INTRODUCTION

Lymphomas are defined as lymphoid cell neoplasms. Traditionally, these are divided into Hodgkin disease and non-Hodgkin lymphoma (NHL). The relative frequency of NHL was 95.4% of malignant lymphoma.1,2 Non-Hodgkin lymphoma affects mostly lymphoid organs, and also affects extranodal sites that do not ordinarily contain lymphoid cells.3 Extranodal lymphomas may vary between the studies with different ethnic groups, comprising 63.3% of NHL cases in Korea.4,5 In a previous study of 2650 cases of extranodal NHL, 1112 (42.0%) cases presented with the disease in the gastrointestinal region.5 The oral cavity involvement in NHL changed from 2.9% in 1998 to 1.9% in 2010 in Korea.1,2

The most frequent subtype of NHL is diffuse large B-cell lymphoma (DLBCL). It constitutes 25%-30% of adult NHLs in Western countries and 42.7% of NHLs in Korea.5,6 Histologically, DLBCL is a neoplasm of large B lymphoid cells with nuclear size equal to or exceeding normal macrophage nuclei or more than twice the size of a normal lymphocyte that has a diffuse growth pattern.6

The etiology of DLBCL remains unknown. It usually arises de novo (primary) but can represent progression or transformation (secondary) of a less aggressive lymphoma.6 The immune deficiency is considered a significant risk factor.7 DLBCL more often occurs in Epstein-Barr virus (EBV)-positive elderly patients than those without an overt immunodeficiency.8

The purpose of this report is to present a case of extranodal DLBCL found in the peri-implant mucosa. Several articles about DLBCL of the oral cavity were reported previously.9,10 To the authors’ knowledge, this is the first report of an oral lymphoma in the peri-implant mucosa.

CASE PRESENTATION

A 55-year-old man was examined at the Department of Otolaryngology, Seoul St. Mary’s hospital in Korea with a complaint of swelling in the left neck region. Physical examination revealed a nontender hard mass in the left palatine tonsil. On computerized tomography (CT) scan, the left palatine tonsil was enlarged, and multiple lymph nodal enlargements were detected close to the left and right upper internal jugular chains. A biopsy was taken from the mass in the left palatine tonsil.

Histopathologic sections showed diffuse infiltration of large atypical lymphoid cells obliterating lymph node architecture (Figure 1a). On immunostaining, the tumor cells were positive for a B-cell marker (CD20), multiple myeloma oncogene 1 (MUM1), and Bcl-2 (Figure 1b–d), but negative for CD10 (Figure 1e). On hematologic analysis, EBV was detected at a high level in the blood (34,963 copies/mL). The serum lactate dehydrogenase (LDH) level was higher (480 U/L) than normal (250–450 U/L).

Prognosis evaluation was performed based on the International Prognostic Index (IPI).11 Five predictors were evaluated: age, serum LDH, sites of involvement, Ann Arbor stage, and Eastern Cooperative Oncology Group performance status (Table 1). The patient was classified as low risk and was expected to have a 73% 5-year survival rate.

Rituximab, cyclophosphamide, hydroxydaunorubicin, oncovin, and prednisolone therapy was performed 6 times. After chemotherapy, complete resolution of the lymphoma was observed with the 1-, 3-, 6-, 9-, 12-, 15-, and 18-month follow-up CT scans. Enlargement of neck lymph nodes was observed at a 21-month follow-up CT scan, and relapsed DLBCL was diagnosed by needle biopsy of the neck lymph node.

At 23 months, the patient was referred to the Department of Periodontics with a complaint of pain and swelling of the peri-implant mucosa of the lower right second molar implant. Patient’s chief complaint was swelling of the peri-implant mucosa and pain when resting. Bleeding on probing and suppuration were observed at the peri-implant mucosa. Clinical evaluation indicated peri-implantitis (Figure 2a). The deepest probing depth was 7 mm. A periapical radiograph showed a crestal bone loss pattern (Figure 2b). A biopsy was performed from the peri-implant mucosa (Figure 3). The patient received additional chemotherapy treatment but did not survive and died 26 months later.

