

原文題目(出處)：	Squamous Cell Carcinoma of the Tongue After Bone Marrow Transplant and Graft-Versus-Host Disease: A Case Report and Review of the Literature J Oral Maxillofac Surg 2008;66-144-7.
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內文：

Introduction



- Allogenic bone marrow transplantation (BMT)
 - ~ Curative therapy for malignant and nonmalignant lymphohematopoietic diseases and other disorders
 - ~ Complication: secondary malignancies(2~8- folds higher rate than general population)



- Secondary malignancies after BMT
 - ~ Lymphoma 、 leukemia: arise in hematopoietic tissue, develop relatively early during the post-transplantation period
 - ~ Secondary solid tumors (such as SCC): uncommon, but appear to increase with time



- Potential risk factors of secondary cancers after BMT
 - ~ **Chronic graft-versus-host disease(GVHD)**
 - ~ Prolonged immunosuppressive therapy
 - ~ Pretransplantation radiation and chemotherapy
 - ~ Antigen stimulation arising from histocompatibility differences between recipient and donor
 - ~ Other factors such as **oncogenic virus infection**

Report of a Case

A 17-year-old woman
First visit: August 2005



Chief Complaint

Referred by her hematologist/oncologist for the evaluation of a tongue lesion



Present Illness

April 2000

- chronic myeloid leukemia was diagnosed

December 2000

- Allogenic BMT was performed
- The conditioning regimen included busulfan and cyclophosphamide, with cyclosporine and prednisolone as GVHD prophylaxis



Six months after transplantation

- Chronic GVHD involving the oral cavity, skin, liver, eyes, and the lungs occurred, and required treatment with cyclosporine and prednisolone
- Recurrent episodes of oral mucositis and xerostomia



Oral Examination

- An ulcerative lesion, 1x2 cm in size, involving the left lateral border of the tongue, among areas of mild mucositis



Treatment course

H-P report

- squamous cell carcinoma
- The metastatic work-up was negative
- T2N0M0, stage II

September 2005

- ipsilateral supraomohyoid neck dissection
- partial glossectomy with reconstruction using a cervical myocutaneous regional flap

Histopathologic examination

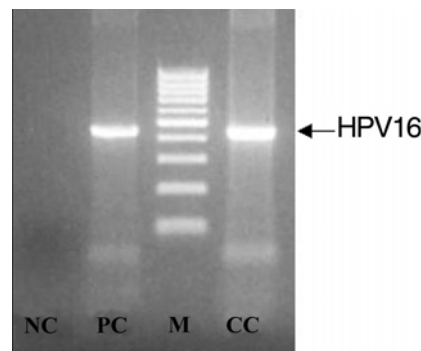
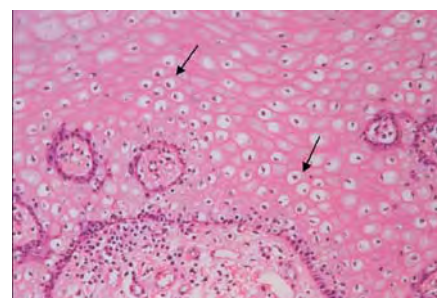
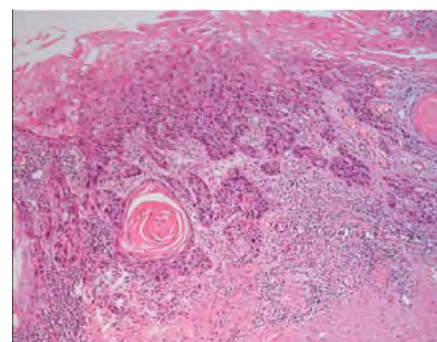
- ~ A moderately differentiated SCC with epithelial koilocytosis (black arrow)
- ~ No metastasis was found in cervical lymph nodes

Polymerase Chain Reaction

- ~ HPV-16 DNA was detected in the excised lesion

Five months after surgery

- The patient had been followed up for 5 months without any evidence of recurrence or metastasis



(NC, negative control; PC, positive control; M, 100 bp ladder; CC, current case)



Discussion



Solid cancer occurrence after BMT recipients:

- 1/3: skin and mucosal neoplasm (50% SCC)
- major risk factor : chronic GVHD
- other risk factors
 - ~ prolonged immunosuppressive therapy (major risk factor for SCC)
 - ~ radiation-based pretransplantation
 - ~ oncogenic viruses infection



Chronic GVHD

- accompanied by chronic inflammation

- Inflammatory cells
 1. Form a tumor microenvironment that facilitates the initial steps of carcinogenesis
 2. Alternatively, these inflammatory cells may be co-opted by neoplastic cells during tumor progression.



