Primary extranodal lymphoma of the maxilla: a case report with imaging features and dynamic data analysis of magnetic resonance imaging

Hidenobu Matsuzaki, DDS, a Naoki Katase, DDS, PhD, b Marina Hara, DDS, c Jun-Ichi Asaumi, DDS, DMSci, d Yoshinobu Yanagi, DDS, e Teruhashi Unetsubo, DDS, PhD, f Miki Hisatomi, DDS, PhD, g Hironobu Konouchi, DDS, PhD, e Toshihiko Takenobu, DDS, PhD, f and Hitoshi Nagatsuka, DDS, PhD, h Okayama, Japan

OKAYAMA UNIVERSITY HOSPITAL AND OKAYAMA UNIVERSITY

Malignant lymphoma is the second-most common malignancy in the head and neck region. Waldeyer’s ring is the most common site of extranodal Hodgkin’s lymphoma (NHL) in that region, and a small percentage of primary extranodal NHL occurs in the oral cavity. The most common sites of extranodal NHL in the oral region are the palate and maxilla, and nearly half of extranodal NHL cases arise from bone. It is difficult to diagnose extranodal NHL because of the variety of its radiological features. We report a case of primary extranodal NHL of the maxilla in a 68-year-old female patient with atypical imaging findings, along with the results of analysis of dynamic magnetic resonance imaging (MRI). (Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2011;112: e59-e69)

Malignant lymphoma is one of the most common non-epithelial tumors of the head and neck region.1,2 Malignant lymphomas are divided into non-Hodgkin’s and Hodgkin’s groups, and approximately 40% of non-Hodgkin’s lymphoma (NHL) arises at extranodal sites outside the lymphoid system.3 The most common site of extranodal NHL in the head and neck region is Waldeyer’s ring.3,5 and 0.2% to 3.0% of primary extranodal NHL arises in the oral region.6,7 The most common sites of extranodal NHL in the oral region are the palate and maxilla; 35% to 50% of extranodal NHL in those areas reportedly arises from bone.8-11 The radiological signs of extranodal NHL involving the jaw bone are lowering of the alveolar margin, diffuse bone destruction, or solitary bone defect; these signs resemble those of periodontal inflammation, osteomyelitis, and other malignant tumors (Tables I and II).5,8,9,11-26,31,34,36 Thus, there are no specific radiological findings for lymphomas.

In this case report, we describe a primary extranodal NHL of maxillary bone that showed atypical radiological features on conventional radiographs, computed tomography (CT), and magnetic resonance imaging (MRI). Furthermore, we report an interesting result of the retrospective analysis of dynamic MRI data.

CASE REPORT

In September 2007, a 68-year-old woman was referred to a general dental practitioner complaining that her upper complete denture fit poorly, along with a painless swelling of the gingival mucosa at the upper-left-side molar region. Her primary doctor diagnosed her with gingival abscess of the left side of the maxillary gingiva on the basis of a periapical radiograph and referred her to our hospital. Her medical history revealed hypertension and type C cirrhosis. She had epistaxis and nasal obstruction, and an intraoral examination revealed a painless elastic soft mass without ulceration from the left anterior to the molar region at the maxilla (Fig. 1). Her weight had decreased 4 to 5 kg within the previous 2 months, as the poor fit of her dentures caused her to eat less.

Conventional radiographs showed a radiolucent area from the maxillary bone of the left-side canine to tuberosity (Fig. 2, A and B). Furthermore, there were partially destroyed portions of the floor of the left maxillary sinus, which was elevated, as was the alveolar process (Fig. 2, A and C). We suspected that this lesion was an intrasosseous malignant tumor on the basis of conventional radiographs showing bone destruction in some parts.
Contrast-enhanced (CE) CT with iohexol was performed as an additional examination. An axial CT (bone window) image revealed a large mass with a partly well-defined margin arising from inside of the maxillary bone with marked expansion and partial perforation of the cortex (Fig. 3, A and B), and there were many continuous internal septalike structures from the expanded marginal cortex (Fig. 3, A-C). On a reconstructed coronal CT image, the mass had an expansive appearance, diffuse bone resorption of the alveolar bone, and elevated maxillary sinus floor and nasal floor (Fig. 3, C). A CE axial CT image showed heterogeneous and weak enhancement of the mass (Fig. 3, E).

