

Tongue cancer developing after haematopoietic stem cell transplantation for treatment of acute promyelocytic leukaemia: A case report

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Abstract

Acute promyelocytic leukaemia (APL) is a form of acute myelogenous leukaemia. APL is characterised by anaemia due to suppression of normal haematopoiesis and infection. Haematopoietic stem cell transplantation (HSCT) is current option for the treatment of haematopoietic malignancies and is proving to be successful. Although HSCT has been effective for the treatment of haematopoietic malignant tumours, chronic graft-versus-host disease (GVHD) but secondary cancers can occur, which is a serious complication and frequently involves the oral cavity and skin. Here, we report the case of tongue cancer occurring 17 years after transplantation in a patient who developed GVHD after haematopoietic stem cell transplantation and APL remission. To the best of our knowledge, this is the first report of secondary oral cancer after HSCT with APL as the primary disease.

Keywords: Chronic graft versus host disease, Haematopoietic stem cell transplantation, Oral squamous cell carcinoma, Secondary cancer.

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Introduction

Haematopoietic stem cell transplantation (HSCT) is currently proving to be an effective treatment for haematopoietic malignancies.¹ However, the development of graft-versus-host disease (GVHD) and secondary cancers after HSCT is a problem.² The risk of developing a secondary cancer after HSCT is reported to be 2.16-fold more than that of developing a normal secondary cancer.¹ Furthermore, secondary cancers developing in the oral cavity and pharynx are reported to be approximately 7–16-fold more common than secondary cancers occurring in other regions of the body.³ Acute lymphocytic leukaemia and chronic myelogenous leukaemia are the most frequently reported primary diseases.³ However, to the best of our knowledge, no reports have described secondary

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oral cancer after HSCT with acute promyelocytic leukaemia (APL) as the primary disease. We, therefore, describe the case of a patient with a history of GVHD after HSCT for treatment of APL who developed tongue cancer 17 years after HSCT.

Case Report

A 56-year-old man presented to Nihon University Itabashi Hospital (Tokyo, Japan) in March 2016 with the chief complaint of left-sided tongue pain. His medical history included APL, chronic GVHD, cytomegalovirus pneumonia, hyperlipidaemia, and hypertension. Regarding tongue lesion, the patient had visited this same hospital in August 2013 for examination of a white lesion. At that time, a histopathologic diagnosis of leukoplakia was made after biopsy of the lesion. The patient was followed-up for some time, but visits to the hospital were interrupted and the next visit for tongue pain was in March 2016.

General findings, in March 2016, showed that the patient was emaciated but well-nourished. Local findings showed an ulcer with induration and contact pain on the left side of the tongue (Figure 1A). Magnetic resonance imaging (MRI) (Figures 1B, 1C) showed a signal-hyperintense region measuring 30×25mm on the left side of the tongue. However, MRI showed no evidence of metastasis in the cervical lymph nodes. Subsequent positron emission tomography-computed tomography (PET-CT) showed no evidence of metastasis to cervical lymph nodes or other regions (date not available). The lesion was biopsied under local anaesthesia. Histopathologic diagnosis of the resulting specimen was highly differentiated squamous cell carcinoma. Based on these results, squamous cell carcinoma of the left tongue (T2N0M0, Stage II) was diagnosed.

In May 2016, partial resection of the left side of the tongue was performed under general anaesthesia. Histopathological examination of the resected specimen revealed a tumour measuring 27×22×8mm. The lesion represented well-differentiated squamous cell carcinoma with infiltration of inflammatory cells (Figure 1D, 1E). The resection margins showed no tumour invasion and no vascular invasion. Postoperative respiratory status and wound healing were excellent and the patient was

discharged on the 12th postoperative day. Periodic follow-up continued after discharge from the hospital. Fourteen months after the surgery, lymph node metastasis was noted on the left side of the neck. Left-sided radical neck

