demographics associated with sinonasal ameloblastomas.

The embryologic derivation of the sinonasal tract and odontogenic apparatus is closely related. The sinonasal tract arises from the ectodermally derived nasal pits that invaginate to cover the oronasal membrane, conchae, primary and secondary palatine processes, and diverticula of the lateral nasal wall. The odontogenic apparatus is a combination of an endophytic proliferation of the basal layer of the ectodermally derived oral cavity epithelium and the mesodermally derived mesenchyme. The sinonasal tract and oral cavity communicate freely until closure of the palate shelves. Although hypothetical, it appears quite likely that this embryologic approximation allows the sinonasal tract mucosa either to incorporate odontogenic epithelium or to acquire cells capable of odontogenesis during development.

The epithelial source of origin for gnathic ameloblastomas still is being debated. Although there are extragnathic ameloblastomas that have been shown to have arisen from misplaced odontogenic rests, there was no evidence in any of our cases of the ameloblastomas arising from a preexisting odontogenic lesion. When considering the possible histogenesis of these sinonasal tract tumors, parallels can be made with peripheral ameloblastomas, which also are believed to originate outside the boundaries of the odontogenic apparatus. In the early 1900s, Bakay proposed the basal cell layer of the surface epithelium as the origin of these peripheral ameloblastomas. Approximately 50 years later, Stanley and Krogh suggested odontogenic epithelial rests outside the jawbone proper as the progenitor cell for peripheral ameloblastomas. In addition, Gardner grouped peripheral
FIGURE 3. (A) Plexiform histologic pattern of ameloblastoma with back-to-back anastomosing cords of epithelium. (B) The columnar peripheral cells with reverse polarity of their nuclei is the most common and recognizable histologic feature of ameloblastoma. Basal cytoplasmic vacuolization and hyperchromasia of the nuclei are additional features. (C) Squamous metaplasia within the center of the ameloblastoma islands is characteristic of the acanthomatous growth pattern.
Ameloblastomas occur after some inductive process on the sinonasal epithelium that results in the neoplastic transformation of retained or acquired odontogenic cells toward ameloblastomatous differentiation. The presence of chronic sinusitis and squamous metaplasia in the areas adjacent to the ameloblastoma could be that initiating event. An argument against this proposal would be that, if true, other types of odontogenic tumors also should be found as primary sinonasal tract neoplasms, but the reality is that this occurs rarely. Alternatively, the ameloblastomatous epithelium could have originated in the submucosa and secondarily extended to involve the surface epithelium rather than originating from this epithelium. However, we could not identify any cell source, such as odontogenic dental lamina, within the submucosa that might represent the source for the development of these tumors. Furthermore, in our departments’ collective experience, odontogenic remnants rarely, if ever, are found in sinonasal mucosal tissues. Although the surface epithelium appears to represent the likely site of origin, the histogenesis for the primary sinonasal ameloblastomas remains unknown.

Given the classic histologic features of these tumors, the differential diagnosis is limited. Of primary importance is to exclude extension into the sinonasal tract from a primary gnathic ameloblastoma. The only other consideration might be a craniopharyngioma. Craniopharyngiomas arise from Rathke’s pouch in the area of the pituitary gland. Histologically, craniopharyngiomas are epithelial neoplasms comprised of centrally situated stellate cells with small nuclei and clear cytoplasm surrounded by a row of basaloid-appearing columnar cells with polarized nuclei in a palisaded arrangement. Degenerative necrobiotic changes, such as ghost cells and calcification, can be identified in the tumor. These features closely resemble the appearance of gnathic ameloblastomas. However, the clinical features of craniopharyngiomas markedly contrast with those of sinonasal tract ameloblastomas so that the lesions should be readily separable.

Primary sinonasal tract ameloblastomas are uncommon tumors. Our findings indicate that ameloblastomas can originate in the sinonasal tract without an association with the gnathic area. These tumors have a distinct predilection for men in the sixth to eighth decades of life. The signs and symptoms are those of unilateral nasal obstruction accompanied by opacification of the adjacent maxillary sinus. The treatment of choice is complete surgical resection. If possible, conservative surgery can be used if an assured complete removal can be performed. Incomplete resection may result in local recurrence. In our
cases, neither distant metastasis nor tumor-related deaths occurred. Based on our histologic findings, there is strong evidence to propose origin of these tumors directly from the sinonasal tract epithelium. However, further studies are indicated to substantiate the histogenesis of these tumors.

REFERENCES