CASE REPORT

Tongue cancer after bone marrow transplantation

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Summary A case of tongue cancer developing in a 33-year-old man 7 years and 7 months after allogenic bone marrow transplantation (BMT) for acute myeloid leukemia is presented. The patient received chemotherapy and total body irradiation of a total dose of 12 Gy in a conditioning regimen. He was affected with chronic graft-versus-host disease after BMT, but had not complained of symptom in the oral cavity. Oral examination showed an ulcerative mass with induration at the right lateral border of the tongue. The mass was diagnosed as a squamous cell carcinoma by biopsy. The tumour was surgically removed. There was no evidence of recurrence or metastasis 9 months after surgery. The necessity of long-term follow-up of the oral cavity in recipients undergoing BMT is emphasized.

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KEYWORDS
Bone marrow transplantation; Graft versus host disease; Secondary malignancy; Squamous cell carcinoma; Oral cancer

Introduction

Bone marrow transplantation (BMT) has become an essential part of the treatment for many cases of malignant and non-malignant hematological disorders, but it is still associated with a wide range of complications. Among the complications following BMT, graft versus host disease (GVHD) is the most important and frequent. The development of secondary malignancies is also reported as one of the complications, and these secondary malignancies are classified into three categories: hematologic malignancies, lymphoproliferative disorders, and solid tumours. The first two are relatively frequent and usually occur soon after transplant, whereas the last is less common and the risk seems to increase over time.\textsuperscript{1–4} Overall, the risk of incidence of secondary solid tumour in patients undergoing BMT is reported to be two to three times greater than in the general population.\textsuperscript{5} About one-third of all secondary solid tumours are skin and mucosal cancers, with squamous cell carcinoma (SCC) representing 50% of these cases.\textsuperscript{1,3–5} However, to our knowledge, only 13 cases of oral squamous cell carcinoma following BMT are reported.\textsuperscript{3,6–14} We present a new case of tongue SCC developing 7 years and 7 months after BMT.
Case report

A 33-year-old man was referred to the Division of Oral and Maxillofacial Surgery, University of Tsukuba Hospital, from the Department of Hematology of the same hospital in June 2005, complaining of contact pain of the tongue. The patient had had acute myeloid leukemia diagnosed in December 1996, when he was 26 years old, and he underwent a BMT from his HLA-identical mother in November 1997, following a conditioning regimen that consisted of chemotherapy (2 days of cyclophosphamide at 3600 mg/day and 2 days of etoposide at 1200 mg/day), and total body irradiation (TBI; total dose of 12 Gy with multiple fractions). After the BMT, the recipient was treated with cyclosporin A at 5 mg/kg for 7 months as immunosuppressive therapy. He was affected with acute graft-versus-host disease (GVHD) in the skin and liver after the BMT, which subsequently became chronic GVHD, which eventually resolved 10 months after BMT. The patient had no oral symptoms during the time he had acute and chronic GVHD, but it was unclear from his records whether or not oral pathologies were present during this time. The patient has received neither immunosuppressive drugs nor medications after the completion of the administration of cyclosporine. He had abandoned smoking and alcohol consumption with 5 years duration before the BMT.

Oral examination showed an ulcerative mass with induration, measuring 21 × 18 mm, at the right lateral border of the tongue (Fig. 1). Lichen planus-like lesions were not observed in the oral or perioral tissues, and his oral hygiene condition was good and well-maintained. There was no clinical lymphadenopathy suspected of being metastasis in the neck. T2-weighted magnetic resonance images depicted a well-demarcated mass with high intensity at the right edge of the tongue (Fig. 2).

A biopsy specimen revealed keratinization and cordlike clusters of alveolar tumour cells infiltrating the muscular layers, indicating a diagnosis of well-differentiated SCC (Fig. 3). The patient underwent partial glossectomy, and skin grafting for the defect in the resected tongue under general anesthesia. The surgical margins of the excised specimen were histologically free of tumour cells. The postoperative course was uneventful, and as of his most recent follow-up examination, 9 months after the surgery, there has been no evidence of recurrence or distant metastasis.

