Dental Research Journal

Review Article

Oral manifestations in transplant patients

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Recieved: June 2013
Accepted: January 2015

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ABSTRACT

Organ transplantation is a widely undertaken procedure and has become an important alternative for the treatment of different end-stage organ diseases that previously had a poor prognosis. The field of organ transplant and hematopoietic stem cell transplant is developing rapidly. The increase in the number of transplant recipients also has an impact on oral and dental services. Most of the oral problems develop as a direct consequence of drug-induced immunosuppression or the procedure itself. These patients may present with oral complaints due to infections or mucosal lesions. Such lesions should be identified, diagnosed, and treated. New treatment strategies permit continuous adaptation of oral care regimens to the changing scope of oral complications. The aim of this review is to analyze those oral manifestations and to discuss the related literature.

Key Words: Hematopoietic stem cell transplantation, immunosuppression, Organ transplantation

INTRODUCTION

An organ transplant is a surgical procedure in which a failing or damaged organ in the body is removed and replaced with a functioning one.[1] Life expectancy of patients who have undergone transplantation has improved dramatically over the years. However, infections are a frequent complication. Risk factors include underlying malignant disease, medical condition of the patient, presence of chronic or latent infections, type of transplant, source of stem cells, use of antimicrobials, mucosal barrier loss, and development of graft-versus-host-disease (GVHD).[2] The oral cavity is an important source of sepsis in immunosuppressed patients, and cytotoxic drugs or the transplant procedure itself has a direct effect on the oral environment. Provision of dental treatment without appropriate management during this time may produce hemostatic and infective complications.[3,4] These complications have a considerable impact on the quality of life and necessitate a multidisciplinary approach aimed at its prevention and management.

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HISTORICAL REVIEW

The first grafting of skin flaps for facial reconstruction of noses and ears date back to around 400 B.C., as indicated by Sushruta in his medical treatise Sushruta Samita.

Gaspare Tagliacozzi is considered to be the father of modern plastic surgery.[2]

In December 23, 1954, the first successful kidney transplant was performed from a living donor between identical twins by Murray *et al*. at the Brigham Hospital, Boston.[5]

In December 3, 1967 Christian Neethling Barnard and his team performed the first human-to-human heart transplant.[6]

CLASSIFICATION

Transplant procedure can be classified as shown in Table 1. Clinical transplant can also be classified as

Table 1: Classification of transplant procedures[7]

Allogeneic transplants	
Autologous transplant	A transplant to and from one's self (autograft)
Isogeneic or syngeneic transplant	Transplantation from an identical twin (isograft)
Allograft	Donors are not genetically identical to the recipient
Xenogeneic transplant	Transplant from donors of one species to recipients of another species (xenograft)

solid organ/tissue transplant and hematopoietic stem cell transplants (HSCT), earlier called bone marrow transplant (BMT).[7]

TRANSPLANT IMMUNOLOGY

The immune response of the body to an allogeneic transplanted organ is T-cell dependent. The first step in response to foreign antigen is T-cell recognition and activation. These activated T-cells then differentiate into effector cells, which are responsible for orchestrating the immune response directed toward the target antigen. Some T-cells differentiate into memory cells, which provide rapid recall responses to antigen re-challenge. Other T-cells may have their effector function silenced or terminated by anergy, apoptosis, or suppression, after interactions with other regulatory cells or soluble factors.[8,9]

The major histocompatibility complex (MHC) codes for antigens like human leukocyte antigen (HLA) system that allow immune cells to identify self from nonself. The MHC presents the strongest immunologic obstacle to all types of allografts. The human T-cell "repertoire" is strongly biased to have cross-reactivity to allogeneic MHC molecules, providing a barrier to organ transplantation and HSCT.[7,9] The main antigens that are important in organ transplantation are the Class I HLA-A, B and the Class II HLA DR antigens.

Allo-recognition is of two types, direct and indirect. In direct allo-recognition, the donor antigen presenting cells (APCs) migrate out of the allograft to secondary lymphoid organs and stimulates T-cells directly. This pathway predominates in the early posttransplant period and is responsible for acute rejection. In indirect allo-recognition, host APCs pick up donor antigens shed from the graft and stimulate host T-cells indirectly.[9]

The immune response to alloantigen is described as a sequence of three signals. The first signal is a presentation of antigen through the MHC class to T-cells. This interaction is highly specific, but has low affinity and requires a second signal (co-stimulation) before T-cell activation can occur. The second signal is provided by ligands on the APC. When both these signals are provided, the T-cell secretes optimum concentrations of interleukin-2 (IL-2). Stimulation of the T-cell receptor without the second signal results in anergy.

Three groups of ligands have been identified:

i. Those responsible for T-cell co-stimulation (CD28/B7)
ii. T-cell adhesion molecules that play an active part in initiating cell-to-cell contacts
iii. T-cell accessory molecules, which stabilize interaction between cytotoxic T-cells and target cell.

