CASE REPORT

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VERRUCOUS CARCINOMA OF THE PARANASAL SINUSES: CASE REPORT AND CLINICAL UPDATE

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Abstract: Background. Verrucous carcinoma is a low-grade malignancy that has been reported to occur in all anatomic sites of the head and neck. Fourteen cases of verrucous carcinoma of paranasal sinus origin have been reported to date in the English literature.

Methods. Case report and retrospective review of all cases of verrucous carcinoma of the paranasal sinuses in the English literature. All authors were contacted to provide missing data and long-term follow-up.

Results. Five of the eight authors contacted responded, and the most current data from all 15 cases were compiled. Eleven of the 15 patients (73%) were men and ranged in age from 35 to 81 years (median, 68 years). The maxillary sinus was the most common paranasal sinus involved (93%). Presentation often occurred late, with 12 of 15 (80%) initially being seen at stage T3 or higher. Surgical excision was the treatment of choice, and median disease-free survival was 54 months.

Conclusions. Verrucous carcinoma of the paranasal sinuses is a rare but potentially curable disease. Treatment is surgical, and prognosis is good with early intervention. © 2004 Wiley Periodicals, Inc. Head Neck 26: 184–189, 2004

Keywords: verrucous carcinoma; paranasal sinuses

Verrucous carcinoma involving the upper aerodigestive tract is most common in the oral cavity, with the glottic larynx being the most frequent nonoral head and neck site.1 Verrucous carcinoma has been reported in almost all anatomic sites in the head and neck, including uncommon sites such as the orbit,2 middle ear,3–5 and temporal bone.6 The incidence varies from 4.5% to 9%, and elderly men are most often afflicted.7 By far, the largest experience comes from India, where verrucous carcinoma is primarily found in the oral cavity.8 Verrucous carcinoma of the nose has been reported to involve the columella,9 nasal septum,10 nasopharynx,11 and, uncommonly, the paranasal sinuses. Our patient represents the fifteenth case of verrucous carcinoma of the paranasal sinuses reported in the literature and along with other reported cases allows a review of patient demographics and long-term treatment outcomes.
CASE REPORT

A 78-year-old previously healthy woman was seen by neurosurgeons with sudden onset headache and confusion. Neurologic examination revealed a grade 3 weakness of the upper and lower limbs on the right side. CT scan was suggestive of slight intracranial bleeding in the left frontal lobe, which was managed conservatively. Blood cultures at this time grew hemolytic streptococci. Subsequent CT scan (4 days later) demonstrated an abscess in the left frontal lobe with subdural empyema. Paranasal sinus cuts revealed a soft tissue mass involving the left maxillary antrum, left ethmoids, and both frontal sinuses (Figure 1).

The patient underwent drainage of the abscess through a frontal burr hole and a right frontal sinusotomy through a Howarth approach to obtain tissue for diagnosis. Culture of the purulent aspirate from the frontal sinus grew *Streptococcus milleri*, and a biopsy specimen from the frontal sinus mass was consistent with verrucous carcinoma (Figure 2).

The postoperative period was complicated by focal seizures; however, the patient progressively improved, and 2 weeks after initial presentation underwent surgical excision of her sinus tumor. The maxilla and ethmoids were mobilized by means of a left lateral rhinotomy incision, and a medial maxillectomy was performed. The frontal sinus was approached through midline forehead extension of the previous incision, and a frontal bone flap was removed. A large mass of tumor was present in both frontal sinuses, and on the right a dehiscence of the posterior wall was noted. The abscess cavity was tapped to evacuate material that had reaccumulated. Subsequent cultures were negative. She required a repeat surgical aspiration of the frontal lobe abscess a week after the sinus surgery but went on to complete recovery. She needed frontal sinusotomy and endoscopic removal of a localized mucocele in the posterior wall of the right frontal sinus after 30 months but is currently tumor free 36 months after surgery.

METHODS

Literature Search and Clinical Update. MEDLINE (1966–2000) and EMBASE (1974–2000) were searched using the following key words: verrucous, carcinoma, cancer, paranasal, sinus, nose, maxilla, ethmoid, frontal, and sphenoid in all fields. All articles on verrucous carcinoma were reviewed, and the references of each article were also scrutinized. Nine articles with 14 patients diagnosed with verrucous carcinoma of the paranasal sinuses were identified.