DISCUSSION

Many studies have focused on oral lymphomas mimicking various oral lesions such as periapical periodontitis,12 periodontal disease,13 gingival swelling,14 dentoalveolar abscess,15 and...
This report presented DLBCL of peri-implant mucosa, comparable to peri-implantitis. The peri-implant mucosa has histologic features different from those of the gingiva: composition of connective tissue, the alignment of collagen bundles, and the distribution of vascular structures in the compartment apical of barrier epithelium. In contrast, immunologically, the gingiva and the peri-implant mucosa have some common features. When both are healthy, the connective tissues contain small amounts of inflammatory cells. The proportion of T cells is higher than that of B cells. This feature implies that local immune systems are primarily regulated by T cells in a healthy state. However, in an inflammatory state, B cells dominate among cells in periodontitis and peri-implantitis lesions. Therefore, metastasis of DLBCL to the peri-implant site could be influenced by continuous B-cell infiltration at the inflammatory peri-implant mucosa.

Peri-implantitis is an inflammatory process of bacterial etiology around an implant, which includes both soft tissue inflammation and progressive loss of supporting bone beyond biologic bone remodeling. It is generally accepted that changes in the level of the crestal bone in conjunction with bleeding on probing with or without concomitant deepening of peri-implant probing depths are important diagnostic factors. Suppuration is a common finding in peri-implantitis sites. In this report, at the first visit, bleeding on probing with suppuration and crestal bone loss was observed during clinical examination and periapical radiograph. It could have been misdiagnosed as peri-implant disease rather than DLBCL. In consequence of the patients’ medical history of lymphoma, a biopsy was performed immediately.

The patient was classified as low risk by IPI. However, in terms of prognosis, the immunophenotype of DLBCL is also important. DLBCL has been subclassified into 3e distinct forms, based on the gene expression profiles: germinal center B-cell like (GCB), activated B-cell like (ABC), and type 3 gene expression (type 3) profiles. Generally, the GCB group has a better prognosis than the ABC and type 3 groups. It is possible to classify DLBCL into the GCB or ABC type using immunohistochemical profiling based on GCB/ABC-related markers (CD10, Bcl-6, and MUM1). In this report, Bcl-2 is also strongly related to a poor prognosis of DLBCL. In this report, DLBCL was positive for Bcl-2 and subclassified in the ABC group (CD10 negative; MUM1 positive). Therefore, although the patient was classified as low risk by IPI, an adverse prognosis was expected based on immunophenotype.

<table>
<thead>
<tr>
<th>Prognostic Factor</th>
<th>Patient</th>
<th>Score</th>
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<tbody>
<tr>
<td>Age (&lt;60 vs ≥60 years)</td>
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<tr>
<td>Serum lactate dehydrogenase level (normal vs &gt;1× normal)</td>
<td>480 U/L</td>
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</tr>
<tr>
<td>Extranodal involvement (&lt;1 site vs &gt;1 site)</td>
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<tr>
<td>Ann Arbor stage (I or II vs III or IV)</td>
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<tr>
<td>ECOG performance status (0 or 1 vs 2–4)</td>
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<td>0</td>
</tr>
<tr>
<td>Total</td>
<td>Low-risk group</td>
<td>1</td>
</tr>
</tbody>
</table>

*ECOG indicates The Eastern Cooperative Oncology Group.
In conclusion, oral lymphoma should be considered in the differential diagnosis of peri-implantitis. A biopsy and pathologic analysis should be performed, especially in patients with hematologic disease.

**ABBREVIATIONS**

ABC: activated B cell  
CT: computerized tomography  
DLBCL: diffuse large B-cell lymphoma  
EBV: Epstein-Barr virus  
GCB: germinal center B cell  
IPI: International Prognostic Index  
LDH: lactate dehydrogenase  
MUM1: multiple myeloma oncogene 1  
NHL: non-Hodgkin’s lymphoma

**FIGURE 2.** (a) Clinical view indicating bleeding on probing and suppuration were observed at first visit. (b) Periapical radiograph indicating alveolar bone loss around the dental implant.

**FIGURE 3.** Histopathology and immunohistochemical staining of biopsy from peri-implant mucosa. (a) Diffuse infiltration of large atypical lymphoid cells (hematoxylin and eosin; original magnification, ×200 and ×400). Tumor cells were positive for CD20 (b) but negative for CD3 (c). Original magnification, ×200, each.
REFERENCES