Discussion

The improvement in the survival rate of BMT patients has resulted in an increased incidence of long-term complications, including the development of secondary malignant solid tumours. One of the most common sites of solid cancers in these recipients is reported to be an oral cavity, and many of these oral cancers has been histologically diagnosed as SCC. Although oral SCC is considered to be frequent as secondary solid tumour in BMT recipients, there were only 13 reported cases of oral SCC following BMT in the
Prolonged use of immunosuppressive drugs may be associated with the development of cancer. Stimulation of the oral mucosa by GVHD may therefore be linked to the development of oral SCC, as many of the reported cases involved a previous chronic GVHD lesion. Chronic GVHD may be predisposing to secondary tumors after BMT in patients under 30 years old, so age is considered as a significant risk factor. The increased use of BMT treatment and better survival of the recipients after BMT are anticipated in future. Oral secondary cancers have the potential to occur in BMT recipients many years after BMT, so the necessity of long-term follow-up of the patients is emphasized to detect cancers early. In addition, BMT patients should be informed of high potential cancer risk and encouraged to adopt a preventive lifestyle, avoiding risk factors such as smoking, alcohol consumption, and poor oral hygiene.

### Table 1: Previously reported cases of oral SCC after BMT

<table>
<thead>
<tr>
<th>Authors</th>
<th>Age of diagnosis (year)</th>
<th>Sex</th>
<th>Location</th>
<th>Primary disease</th>
<th>Interval (year)</th>
<th>Oral GVHD</th>
<th>TNM classification</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bradford et al.</td>
<td>29</td>
<td>F</td>
<td>Tongue</td>
<td>FA</td>
<td>10</td>
<td>+</td>
<td>T4N0M0</td>
<td>R+C+S</td>
</tr>
<tr>
<td>Lishner et al.</td>
<td>41</td>
<td>M</td>
<td>Buccal mucosa</td>
<td>AA</td>
<td>6</td>
<td>+</td>
<td>T4N0M0</td>
<td>S</td>
</tr>
<tr>
<td>Socie et al.</td>
<td>29</td>
<td>M</td>
<td>Oral cavity</td>
<td>AA</td>
<td>5</td>
<td>+</td>
<td>NS</td>
<td>S</td>
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<tr>
<td>Flowers et al.</td>
<td>12</td>
<td>M</td>
<td>Tongue</td>
<td>FA</td>
<td>6</td>
<td>—</td>
<td>NS</td>
<td>S</td>
</tr>
<tr>
<td>Millen et al.</td>
<td>12</td>
<td>M</td>
<td>Tongue</td>
<td>FA</td>
<td>10</td>
<td>+</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>Otsubo et al.</td>
<td>18</td>
<td>F</td>
<td>Buccal mucosa</td>
<td>AA</td>
<td>8</td>
<td>+</td>
<td>T3N0M0</td>
<td>S</td>
</tr>
<tr>
<td>Kawabe et al.</td>
<td>53</td>
<td>M</td>
<td>Floor of the mouth</td>
<td>CML</td>
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<td>+</td>
<td>T1N0M0</td>
<td>S</td>
</tr>
<tr>
<td>Zhang et al.</td>
<td>35</td>
<td>M</td>
<td>Tongue</td>
<td>CML</td>
<td>8</td>
<td>+</td>
<td>T3N0M0</td>
<td>S+R</td>
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<tr>
<td>Abdelsayed et al.</td>
<td>14</td>
<td>M</td>
<td>Tongue</td>
<td>ALL</td>
<td>8</td>
<td>—</td>
<td>T2N0M0</td>
<td>S</td>
</tr>
<tr>
<td>Noji et al.</td>
<td>18</td>
<td>M</td>
<td>Tongue</td>
<td>ALL</td>
<td>11</td>
<td>+</td>
<td>T2N0M0</td>
<td>S</td>
</tr>
<tr>
<td>The present case</td>
<td>33</td>
<td>M</td>
<td>Tongue</td>
<td>AML</td>
<td>7</td>
<td>—</td>
<td>T2N0M0</td>
<td>S</td>
</tr>
</tbody>
</table>

FA, Fanconi’s anemia; AA, aplastic anemia; ALL, acute lymphocytic leukemia; AML, acute myeloid leukemia; CML, chronic myeloid leukemia; NS, not stated; S, surgery; R, radiation; C, chemotherapy.

References