Data extracted from each study included age and sex, site and stage of the tumor, treatment, and the current status of each patient. These data fields were not always available in all publications. Therefore, all authors except one (Newman et al12) were contacted for further information. Care was taken to ensure that the UICC TNM system (1997)13 was uniformly used for staging. Five of the eight authors contacted responded with all the necessary information.
RESULTS

Information regarding treatment outcome was available in 14 of the 15 patients reported. One of the patients\textsuperscript{12} died in the immediate postoperative period secondary to sepsis. In 10 patients the long-term outcome status could be ascertained by directly contacting the authors. This included information not present in the original case report and long-term follow-up data. Information regarding age, sex, and stage was not available for one patient\textsuperscript{14} (Table 1). The age of the remaining patients ranged from 35 to 81 years (median, 68 years), and a male predominance was noted (11 M:4 F). The maxillary sinus was the most common site, being involved in all patients except one (Table 1). The frontal sinus was solely involved in one patient and was involved additionally with the maxillary and ethmoid sinuses in one other case. It is notable that both patients with frontal sinus involvement had intracranial extension. However, no patient had regional or systemic metastatic disease develop. Four of the patients with verrucous carcinoma also had synchronous or metachronous inverting papilloma.

Twelve (80\%) of the 15 patients had advanced-stage disease (stage III/IV). None of the patients had cervical node involvement or demonstrated evidence of distant metastases. Surgery was the initial treatment in all but one case (Table 1). This patient\textsuperscript{15} was offered but refused surgery. He was treated with palliative radiation therapy (35 Gy in 12 sittings extended over 2 weeks), followed by chemotherapy (four cycles of methotrexate, 80 mg every 2 weeks, and six cycles of bleomycin, 15 mg every 2 weeks). He remained free of tumor for 36 months and was subsequently lost to follow-up. Three patients received postsurgical radiation therapy. No patient treated with radiation therapy had subsequent anaplastic transformation of their tumor develop. Disease-free survival ranged from 4 to 135 months (median, 54 months).

<table>
<thead>
<tr>
<th>Author/year (ref)</th>
<th>Age/gender</th>
<th>Site</th>
<th>Stage</th>
<th>Treatment</th>
<th>Current status</th>
<th>Follow-up (mo)</th>
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<tr>
<td>Elliot 1973\textsuperscript{14}</td>
<td>?</td>
<td>Maxilla</td>
<td>?</td>
<td>Infraorbital maxillectomy radiation (40 Gy)</td>
<td>NED</td>
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<tr>
<td>Newman 1983\textsuperscript{12}</td>
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<td>Frontal</td>
<td>T4</td>
<td>Osteoplastic excision hemimaxillectomy ethmoidectomy</td>
<td>DOC (Postop death)</td>
<td>7 d</td>
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<td>Bacon 1989\textsuperscript{26}</td>
<td>60/M</td>
<td>Maxilla and ethmoid</td>
<td>T3</td>
<td>Hemimaxillectomy ethmoidectomy</td>
<td>—</td>
<td>Not reported</td>
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<tr>
<td>Daoud 1991\textsuperscript{12}</td>
<td>72/F</td>
<td>Maxilla</td>
<td>T3</td>
<td>Extended Caldwell-Luc procedure</td>
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<tr>
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<td>Maxilla</td>
<td>T3</td>
<td>Total maxillectomy</td>
<td>DOD</td>
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<td>T4</td>
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<td>Maxilla</td>
<td>T2</td>
<td>Partial maxillectomy</td>
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<td>79/M</td>
<td>Maxilla</td>
<td>T3</td>
<td>Medial maxillectomy radiotherapy</td>
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<td>T2</td>
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<td>T4</td>
<td>Medial maxillectomy</td>
<td>NED</td>
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<td>NED</td>
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<td>Present case</td>
<td>74/F</td>
<td>Maxilla, ethmoid and frontal</td>
<td>T4</td>
<td>Medial maxillectomy osteoplastic flap</td>
<td>NED</td>
<td>36</td>
</tr>
</tbody>
</table>

Abbreviations: DOD, died of disease; DOC, died of other causes; F, female; M, male; NED, no evidence of disease.

*Survival figures updated (Mar 2001) by personal communication with authors.
DISCUSSION

Friedell and Rosenthal\textsuperscript{16} initially described verrucous carcinoma in a series of eight cases of oral cancer with a papillary verrucoid appearance. Characterized in greater detail by Ackerman in 1948,\textsuperscript{17} the discrepancy between the histologic pattern and clinical behavior is the hallmark of this tumor. Often described as a distinct variant of squamous cell carcinoma, verrucous carcinoma is a rarely metastasizing, locally invasive neoplasm composed of squamous cells that lack cytologic features of malignancy. Grossly, it is an exophytic, fungating, and broadly implanted tumor that is locally invasive. Histologic findings reveal marked hyperkeratosis with papillary fronds, lack of cellular atypia, and pushing borders with surrounding inflammatory reaction. Enlarged regional lymph nodes are often due to inflammation rather than tumor invasion.\textsuperscript{1} Not confined to the head and neck, verrucous carcinoma has been described in the skin, male and female genitalia, anal canal, uterine cervix, bladder and renal pelvis, and esophagus.\textsuperscript{7} Tobacco plays a significant role in the pathogenesis of verrucous carcinoma of the aerodigestive tract. More than one third of the patients in Ackerman's original report\textsuperscript{17} were tobacco chewers, and the relationship between smokeless tobacco and verrucoid oral lesions has been established in several other studies. The habitual chewing of “paan,” a mixture of betel leaf, lime, betel nuts, and tobacco, has long been implicated in the high incidence of verrucous-type oral cancers in India.\textsuperscript{18} As Ferlito and Recher\textsuperscript{19} reported, tobacco use is not a reasonable explanation for verrucous carcinoma that arises in skin, genitals, and other nonaerodigestive tract sites.