We performed CE MRI with gadodiamide, including dynamic studies. MR images revealed a large mass with no signal intensity in areas of internal septalike structures, and which showed almost homogeneous isointensity on a T1-weighted image (WI), heterogeneous isointensity to hyperintensity on a short TI inversion recovery (STIR) image, and heterogeneous slight enhancement on CE-T1WI (Fig. 4, A-C).

At that point, we misdiagnosed this lesion as odontogenic myxoma or glandular tumors based on the CT findings of septalike structures and MRI findings of weak enhancement of the mass.

An incisional biopsy with the use of local anesthesia was performed based on the clinical diagnosis of odontogenic tumor. Histologic findings of the biopsy specimen revealed that the tumor cells consisted of uniform proliferation of atypical lymphoid cells, which did not indicate its odontogenic/salivary-gland origin, but gave an impression of a hematolymphoid origin. The tumor cells were large and showed nuclear atypia (Fig. 5, A). Immunohistochemical analysis demonstrated that the tumor cells were positive for CD20, CD79/H9251, and CD10, but negative for cytokeratin (CK) AE1/AE3, vimentin, S-100, CD3, and CD5 (Fig. 5, B-F). From these findings, the tumor was finally diagnosed as diffuse large B-cell lymphoma.

For treatment, the patient was transferred to a hospital she had already been visiting for hypertension and type C cirrhosis. In that hospital, she received bone marrow aspiration and 18 F-fluorodeoxyglucose-positron emission tomography. As a result, there were no malignant signs in any other organs, and she finally was diagnosed at clinical stage IVB with maxillary bone resorption.

After treatment with 3 courses of systemic chemotherapy with pirarubicin, cyclophosphamide, vincristine, prednisolone, and rituximab, her condition went into remission.

### DYNAMIC DATA ANALYSIS

We misdiagnosed this lesion as odontogenic myxoma or glandular tumor, because we observed only early-phase data from dynamic studies at the time of initial diagnosis. After diagnostic confirmation by biopsy, we created a contrast index (CI) curve to analyze dynamic data retrospectively.

We created the CI curve using dynamic images so as to observe the flow pattern of contrast medium into the tumor mass. The region of interest (ROI) was drawn to include the maximal region of the tumor mass using the...
The mean signal intensity on the ROI of each lesion was calculated using a workstation (Synapse Vincent, FUJIFILM Medical Co, Ltd., Tokyo, Japan.). The CI was calculated using the formula

\[ \text{CI} = \frac{\text{signal intensity [postcontrast] – signal intensity [precontrast]}}{\text{signal intensity (precontrast)}} \]

The CI was then plotted on a time course to obtain the CI curve (Fig. 6). We defined CImax as the CI at maximal enhancement and CIpeak as the inequality CI > 0.9 CImax. Tmax and Tpeak were defined as the times corresponding to CImax and CIpeak, respectively. The washout ratio (WR<sub>600</sub> and WR<sub>1200</sub>), expressed as a

