Revista Brasileira de Hematologia e Hemoterapia
Brazilian Journal of Hematology and Hemotherapy

www.rbhh.org

Case report

Oral cancer after prolonged immunosuppression for multiorgan chronic graft-versus-host disease

*Renata Lins Fuentes de Araújo, Karine de Fátima Lyko, Vaneuza Araújo Moreira Funke, Cassius Carvalho Torres-Pereira**

Universidade Federal do Paraná (UFPR), Curitiba, PR, Brazil

ARTICLE INFO

Article history:
Received 10 June 2013
Accepted 2 August 2013

Keywords:
Mouth neoplasms
Bone marrow transplantation
Leukemia
Myeloid
Graft-versus-host disease

ABSTRACT

Long-term survivors of hematopoietic stem cell transplantation are recognized as a risk group for malignization. Malignant oral neoplasms are increasingly being reported in the literature as a consequence of lesions of chronic graft-versus-host disease, and prolonged multidrug treatment to control its manifestations. This report describes a 43-year-old patient who, after allogeneic bone marrow transplantation, developed an oral squamous cell carcinoma secondary to the use of azathioprine, cyclosporine, prednisone, and tacrolimus, associated with multiorgan chronic graft-versus-host disease involving the oral mucosa, skin, eyes, and liver. This report aims to discuss the possible role of immunosuppressant therapy for chronic graft-versus-host disease on the development of oral squamous cell carcinoma, and the relevance of a close oral follow-up of patients to detect dysplastic or malignant alterations at an early stage.

Introduction

Chronic myeloid leukemia (CML) is a clonal myeloproliferative disorder characterized by the presence of a reciprocal translocation between chromosomes 9 and 22 (Philadelphia chromosome), which leads to the appearance of a new hybrid gene (BCR-ABL) with tyrosine kinase activity. Current initial therapy is the administration of the tyrosine kinase inhibitor, imatinib mesylate, but in some cases, particularly for refractory or advanced phase disease, hematopoietic stem cell transplantation (HSCT) can be indicated as a curative treatment. However, there is concern about late complications of this procedure, such as chronic graft-versus-host disease (cGVHD) and the development of malignancies secondary to radiotherapy, chemotherapy, and prolonged immunosuppressive treatment.[1,2]

*Corresponding author at: Programa de Pós-Graduação em Odontologia e Departamento de Estomatologia, Universidade Federal do Paraná, Av. Lothário Meissner, 632, Jardim Botânico 80210-170, Curitiba, PR, Brazil.
E-mail address: cassius@ufpr.br (C.C.T. Pereira).

1516-8484/$ - see front matter
DOI: 10.5581/1516-8484.20140016

One of the most common late complications after HSCT is graft-versus-host disease (GVHD). Studies demonstrate that patients who develop cGVHD have higher risk of developing solid tumors such as oral squamous cell carcinoma (SCC), mainly because of the immunosuppressive treatment, which generally includes cyclosporine, tacrolimus, and corticosteroids.[2,3]

The current report describes a patient with multiorgan cGVHD, who developed oral SCC after prolonged and combined immunosuppressant drug therapy.

Case report

In 2008, a 43-year-old Caucasian male patient was referred for an oral medical consultation from a bone marrow transplantation unit, with the chief complaint of widespread oral pain, mainly of the palate, and difficulty to open his mouth. In 1999, the patient had been diagnosed with CML and started treatment with hydroxyurea to control the leukocyte count. Three years later he started taking imatinib mesylate, which was maintained for 14 months. As there was no response to high doses of imatinib or its association with cytarabine, the patient was submitted to a HSCT in 2003. The cell donor was his sister and they were fully matched. The patient progressed with acute GVHD (aGVHD), followed by extensive multiorgan cGVHD. In 2004, the CML relapsed, despite severe cGVHD. At that time, there was no other available option and the patient returned to imatinib therapy (400 mg/day), which was maintained until 2009, with an unexpected complete molecular response.

An extra oral examination revealed diffuse hypochromic and hyperchromic skin lesions (Figure 1), and palpable submandibular and cervical lymph nodes. The oral examination revealed a very poor hygiene status, scleroderma with a severe limitation of mouth opening, severe mucosal atrophy and ulcerations, absence of tongue papillae, a pseudomembrane on the anterior third part of the left buccal mucosa, and an indurated retrocomissural ulcerated nodule of approximately 1 cm in diameter (Figure 2). The panoramic radiographic image showed residual root fragments and loose teeth (Figure 3).

