Oral Manifestations of Immunodeficiencies and Transplantation Medicine

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KEYWORDS

• Hematopoietic cell transplant • Solid organ transplant • Immunocompromised • Oral complications of transplant

KEY POINTS

- Patients who have received a stem cell or solid transplant are acutely and often chronically immunosuppressed.
- Signs and symptoms of immunosuppression can often present in the oral cavity.
- Oral manifestations of immunocompromised patients include mucositis, infections (viral, fungal, and bacteria), and increased risk of oral cancer.
- Early recognition and treatment of oral manifestations of immunodeficiencies secondary to stem cell or solid organ transplant improves quality of life of patients.

Introduction

Solid organ transplantation and hematopoietic cell transplantation (HCT) are becoming increasingly more popular treatments options for various diseases. Solid organs are transplanted from a donor to the body of a recipient to replace a missing or damaged organ. Solid organs that have been successfully transplanted include kidney, liver, heart, lung, pancreas, intestine, and thymus. HCT is the administration of hematopoietic progenitor cells used to reconstitute the bone marrow in hematologic disorders, including hemoglobinopathies, bone marrow failure syndromes, and several malignancies (eg, leukemias, lymphomas).

Oral complications after transplantation can be characterized as early (or acute) or late (or chronic). Early effects tend to develop during treatment and are mainly due to direct tissue toxicity. They usually last days to months and are self-limiting. Late effects occur months to years after treatment, are long-lasting and cause permanent tissue damage and significant morbidity. Several oral complications are secondary to immunosuppression and their presentation is similar to that seen in immunocompromised human immunodeficiency virus (HIV) patients.

Orofacial care providers (eg, dentists, oral medicine specialists, and oral surgeons) can play an important role in the cancer or transplant care team by recognizing and diagnosing oral complications. It is important to be able to recognize and treat these complications because some can contribute to increased morbidity and mortality.

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Early effects

Mucositis

Mucositis is a common early complication of HCT, affecting 60% to 85% of patients. This is due to the conditioning regimen of high-dose chemotherapy administered before HCT. Mucositis occurs approximately 1 week after conditioning and clinically appears intraorally as diffuse painful ulcerations mainly affecting the nonkeratinized mucosa (buccal mucosa, soft palate, and lateral and ventral tongue) (Fig. 1). Mucositis can also affect the gastrointestinal tract (GI) causing many GI-related symptoms, including intestinal cramping and diarrhea. Patients at increased risk of mucositis are those who received total body irradiation as part of their conditioning regimen, have an unrelated donor, or are receiving methotrexate as graft versus host disease (GVHD) prophylaxis.

Because these patients are immunocompromised, mucositis can put the patient at risk for infection and bacteremia. Patients may require total parenteral nutrition due to oral pain and poor oral intake. Mucositis is also associated with increased length of hospital stay and cost of care.

Management strategies are mostly palliative and include systemic opioids and topical agents such as topical anesthetic, Caphosol (EUSA Pharma, Hemel Hempstead, United Kingdom), GelClair (Midatech Pharma US Inc, Raleigh, NC, USA), and MuGard (AMAG Pharmaceuticals, Waltham, MA, USA). Palifermin is a keratinocyte growth factor approved by the US Food and Drug Administration (FDA) for prevention of mucositis. Cryotherapy can also be useful in preventing mucositis secondary to fluorouracil (5-FU). Oral mucositis peaks between days +7 to +14 after HCT and resolves in the next week when normal hematopoiesis resumes.[1,2]

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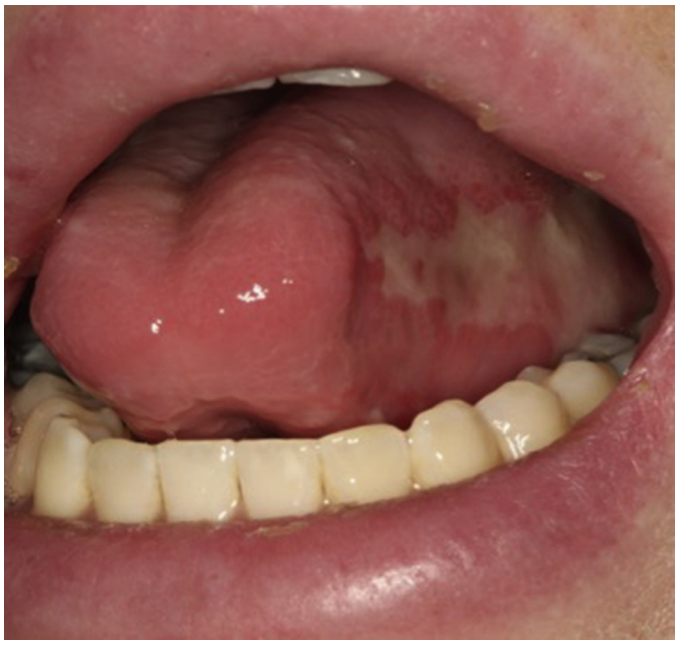

Fig. 1 Mucositis affecting the left tongue in a patient shortly after HCT before engraftment.

Infection

Infections can be both an early and late complication of solid organ or HCT. Early infections typically occur within first 30 days of transplant and include fungal, viral, and bacterial infections. After this period, patients are at higher risk for opportunistic infections. Late infections include encapsulated organisms. The following section discusses the most common oral infections encountered in this patient population.