### Table II. Clinical and radiologic features of extranodal non-Hodgkin’s lymphomas in published cases

<table>
<thead>
<tr>
<th>First author (year)</th>
<th>Ref</th>
<th>Sex</th>
<th>Age</th>
<th>Loc</th>
<th>X-P findings</th>
<th>CT findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>M 44</td>
<td></td>
<td></td>
<td></td>
<td>Mand</td>
<td>Extensive lytic process</td>
<td>—</td>
</tr>
<tr>
<td>M 29</td>
<td></td>
<td></td>
<td></td>
<td>Mand</td>
<td>Irregular radiolucent pattern</td>
<td>—</td>
</tr>
<tr>
<td>F 44</td>
<td></td>
<td></td>
<td></td>
<td>Max</td>
<td>Extensive, invasive, poorly define lytic lesion</td>
<td>—</td>
</tr>
<tr>
<td>M 42</td>
<td></td>
<td></td>
<td></td>
<td>Max</td>
<td>Extensive destruction</td>
<td>—</td>
</tr>
<tr>
<td>F 54</td>
<td></td>
<td></td>
<td></td>
<td>Max</td>
<td>Poorly defined lytic lesion</td>
<td>—</td>
</tr>
<tr>
<td>F 80</td>
<td></td>
<td></td>
<td></td>
<td>Max</td>
<td>Destruction of the maxillary tuberosity</td>
<td>—</td>
</tr>
<tr>
<td>Macintyre (1986)</td>
<td>[23]</td>
<td>F</td>
<td>52</td>
<td>Mand</td>
<td>Poorly defined osteolytic lesion</td>
<td>—</td>
</tr>
<tr>
<td>M 79</td>
<td></td>
<td></td>
<td></td>
<td>Mand</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>F 3</td>
<td></td>
<td></td>
<td></td>
<td>bil.</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>M 8</td>
<td></td>
<td></td>
<td></td>
<td>MS</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>F 30</td>
<td></td>
<td></td>
<td></td>
<td>SS</td>
<td>A mass without definite bony destruction</td>
<td>—</td>
</tr>
<tr>
<td>M ING</td>
<td></td>
<td></td>
<td></td>
<td>Mand</td>
<td>Vague, diffuse radiolucent and abnormal trabecular pattern</td>
<td>—</td>
</tr>
<tr>
<td>Shlansky-Goldberg (1988)</td>
<td></td>
<td>M</td>
<td>89</td>
<td>MS</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Kawasaki (1990)</td>
<td>[18]</td>
<td>F</td>
<td>60</td>
<td>Mand</td>
<td>Extensive change and radiolucent</td>
<td>—</td>
</tr>
<tr>
<td>M 75</td>
<td></td>
<td></td>
<td></td>
<td>Max</td>
<td>Extensive destruction of the anterior floor</td>
<td>—</td>
</tr>
<tr>
<td>Barber (1992)</td>
<td>[29]</td>
<td>M</td>
<td>40</td>
<td>Mand</td>
<td>Well-defined widening of the mandibular canal</td>
<td>—</td>
</tr>
<tr>
<td>Kololotronis (2005)</td>
<td>[15]</td>
<td>F</td>
<td>50</td>
<td>Mand</td>
<td>Irregular radiolucent pattern throughout the ramus</td>
<td>—</td>
</tr>
<tr>
<td>Nassenstein (2005)</td>
<td>[31]</td>
<td>M</td>
<td>9</td>
<td>Max</td>
<td>—</td>
<td>Tumor with destruction of maxilla and infiltration of the subcutaneous fat</td>
</tr>
<tr>
<td>Valenzuela-Salas (2008)</td>
<td>[33]</td>
<td>M</td>
<td>5</td>
<td>Max</td>
<td>—</td>
<td>A faint ill-defined radiolucent area in the maxilla</td>
</tr>
<tr>
<td>Calvalvante (2009)</td>
<td>[34]</td>
<td>F</td>
<td>6</td>
<td>Max</td>
<td>Poorly defined radiolucent lesion</td>
<td>Perforation of buccal and lingual cortical plate</td>
</tr>
<tr>
<td>Nikgoo (2009)</td>
<td>[35]</td>
<td>M</td>
<td>31</td>
<td>MS</td>
<td>Ill-defined radioluencies with remaining bony trabeculae</td>
<td>A mass with destruction of sinus walls</td>
</tr>
</tbody>
</table>

Ref, reference; Loc, location; X-P, conventional radiographs; —, information not given; Max, maxilla; Mand, mandible; MS, maxillary sinus; SS, sphenoidal sinus.
percentage, was defined as follows: $C_{\text{Imax}} = C_{\text{I600s}}/C_{\text{Imax}} \times 100(\%)$ and $C_{\text{Imax}} = C_{\text{I1200s}}/C_{\text{Imax}} \times 100(\%)$, where $C_{\text{I600s}}$ and $C_{\text{I1200s}}$ represent the CI at 600 seconds and 1200 seconds after contrast medium administration.

