Primary Intraosseous Carcinoma of the Jaws

Narcisse Zwetyenga, MD; Jacques Pinsolle, MD; Janine Rivel, MD; Claire Majoufre-Lefebvre, MD; Alain Faucher, MD; Vincent Pinsolle, MD

Objectives: To present 8 new cases of primary intraosseous carcinoma of the jaws and to review the literature for an analysis of treatment modalities and patient outcomes.

Data Sources: A MEDLINE search from 1970 to 1999. The articles chosen and the study of the references of every one that produced additional articles provided database information for 28 patients. Eight new patients from our institutions were added.

Study Selection: Our criteria of inclusion included the absence of ulceration of the oral mucosa, a negative result in the search for a distant primary tumor, and convincing histological documentation.

Data Extraction: The variables of the analysis included age, sex, site of the tumor, condition of the oral mucosa, tumor size, neck status, treatment modalities, recurrences, and survival.

Data Synthesis: Twenty-eight patients were identified in the literature, for a total of 36 patients. There were 28 males (78%) and 8 females (22%) ranging in age from 4 to 76 years (mean, 54 years). The tumor site was the mandible in 33 patients (92%) and the maxilla in 3 (8%). Of the 34 patients treated, 19 (56%) had recurrences. Overall 2- and 4-year survival was 60.5% and 39.9%, respectively. Patients who underwent radical surgery and postoperative radiotherapy (n=11) had a 2- and 3-year survival probability of 61.3% and 40.9%, respectively, whereas in the remaining patients (n=25), the rates were 59.7% and 31.3%, respectively (P=.60).

Conclusions: Strict diagnostic criteria must be applied. The prognosis associated with primary intraosseous carcinoma of the jaws is poor and suggests the need for aggressive treatment.


Primary intraosseous carcinoma (PIOC) of the jaws is a rare tumor presumably developing from residues of the odontogenic epithelium. It is one of the odontogenic carcinomas arising in the jaws, which are divided into 4 types: (1) malignant ameloblastoma, (2) PIOC, (3) malignant variants of other odontogenic epithelial tumors, and (4) malignant changes in odontogenic cysts. Only a few cases have been reported in the literature. Some reports include an exhaustive review of the published cases to define the diagnostic criteria. However, information about treatment modalities, patient outcomes, and comparisons with other oral cavity primary sites of squamous cell carcinoma are rarely available. The tumor usually presents as a painful swelling in the jaw area, but may be asymptomatic and found on a routine panoramic radiograph. The diagnostic criteria are now well-defined: no ulceration of oral mucosa should be observed (Figure 1), and another primary site should be excluded. The tumor seems to arise from any residual odontogenic epithelium, such as remnants of the dental lamina or of the Hertwig root sheath. Microscopically, most PIOCIs show the same histological features as squamous cell carcinoma of any squamous epithelium (eg, the oral mucosa). The tumor is composed of sheets; islands; and strands of squamous cells with marked cellular pleomorphism, nuclear hyperchromatism, and mitotic activity. In a few cases, however, the tumor has a distinctly odontogenic pattern, with basal-type cells arranged in alveoli or in a plexiform pattern with palisading of the peripheral cells (Figure 2). The standard treatment includes surgery and/or radiation therapy, and the prognosis is severe.

We reviewed information about cases of intraosseous carcinoma from published reports and performed an analysis of the data including 8 new cases from our institutions. The aims of the study were to confirm the diagnostic criteria, to assess the difficulty of staging such tumors and of determining patient outcomes, and to try to define a consistent method of treatment.

RESULTS

The tumors of the 8 cases from our institutions were all located in the mandible, with only 1 anterior location. The first symptom was swelling in the mandibular area in 7 cases, which was painful in 3. One tumor was found on a routine panoramic ra-

From the Departments of Maxillofacial and Plastic Surgery (Drs Zwetyenga, J. Pinsolle, and Majoufre-Lefebvre) and Pathology (Dr Rivel), Centre Hospitalier Universitaire de Bordeaux, and the Department of Surgery, Institut Bergonie (Drs Faucher and V. Pinsolle), Bordeaux, France.
MATERIALS AND METHODS

Two sources were used to identify well-documented case reports of PIOC. A MEDLINE search from 1970 to 1999 was performed first. The choice was based on the reports of treatment methods and survival data for individual patients. The articles chosen and the study of the references of every one that produced additional articles amounted to 27, 3, 8, 10, 21, 22 of which presented 28 identified cases of 63 reported cases. Thirty-five cases from different reports were rejected owing to a lack of a search for another primary site,10,13,18,23 different histological features,20,21,27,28 the presence of an ulceration of the oral mucosa,21 or a tumor arising from an odontogenic cyst.23,28 Individual patient data, and not results of series, were entered into the database.

Meanwhile, we reviewed in our files 15 cases with the suspected diagnosis of PIOC. Careful assessment of the clinical criteria eliminated 4 cases. Of the 11 remaining cases, 3 were eliminated after a new histological examination of the specimens. Therefore, 8 new cases were identified and added to the 28 previous cases, so a total of 36 cases were included in the statistical analysis.