Prolonged immunosuppressive therapy
Azathioprine, combined with **cyclosporine** and **steroids** → risk factor of SCC development



Radiation-based pretransplantation
The risk of cancer in transplant recipients that underwent irradiation has been reported to be elevated **18.4-fold**



Oncogenic viruses in many post-transplant solid cancers

- **HPV-16 (most common in HPV positive)**
- Hermann et al reported a case of oral SCC coinfecting with HPV-18 and EBV



21 oral SCC cases that developed in patients who had undergone allogeneic BMT

- ~ **The tongue** was the **most commonly affected site** (11 cases)
- ~ **The great majority of cases** (18 cases) had **chronic GVHD**, which was being treated mostly with cyclosporine, prednisolone, and azathioprine
- ~ Reasons for BMT were leukemia (8 cases), aplastic anemia (6 cases), Fanconi's anemia (6 cases), and non-Hodgkin's lymphoma (1 case)
- ~ Fanconi's anemia
 - several studies have reported that SCC develops in Fanconi's anemia patients before the administration of any treatment for anemia
 - in this context, it remains unanswered as to whether carcinoma is caused by BMT factors, the nature of Fanconi's anemia, or by both
- ~ Oncogenic virus infection was evaluated in 11 cases (HPV:4 cases, no EBV)



We recommend that BMT recipients should be closely followed to ensure the early detection of oral cancer, particularly in those with a chronic GVHD and/or HPV infection.

Table 1. ORAL SQUAMOUS CELL CARCINOMAS IN BONE MARROW TRANSPLANTATION PATIENTS

Reference	Age at Diagnosis (yrs/gender)	Location	Oral Chronic GVHD	Interval Between BMT and Oral Cancer (yrs)	Medication for Chronic GVHD	Oncogenic Virus Detection	Reason for BMT
Lishner et al, ¹¹ 1990	41/M	Buccal mucosa	Yes	6	P, A	Negative	AA
Bradford et al, ⁹ 1990	29/F	Tongue	Yes	10	Steroids	HPV	A
Socie et al, ¹² 1991	29/M	Oral cavity	Yes	5	Cs	NA	AA
	20/M	Lip	Yes	8	MTX	NA	AA
	12/M	Tongue	No	6	Cs	NA	FA
Flowers et al, ¹³ 1992	30/F	Tongue	Yes	10	P, A	NA	FA
	25/F	Tongue	No	12	None	NA	FA
Lowsky et al, ¹⁴ 1994	31/F	Tongue	Yes	11	Cy, Cs, P, A	NA	AA
	27/F	Mouth	Yes	6	P, A	NA	AA
Otsubo et al, ¹⁵ 1997	20/F	Gingival	Yes	4	Cs, P	NA	AA
Millen et al, ¹⁶ 1997	18/F	Buccal mucosa	Yes	9	Cs, A	NA	FA
Jansisyanont et al, ¹⁷ 2000	24/F	Tongue	Yes	15	None	NA	FA
Abdelsayed et al, ¹⁸ 2002	24/M	Buccal mucosa	Yes	2	NA	Negative	ALL
	14/M	Tongue	Yes	8	NA	Negative	ALL
Zhang et al, ⁸ 2002	35/M	Tongue	Yes	8	None	Negative	CML
	47/M	Lower lip	Yes	7	Cs, P	HPV18	CML
	54/M	Lower lip	Yes	5	None	HPV16, 18	AML
Szeto et al, ⁵ 2004	45/M	Tongue	Yes	6	Steroid, Thal, A	Negative	AML
	50/M	Tongue	Yes	2	Steroid, Thal, A	Negative	AML
Demarosi et al, ⁷ 2005	53/F	Gingiva	Yes	5	Cs, P	Negative	NHL
Current case	17/F	Tongue	Yes	5	Cs, P	HPV16	CML

Abbreviations: P, prednisolone; A, azathioprine; Cy, cyclophosphamide; Cs, cyclosporine; MTX, methotrexate; Thal, thalidomide; NA, not available; HPV, human papillomavirus; AA, aplastic anemia; FA, Fanconi's anemia; ALL, acute lymphoblastic/lymphocytic leukemia; AML, acute myeloid leukemia, CML, chronic myeloid leukemia; NHL, non-Hodgkin's lymphoma.

題號	題目
1	Which type of HPV has been found to be associated with oropharyngeal squamous-cell carcinoma? (A) HPV 2 (B) HPV 6 (C) HPV 11 (D) HPV 16
答案(D)	出處：Oral and Maxillofacial Pathology 2 nd edition/Sapp. Eversole. Wysocki. p223
題號	題目
2	Which of the following is the most common location for intraoral squamous cell carcinoma? (A) Upper labial mucosa, maxillary gingival, and hard palate (B) Lower labial mucosa, maxillary gingiva, and buccal mucosa (C) Lower lip, ventrolateral tongue, and floor of the mouth (D) Anterior tongue, mandibular gingiva, and retromolar area
答案(C)	出處：Oral Pathology for the Dental Hygienist 4 th edition p290