The CI curve in our case increased rapidly, reaching a CIpeak at 90 seconds and $C_{\text{Imax}} (=1.08)$ at 120 seconds. After that, the CI curve showed a nearly sustained plateau until 600 seconds, and then gradually decreased to 1200 seconds. The washout ratios were 6.5% of WR600 and 21.1% of WR1200; washout of contrast medium was almost invisible.

DISCUSSION

Malignant lymphoma is the second-most common malignancy in the head and neck region, followed by squamous cell carcinoma. Approximately 40% of NHL arises from extranodal sites outside the lym-
Fig. 3. CT images. A and B, The axial image with the bone window shows a large mass with a partly well-defined margin in the left maxilla to the palate. The lesion is markedly expanded to the bucco-palatal side with partial perforation of the cortex. C, The reconstructed coronal image with the bone window, showing the tumor has elevated the nasal floor and the floor of the left maxillary sinus with perforation of the cortex and expands into the left maxillary sinus and nasal cavity. A, B, D, There are many continuous internal septalike structures from the marginal expanded cortex. D, E, The contrast-enhanced axial image shows heterogeneous weak enhancement within the tumor.
phoid system,\(^3\)\(^4\) and the most common site of extranodal NHL in the head and neck region is Waldeyer’s ring.\(^3\)\(^5\) The average age of patients with extranodal NHL in the oral region has been reported to be about 50 to 70 years, and a sex difference in the incidence of extranodal NHL in that region has been variously reported.\(^6\)\(^8\)\(^10\)\(^12\)\(^13\)\(^15\)\(^26\)\(^37\)\(^39\)

In the oral cavity, 15% to 45% of NHL occurred in the mandible and maxilla.\(^14\)\(^40\)\(^42\) Eisenbud et al.\(^10\)\(^11\) reported that about 45% of extranodal NHL in the oral region arose from the jaw bone. Furthermore, van der Waal et al.\(^9\) reported that about 35% (14/40) of primary extranodal NHL in the oral region arose from the jaw bone. They also reported that all cases in the mandible

---

**Fig. 4. MR images.**

A, T1WI shows almost homogeneous isointensity with no signal intensity areas of internal septalike structures. B, STIR image shows heterogeneous isointensity to hyperintensity. C, On CE-T1WI, the tumor shows slight heterogeneous enhancement.
Fig. 5. Histopathological findings. A, The tumor was composed of large, atypical lymphoid cells, replacing gingival connective tissue, indicating hematolymphoid origin (hematoxylin-eosin stain, ×400). Immunohistochemistry revealed that the tumor cells were positive for CD20 (B; CD20 immunohistochemical stain) and CD79α (C; CD79α immunohistochemical stain, ×200), but negative for CD3 (D; CD3 immunohistochemical stain, ×200), CK AE1/AE3 (E; Cytokeratin AE1/AE3 immunohistochemical stain, ×400), Vimentin (F; Vimentin immunohistochemical stain, ×200), and S-100 (G; S-100 immunohistochemical stain, ×200). H, Ki-67 index was remarkably high (Ki-67 immunohistochemical stain, ×200).
arose from the bone, but most of the cases in the maxilla (20/27) arose from soft tissue. Wolvius et al. also reported that the incidence of primary extranodal NHL that arose from mandible bone was higher than that in maxilla. We thought that our case arose from inside the jaw bone, because the center of the lesion existed in the maxilla, although this NHL had diffuse bone resorption of alveolar bone and elevated maxillary sinus floor and nasal floor.