The dilemma in the diagnosis of verrucous carcinoma is well known. Small superficial biopsy specimens can be mistakenly reported as benign hyperplasias or as hyperkeratotic, acanthotic squamous proliferations. Conversely, exophytic, papillomatous, or verrucoid-appearing neoplasms that histologically demonstrate well-differentiated, infiltrating squamous cell carcinomas have been mistakenly called verrucous carcinoma.\textsuperscript{20} In an attempt to better differentiate the two tumors, Drachenberg et al\textsuperscript{21} studied the expression of bcl-2 and p53 in squamous cell carcinoma and verrucous carcinoma of the oral cavity in an attempt to positively diagnose one lesion from the other. They concluded that the two lesions exhibited different levels and patterns of gene expression, and these additional parameters can be occasionally diagnostically helpful in cases of doubt, although caution should be applied because of some overlap. This emphasizes the need for close communication between the surgeon and pathologist to establish the correct diagnosis in these cases.

An association between human papillomavirus (HPV) and verrucous carcinoma has also been proposed. However, results have been inconsistent. Although HPV types 6, 11, 16, and 18 have been detected to varying degrees in verrucous carcinoma of the oral cavity and the larynx,\textsuperscript{22,23} Orvidas et al\textsuperscript{24} could detect no HPV in association with nasal and paranasal sinus verrucous cancers using the polymerase chain reaction technique. Only one case of a hybrid tumor (elements of both verrucous carcinoma and typical squamous cell carcinoma on histologic evaluation) in the paranasal sinus has been described until now\textsuperscript{25} but has not been included in the review, because these tumors behave more like squamous cell cancers. Of interest is the patient reported by Bacon et al,\textsuperscript{26} who had been treated 10 years before the diagnosis of verrucous carcinoma by intranasal polypectomy. The diagnosis of verrucous carcinoma was only made on the second visit when a hemimaxillectomy was performed. Retrospective review of the initial polypectomy specimen confirmed it to be a verrucous carcinoma.

Surgery has been the mainstay of treatment of this neoplasm, with all but one of these 15 patients undergoing surgical excision of their tumor as the primary mode of therapy. Despite the advanced stage in 79% of the patients, surgery alone has provided median survival approaching 5 years. Verrucous carcinoma spreads on a broad front, tending not to infiltrate. It is, therefore, more amenable to surgical extirpation with negative margins and would not need adjunctive radiation therapy. It seems from the review that this goal has been achieved in most, with only two of the 15 patients receiving postoperative radiation. Judging from the treatment results of this small population, we would recommend that radiation be limited to those patients in whom there are concerns of residual disease.

Fears of “anaplastic transformation,”\textsuperscript{27} reported to be as high as 30%, have lead many to abandon radiation therapy as a treatment for verrucous carcinoma. In a review of primary radiotherapy as an appropriate option for the management of verrucous carcinoma, Ferlito et al\textsuperscript{28} concluded that the incidence of anaplastic transformation was low, but when it occurred after ra-
radiation, all patients died within 3.3 years of diagnosis, and disseminated disease was detected in most cases at the time of death. Dissemination has not been noted to occur in the absence of anaplastic transformation. Anaplastic transformation has also been reported in nonirradiated patients after surgery or cryosurgery and also in untreated verrucous carcinoma. This is likely due to an incorrect diagnosis of verrucous carcinoma and calls into doubt whether anaplastic transformation actually occurs. The diagnosis remains the fundamental problem; without a correct diagnosis of verrucous carcinoma, appropriate treatment cannot be carried out.

CONCLUSIONS

Verrucous carcinoma of the paranasal sinuses is a rare tumor that behaves similar to verrucous carcinoma elsewhere in the aerodigestive tract. It has been associated with inverting papilloma, and one true hybrid tumor has been reported. Verrucous carcinoma of the paranasal sinuses does not metastasize, and surgical excision remains the mainstay of treatment. The role of radiation therapy in these tumors has yet to be defined but may be indicated for patients unwilling or ineligible for surgical treatment.

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