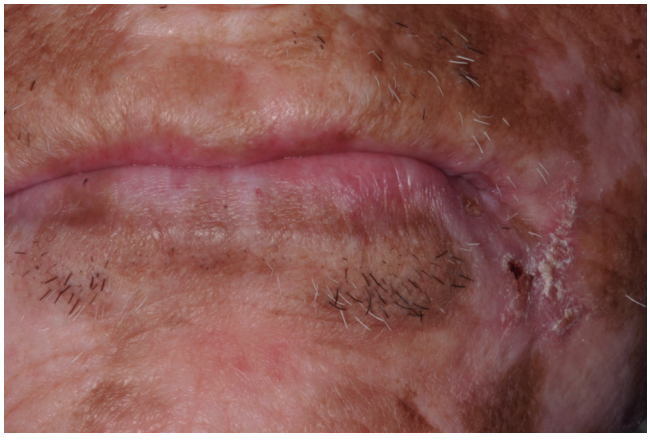

Figure 1 – Diffuse hypochromic and hyperchromic skin lesions characteristic of chronic cutaneous graft-versus-host disease.

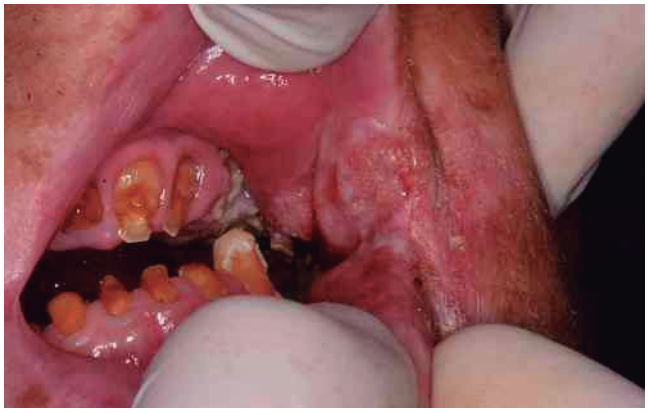

Figure 2 – Indurate and asymptomatic retrocomissural lesion. Poor oral hygiene was evident with multiple acute carious lesions, the accumulation of gross biofilm, gingivitis and restricted mouth opening.

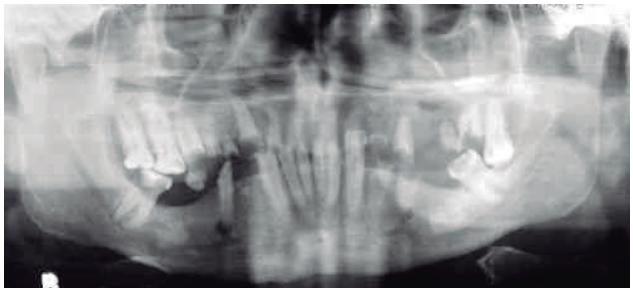

Figure 3 – Panoramic radiograph showing the poor dental status.

The patient was taking imatinib mesylate (400 mg/day), prednisone (20 mg) on alternate days, trimethoprim and sulfamethoxazole (TMP/SMX) (80/400 mg/day), tacrolimus (4 mg/day), azathioprine (100 mg/day), and morphine (240 mg/day). Information on drugs, dosage and time is summarized in Table 1.

Table 1 - Immunosuppressant treatment for acute and chronic graft-versus-host disease.

Year	Drug	Dosage	Prescription (days)
2003-2005	Cyclosporine[a]	200-800 mg	458
	Prednisone	> 5 mg/kg/day	708
2005	Mycophenolate mofetil	1 g	30
2006	Cyclosporine	300 mg	270
	Prednisone	> 5 mg/kg/day	240
	Azathioprine	100 mg	285
2007	Cyclosporine	300 mg	45
	Prednisone	> 5 mg/kg/day	345
	Azathioprine	100 mg	365
	Tacrolimus	2-4 g	330
2008-2009	Prednisone	> 5 mg/kg/day	395
	Azathioprine	100 g	395
	Tacrolimus	2-4 g	395

[a] Dosage used to keep serum level between 200-400 mg/kg.