Viral

Human herpes virus

There are 8 viruses in the herpes family, which are pathogenic to humans, 6 of which can present clinically in the head and neck region.

Herpes simplex virus (HSV), including HSV-1 and 2, and human herpes virus (HHV), including HHV-1 and HHV-2, can present as a primary infection or as recrudescent of a latent infection. Primary herpetic gingivostomatitis presents acutely with painful coalescing ulcers, which can affect any oral mucosal surface and is often associated with systemic signs (eg, malaise, lymphadenopathy, and fever). Primary infections usually occur in children and young adults. Antiviral therapy can reduce viral shedding and shorten the duration of ulceration.

Recrudescent HSV usually presents as clustered coalescing ulcers on keratinized surfaces, such as the lips, in recurrent herpes labialis or gingival tissue, palatal mucosa, or dorsal tongue (Fig. 2). In immunocompromised patients (eg, individuals who undergo HCT), nonkeratinized tissue can also be involved and may present as single or multiple, larger (>0.5 cm) ulcers. Antiviral prophylaxis is common in immunocompromised patients but recrudescence of HSV can still occur. Due to this atypical presentation, the diagnosis can be challenging and lead to delay in treatment, putting the patient at risk for disseminated disease. Viral cultures of active lesions can be helpful in diagnosis but does not distinguish between viral shedding and recrudescence. Exfoliative cytology can also be performed, which can give a diagnosis within hours. Biopsy of the lesion can be useful in those cases that do not respond to therapy or in patients in whom the clinical diagnosis remains unclear. Treatment includes pain management, supportive care, and antiviral therapy.

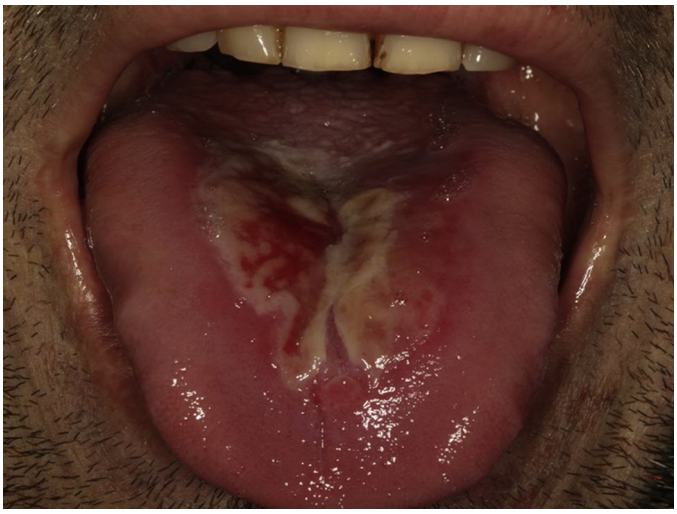

Fig. 2 HSV-related ulceration of the dorsal tongue in an immunocompromised patient.

Varicella-zoster virus (VZV; HHV-3) causes primary varicella and, as a recurrent infection, causes herpes zoster (shingles) in 10% to 20% of cases. Primary infections usually occur in childhood but have become uncommon due to the VZV vaccine, which was approved by the FDA in 1995. Primary infections are accompanied by flu-like symptoms and pruritic papular rash followed by vesicle formation.

Herpes zoster can cause small ulcers that are similar in appearance to oral HSV but are almost always unilateral and along 1 nerve dermatome. Herpes zoster affecting the skin presents as grouped vesicles or crusted lesions on an erythematous base. Viral culture can differentiate between an HSV or VZV infection. Herpes zoster infections require systemic antiviral therapy at greater doses than treatment of HSV infections.

Epstein-Barr virus (HHV-4) has been linked with many conditions, such as infectious mononucleosis; some cancers, including nasopharyngeal carcinoma; lymphoproliferative disorders; and oral hairy leukoplakia (OHL) (Fig. 3). OHL is a benign condition that presents as a white corrugated papule or plaque

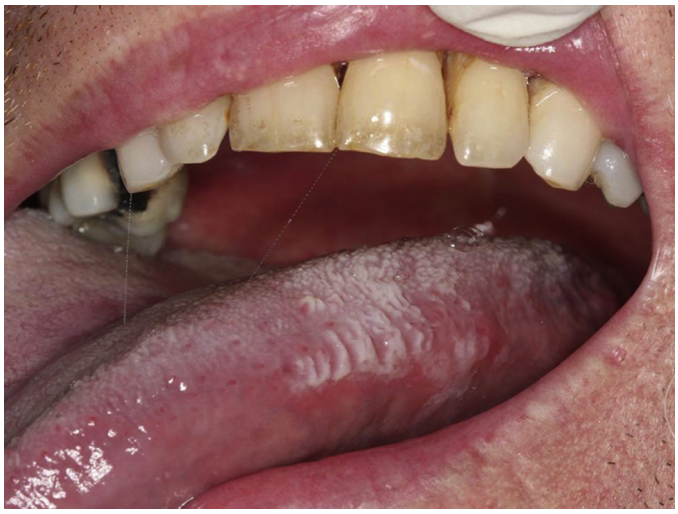

Fig. 3 White corrugated plaques of the left lateral tongue in an HIV patient with OHL.