Our criteria of inclusion were the absence of ulceration of the oral mucosa, a negative result in the search for a distant primary tumor, and convincing histological documentation.2,3 The analytical variables included age, sex, site of the tumor, condition of the oral mucosa, tumor size, neck status, treatment modalities, recurrences, and survival. All patient data were recorded on a computer file (MEDLOG). Survival and recurrence data were analyzed with Statistical Product and Service Solutions software (SPSS Inc, Chicago, Ill). The survival probabilities were calculated with the actuarial method. The Wilcoxon (Gehan) test was used for comparison between factors.

2-18 months). Ten patients (28%) had clinically homolateral positive neck nodes at the time of the diagnosis, 7 in the submandibular triangle and 3 in the lateral neck. Follow-up information was available for 35 patients (mean follow-up, 29 months). As for radiographic features, osteolytic bone changes were noted in all patients. The margins were irregular in 22 patients (63%) and regular in 10 (29%); no precision was available for 3 patients (9%) (percentages total >100 because of rounding). Five patients (14%) had a pathological fracture of the mandible.

Data about treatment modalities were available for 34 patients and are as follows:

<table>
<thead>
<tr>
<th>Treatment Modality</th>
<th>No. (%) of Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Surgery</td>
<td></td>
</tr>
<tr>
<td>Alone</td>
<td>16 (47)</td>
</tr>
<tr>
<td>Plus radiotherapy</td>
<td>13 (38)</td>
</tr>
<tr>
<td>Plus radiotherapy and chemotherapy</td>
<td>2 (6)</td>
</tr>
<tr>
<td>Plus chemotherapy</td>
<td>2 (6)</td>
</tr>
<tr>
<td>Definitive radiotherapy</td>
<td>1 (3)</td>
</tr>
<tr>
<td>Total</td>
<td>34 (100)</td>
</tr>
</tbody>
</table>

Surgery at the tumor site consisted of hemimandibulectomy in 23 patients, marginal mandibulectomy in 5, curettage in 2, and maxillectomy in 3 (for tumors of the maxilla). In the 33 patients treated by surgery, 23 underwent a neck dissection (22 primary and 1 radical dissection). In 10 (43%) of them, there was histological evidence of node metastasis in the neck specimen. Ten patients underwent mandibular reconstruction. Of the 34 patients treated, 19 (56%) had recurrences; 12 experienced a local recurrence in a mean delay of 7.8 months (range, 1-36 months), 2 had a neck recurrence, and 5 had distant metastases (2 bone and 3 lung metastases). The 2-year probability of nonrecurrence was 51.0%. None of these recurrences could eventually be controlled. The estimated overall 2-year survival was 60.5%. Patients who underwent radical surgery and postoperative radiotherapy (n = 11) had a 2- and 3-year survival probability of 61.3% and 40.9%, respectively, whereas in the remain-
ing patients (n=25), the rates were 59.7% and 31.3%, respectively (P=.60). The median survival was 40.6 months in the former and 29.6 months in the latter. The comparison of estimated survival between patients who underwent a neck dissection and the other patients was not statistically significant (P=.81). The study of prognostic factors was not significant.

**COMMENT**

Primary intraosseous carcinoma is a rare tumor whose diagnostic criteria have been well-defined and must be fully applied to confirm any new case. To eliminate an oral cavity cancer (particularly originating in the gum) with osseous involvement, no ulceration of the oral mucosa should be observed. Moreover, excluding a metastatic lesion of the bone for another primary site necessitates a careful physical examination and a chest radiograph with a posttreatment observation period of at least 6 months. In the event of an early death, an autopsy reporting no evidence of another primary site is mandatory. Moreover, the pathologist must differentiate the lesion from a malignant ameloblastoma or "other carcinomas arising from the odontogenic epithelium including those arising from odontogenic cysts. More than two thirds of the patients are aged 50 years or older, but the tumor may arise in young patients (there were 2 patients <20 years), unlike oral cavity carcinomas, which are exceptional in the first 2 decades of life. The male-female ratio is 3.5:1, but the classic oral mucosa carcinoma background of alcohol or tobacco abuse is not present. The predominant location is the posterior part of the mandible, which is similar to benign tumors and odontogenic cysts. However, in the anterior cases, the origin might be epithelial remnants in the deeper structures during the fusion of the facial processes, which is at variance with the World Health Organization's definition. Yet, remnants of the dental lamina can be found in a median location. The tumor usually presents as possibly painful swelling in the jaw area, but may be asymptomatic and found on a routine panoramic radiograph. In most cases, the diagnostic delay is due to previous teeth removal without a panoramic radiograph and to having attributed the symptoms to operative complications. The radiographic features show great variations in size and shape, but in many cases a large tumor is found. Histologically, it may be difficult to decide whether the tumor should be classified as a PIOC or as a malignant ameloblastoma when it presents an odontogenic pattern. The diagnosis of malignant ameloblastoma can be made if there is histological evidence of a previous tumor. If not, the diagnosis is differentiated squamous carcinoma. A definite diagnosis of PIOC is possible only with reliable clinical and radiographic data.