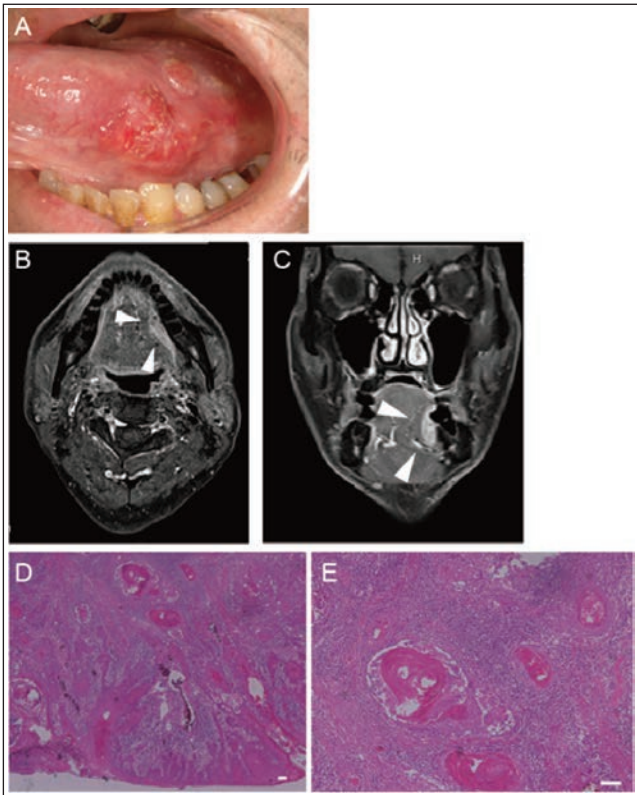


Figure-1: A) Intra-oral findings at initial examination, revealing left tongue carcinoma. B, C) Magnetic resonance imaging (MRI) shows a hyperintense mass measuring 30@25mm on axial (B) and coronal (C) T1-weighted imaging. D, E) Histopathology of the surgical specimen. D) Extension of the epithelial leg is observed. In addition, carcinoma cell proliferation with a high N/C ratio [Nucleocytoplasmic ratio: area of nucleus/(area of cell - area of nucleus)] is observed. Furthermore, inflammatory cell infiltration is observed under the epithelium. Scale bar, 100 μ m. E) Atypical cells with enlarged nuclei form cancerous foci. In addition, multiple cancer pearls are observed. Scale bar, 100 μ m.



Figure-2: Findings for submandibular region metastases
A mass with contrast effect is revealed in the submandibular region.
A) CT, axial cross-section. B) CT, coronal cross-section.

dissection was, therefore, performed. Two years and five months after resection of the left-sided tongue cancer, recurrence was seen in the submandibular region. MRI showed signal hyperintensity in the submandibular region (Figure 2). The patient requested transfer to a palliative ward at another hospital after discussing subsequent treatment. Three years and three months after resection of the left-sided tongue cancer, the patient died of multiple-organ failure due to tumour progression. Verbal consent from the patient to publish the case report was obtained.

Discussion

APL is a type of acute myelogenous leukaemia (AML), accounting for 10% of AML. APL is characterised by the neoplastic proliferation of promyelocytes with a unique cellular morphology in the bone marrow and peripheral blood.⁴ APL is further defined as being accompanied by promyelocytic leukaemia-retinoic acid receptor alpha (PML-RARA), a repetitive chromosomal abnormality.⁴ The age of peak susceptibility is between 10 and 30 years.⁵ Symptoms of APL include anaemia due to suppression of normal haematopoiesis, pancytopenia, weakness, easy fatigability, infections, and bleeding complications such as gingival bleeding, epistaxis, excessive menstrual bleeding, and bruising.⁵ Treatment of APL has improved dramatically with the advent of all-trans retinoic acid. In addition, Arsenic trioxide is the first choice to avoid APL relapse, reportedly achieving a remission rate of 80–90% or more.⁶ After remission, consolidation therapy with Arsenite and allogeneic HSCT is recommended if bone marrow PML-RARA yields a positive result.⁴ The patient in our case experienced relapse after remission and underwent HSCT.

Secondary cancer after HSCT is a serious complication. Curtis et al reported a significantly increased risk of developing secondary cancer (2.1-fold) after HSCT among 28,874 bone marrow transplant patients.² Furthermore, the risk of cancer of the oral cavity and pharynx was reported as about seven-fold that of cancers occurring in other parts of the body.² The development of oral cancer after HSCT has also been reported as a risk factor for bone marrow transplantation at a young age, after total-body irradiation, long-term use of immunosuppressive drugs, chronic GVHD, male gender, and viral infections.⁷ In particular, administration of immunosuppressive drugs after bone marrow transplantation, has been reported to increase carcinogenicity due to decreased immune surveillance against cancer.⁸ Furthermore, among the various immunosuppressants, Azathioprine has been reported to increase the risk of secondary cancers.⁸ Fortunately, Tacrolimus was administered in this case, representing an agent not identified as problematic in the previous report. Furthermore, the patient in this case had no history of total-

body irradiation. However, chronic GVHD, male gender, and a history of viral infections were present, which are known risk factors for development of secondary cancer. These were believed to have possibly contributed to the development of secondary cancers in this case.

A literature search for reports of secondary cancers developing in the oral cavity after HSCT failed to identify any reports of APL as the primary disease, and this case seems to represent the first account.

Oral lesions due to chronic GVHD after HSCT are reported in approximately 82% of patients.⁹ The main symptoms are reported as diverse changes in the oral cavity, including lichen planus-like changes, platelet leukoplakia and sclerotic changes.⁹ In the present case, leukoplakia was initially observed and histopathological examination of the tumour showed a highly lymphocytic infiltrate. Chronic inflammation was thus presumably involved. In addition, the tongue is the most common site of oral cancer after HSCT, followed by the gingiva.² The time from HSCT to the development of oral cancer reportedly ranges from two to over 17 years,¹⁰ with an average of eight years.¹⁰ In the present case, 17 years passed before tongue cancer developed, and the patient had a long interval until the development of secondary cancer. Secondary cancers that develop in the oral cavity after HSCT are treated according to the usual procedures for oral cancer. The treatment results show a good prognosis, with a five-year survival rate of about 70%.¹⁰

The number of patients treated with HSCT for haematopoietic malignancy continues to increase with improved outcomes. In addition, oral secondary cancers can develop after a long period, as in this case. Careful long-term follow-up is, therefore, important.

Conclusion

We encountered a case of chronic GVHD after HSCT in a patient with APL who developed tongue cancer approximately 17 years after transplantation. This is the first report to describe secondary oral cancer after HSCT with APL as the primary disease.

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Author Contribution:

HK, SA, EC, KY: Conception, design, acquisition, analysis, interpretation of data, literature search, data collection, drafting, revising it critically, final approval.

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