The radiological features of NHL involving the jaw bone revealed the lowering of the alveolar margin and diffuse bone destruction or solitary bone defect, and these findings resembled those of periodontal inflammation, osteomyelitis, and other malignant tumors (Tables I and II). These radiological findings revealed that almost all NHLs involving the jaw bone tend to have ill-defined margins. On the other hand, there are few reports about NHL with well-defined margins (Tables I and II), and in these reports, all cases in which the location was known occurred in the mandible; however, there are no reports of cases in the maxilla to our knowledge. In the radiographic appearance in our case, the margin of the lesion was not so clear in the conventional radiographs but was partly well defined in CT images, which differed between inflammation and malignant tumors. Furthermore, CT images revealed many continuous internal septalike structures from the expanded marginal cortex in the tumor mass. Some authors have reported the presence of calcifications in lymphoma as a rare finding. In our case, we considered that the internal septalike structures were not so much calcifications as bone, based on the CT images. Some authors have reported that bone remained in tumor masses on CT images of the paranasal sinus because the tumor permeated the wall without aggressive bony destruction (Tables II and III). We considered that our finding, which showed many internal septalike structures in the tumor mass, was similar to those reports. We thought of these structures as an atypical radiological finding, because our search of the literature turned up no similar cases. We misdiagnosed her condition even though there was bone resorption in the alveolar bone and on the floor of maxillary sinus. This was because we thought these structures were internal septa as a typical finding of odontogenic myxoma.

MR images of extranodal lymphomas in the head and neck region have shown homogeneous isointensity to hyperintensity on T1WI, isointensity on T2WI, and various levels of enhancement on CE-T1WI (Table III). The MRI results in our case were similar to these reports, which showed homogeneous isointensity on T1WI and heterogeneous slight enhancement on CE-T1WI. Moreover, an STIR image showed heterogeneous isointensity to hyperintensity. We previously reported dynamic CE MRI of ameloblastomas, odontogenic myxomas, glandular tumors, squamous cell carcinomas, and lymphomas at the head and neck region. The CI curve in the present case showed that Tpeak and T max. were 90 seconds and 120 seconds, respectively; these findings were similar to those for malignant tumors (squamous cell carcinoma, mucoepidermoid carcinoma, adenoid cystic carcinoma, and lymphoma) that we have reported. On the other hand,
there were some differences between the present case and that one. The first was the value of CI\text{max} in the early phase of dynamic MRI. CI\text{max} in this case was 1.08; this value was lower than those for head and neck malignant tumors except lymphomas. Even though we previously reported that CI\text{max} of lymphomas tended to be less than 2.0,\textsuperscript{56} we misdiagnosed this lesion based on the features of low CI\text{max} and atypical CT findings. The second point was the washout rate of contrast medium in the late phase. The low washout rate (WR\text{600} = 6.5\%) in our case was a unique finding, even though almost all cases of malignant tumors had rates higher than 10\% at 300 seconds after contrast medium administration. We suspected our case as odontogenic myxoma based on the CT findings, but the signal intensities of myxoma had features that gradually increased over time.\textsuperscript{60} At the time of initial diagnosis, we should have checked the dynamic MRI data. However, the finding of the low washout ratio did not necessarily correspond to our reports about malignant lymphoma, and it is the same for CI\text{max}; there were some cases with ratios higher than 2.0.\textsuperscript{55,56} However, such various dynamic MRI findings, including those in the present case, were not consistent with the enhancement patterns on CE-T1WIs that have been reported.\textsuperscript{48,52,53} In other words, these diversities might be characteristics of malignant lymphoma. Therefore, we thought it might be important to know about these diversities, including CT findings of the present case, for the diagnosis of malignant lymphoma.

CONCLUSIONS

We have reported a case of primary extranodal NHL of the maxilla in a 68-year-old female patient. It was difficult to diagnose this case as lymphoma because the lesion showed atypical radiological features. Although we misdiagnosed this patient because of the CT finding of bone remaining in the tumor mass as occurs in internal septa, that finding might be a characteristic of malignant lymphoma. Our patient’s MR findings were similar to those in the literature, but the retrospective analysis of dynamic data showed atypical findings. These results suggested that NHL had a variety of radiological findings, and this was considered to be a characteristic of NHL. Therefore, we considered that dynamic MRI, especially the observation of CI\text{max} and the washout ratio, was useful for the diagnosis of extranodal NHL in the head and neck region.

REFERENCES

2. Duurkens V, Wagener DJ, van den Broek P, Bogman MJ, Kazem...


39. Matthews JB, Basu MK. Primary extranodal lymphoma of the