No conclusion can be drawn from this study regarding prognostic factors owing to the few patients enrolled. However, the number was large enough and the follow-up long enough to evaluate local and general results. Apart from age and general status or delay in establishing the correct diagnosis, we suspect that, as in oral cavity squamous carcinoma, the tumor extension (herein equivalent to a T4 tumor) and neck node involvement are of the utmost importance. In fact, there is a problem concerning the staging of such tumors. Since they are squamous carcinoma, they cannot be classified as primary bone tumors even if their location is intraosseous. Also, they cannot be classified according to the international classifications of head and neck squamous carcinomas because every tumor would be classified T4 regardless of its size since they are closely in contact with the bone marrow, with a high risk of neck node involvement, thus accounting for their poor outcome. The only possibility seems to be to report the tumor size on computed tomographic scanning.

As for treatment, there is no consensus so far. Standard treatment includes surgery and/or radiation therapy, and the prognosis is severe. All our patients but 1 were treated with a neck dissection and postoperative radiotherapy: A, alive without disease; N+, histological node involvement with extracapsular spread; FND, functional neck dissection; PM, pulmonary metastases; and ellipses, data not applicable.

---

**Details of the Patients From Our Institutions**

<table>
<thead>
<tr>
<th>Patient No./ Sex/Age, y</th>
<th>Tumor Size, cm</th>
<th>Neck Status</th>
<th>Neck Dissection</th>
<th>Postoperative RT Dose, rad (Gy)</th>
<th>Follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Time, mo</td>
<td>Status</td>
</tr>
<tr>
<td>1/M/74</td>
<td>3</td>
<td>N0</td>
<td>SOHND</td>
<td>6500 (65)</td>
<td>D (LR)</td>
</tr>
<tr>
<td>2/M/59</td>
<td>8</td>
<td>N0</td>
<td>SOHND</td>
<td>6000 (60)</td>
<td>84</td>
</tr>
<tr>
<td>3/M/71</td>
<td>4</td>
<td>N1 (N+R+)</td>
<td>FND</td>
<td>6000 (60)</td>
<td>35</td>
</tr>
<tr>
<td>4/M/66</td>
<td>5</td>
<td>N0</td>
<td></td>
<td></td>
<td>20</td>
</tr>
<tr>
<td>5/F/73</td>
<td>6</td>
<td>N0</td>
<td>SOHND</td>
<td>6000 (60)</td>
<td>156</td>
</tr>
<tr>
<td>6/M/50</td>
<td>8</td>
<td>N2 (N+R+)</td>
<td>FND</td>
<td>6000 (60)</td>
<td>32</td>
</tr>
<tr>
<td>7/M/66</td>
<td>4</td>
<td>N0 (N+R+)</td>
<td>SOHND</td>
<td>6500 (65)</td>
<td>9</td>
</tr>
<tr>
<td>8/M/40</td>
<td>7</td>
<td>N0</td>
<td>SOHND</td>
<td>6500 (65)</td>
<td>32</td>
</tr>
</tbody>
</table>

*RT indicates radiotherapy; SOHND, supraomohyoid neck dissection; D, deceased; LR, local recurrence; A, alive without disease; N+R+, histological node involvement with extracapsular spread; FND, functional neck dissection; PM, pulmonary metastases; and ellipses, data not applicable.*
treated with radical surgery, neck dissection, and postoperative radiotherapy. The only exception was a patient with an initially false diagnosis of ameloblastoma. Of the 7 patients who underwent the complete treatment sequence, only 1 experienced a local recurrence. Two patients died of pulmonary metastases, and in both there was histological neck node involvement with extracapsular spread. The mainstay of treatment remains surgery, owing to the intraosseous location of the tumor, which proscribes definitive radiation therapy. Postoperative radiotherapy seems to be useful. In fact, 2 arguments favor combined treatment. First, because PIOC is clearly similar to locally advanced squamous carcinoma of the oral mucosa, particularly T4 gum carcinoma, the same aggressive treatment seems to be recommendable.34 Second, while the comparison of survival according to the treatment modalities is not statistically significant, the trend is in favor of radical surgery and postoperative radiotherapy. Therefore, for mandibular tumors, hemimandibulectomy with neck dissection (functional or radical, according to the neck status) can be suggested along with postoperative radiotherapy including the primary site and bilateral neck areas.5,8 This attitude is justified by the need to obtain safe margins in the primary site and the high risk of neck node involvement with a tumor closely in contact with the bone marrow. As for tumors in the maxilla, maxillectomy seems mandatory, but neck dissection might be optional because of the different lymphatic drainage mechanisms at this site.

CONCLUSIONS

Primary intraosseous carcinoma is a rare tumor that behaves like a locally advanced carcinoma of the oral cavity. Strict diagnostic criteria must be applied, with primary emphasis on the nonconnection of the tumor with the oral mucosa and on the histological features. The prognosis associated with PIOC of the jaws is poor and suggests the need for aggressive treatment. Surgery and postoperative radiation therapy seem to provide the best results.

Accepted for publication March 16, 2001.


We thank Veronique Picot for performing the statistical analysis.

REFERENCES