The third signal in T-cell activation is the interaction of IL-2 with its T-cell receptor. IL-2 results in a number of intracellular events that lead to DNA synthesis as well as T-cell differentiation.[9]

Organ transplantation can lead to rejection. It is classified according to the time of occurrence as:

a. Hyperacute rejection occurring within 24 h of reperfusion is usually caused by antibodies present in the recipient at the time of transplantation.
b. Antibody mediated rejection (humoral/vascular rejection) occurs days, weeks or months after transplantation and is caused by antibodies produced after transplantation.
c. Chronic rejection occurs month to years after transplantation, caused by repeated inflammation and injury from immune-mediated and nonimmune-mediated causes.[9,10]

ORAL MANIFESTATIONS

Cytotoxic treatment performed prior to transplantation results in transient neutropenia and thrombocytopenia causing risk of infection.[3,4] The oral cavity is the most frequently affected site after BMT and the second most affected site after peripheral blood stem cell transplant.[11]

CLASSIFICATION

The oral lesions are broadly classified in Table 2.[7] Majorana *et al.* divided the HSCT process into five stages based on physiologic and biological events or therapy-related toxicity affecting the oral cavity [Table 3].[12]

Table 2: Classification of oral lesions in transplant patients[7]

Infectious	Noninfectious
HSV infection	Neoplasms
VZV virus infection	SCC
Epstein-Barr viruses	Lymphoma
CMV infection	Kaposi's sarcoma
Bacterial infections, including dentoalveolar abscesses, dental caries	Graft versus host disease
Candidiasis	Oral mucositis
Deep fungal infections	Salivary gland dysfunction
Aspergillosis	Developmental tooth defects
Cryptococcosis	
Mucormycosis	
Blastomycosis	

HSV: Herpes simplex virus; VZV: Varicella-zoster; CMV: Cytomegalovirus; SCC: Squamous cell carcinomas.

INFECTIONS

More than 80% of transplant recipients develop at least one infection and 40% of deaths are due to complications of infections occurring alone or following rejection. About 55% of posttransplant infections are caused by bacterial agents, 30% viral and 15% fungal.[13] Signs of oral infection may be muted due to decreased inflammatory response, or may be exaggerated. The presentation of an infection depends upon the patient's level of immunosuppression and the ability to mount an immune response.[7] Two main mechanisms play a role in the risk for infection. One depends on nonspecific defenses such as the integrity of surface barriers, which is damaged by intensive conditioning regimens. The other major defense is the immune system, which results from activity of granulocytes, monocytes, macrophages, natural killer (NK) cells, T-cells, and complement, which become deficient after HSCT. Uncomplicated recovery starts with healing of the mucosal tissues and recovery of granulocytes and NK cells about 2-week after myelo-ablative conditioning. T-cell and B-cell immune responses against viral, bacterial, and fungal organisms may be suppressed for a prolonged period of time, particularly if GVHD develops.[2]

Infections, which occur after transplantation are categorized into three phases:[14,15]

a. First posttransplantation month: These include candida species, herpes simplex virus (HSV) and nosocomial bacteria. However, the incidence has decreased significantly with the use of prophylactic antiviral medications.

Table 3: Oral manifestations according to different stages of HSCT process[12]

Staging based on therapy-related toxicity affecting the oral cavity
Stage 1: Pretransplant
Oral mucosal diseases
Dental decay
Periodontal infections
Endodontic infections
Oral manifestations of malignancy
Leukemia, lymphoma
Oral manifestations of systemic conditions - immunosuppression, pancytopenia
Stage 2: Conditioning to early engraftment (days: −10-+21)
Mucositis
Viral infections: HSV
Fungal: Candida, aspergillus
Bacterial: Gram-negative
Xerostomia, hemorrhage
aGVHD
Stage 3: Early engraftment to recovery of circulating counts (days: +21-+100)
Mucositis (resolving)
Hemorrhage
GVHD: Acute and chronic
HSV, CMV, VZV
Fungal: *Candida*, *Aspergillus*, *Mucormycosis*
Bacterial infection
Xerostomia
Recurrence of cancer
Stage 4: Recovery of circulating counts to immune reconstitution (days: +100-365)
Chronic GVHD
Viral infections: VZV, HPV, HSV
Fungal: *Candida*
Xerostomia
Recurrence of cancer
Dental/skeletal growth and development
Stage 5: Long-term survival (1 year or longer after transplant)
Xerostomia
Dental/skeletal growth and development
Second primary malignancy

HSCT: Hematopoietic stem cell transplants; aGVHD: Acute graft versus host disease; GVHD: Graft-versus-host-disease; HSV: Herpes simplex virus; CMV: Cytomegalovirus; VZV: Varicella-zoster; HPV: Human papilloma virus.

b. During 1-6 months posttransplantation, in addition to earlier infections, new infections produced by intracellular/opportunistic pathogens including cytomegalovirus (CMV), HSV six, *Pneumocystis carinii*, and *Cryptococcus* neoformans appear. Oral candidiasis and recurrent herpetic stomatitis also occur.
c. In the third phase (>6 months), the risk of infection varies, depending on the course during the first two phases and the state of immunosuppression.

Herpes simplex virus is the most common viral pathogen causing oral infections in transplant patients and usually occurs 2-6 weeks posttransplant[7] and is more severe than in nonimmunocompromised patients.[16] Recipients of matched unrelated/ mismatched allo-HSCT are more at risk of acquiring infections with HSV than patients who have undergone matched related allo-HSCT.[17] The reported prevalence of oral HSV lesions in renal transplant patients is 0-11.3%,[18-20] whereas in BMT patients is 37-57%.[21] Primary and recurrent oral HSV infections are characterized by clustered vesicles on an erythematous base, which rapidly rupture leaving an ulcerated area. Recrudescent HSV-1 lesions are more extensive, aggressive, slow-healing, and painful. They appear slightly depressed with raised borders. Vesicles or satellite ulcers measuring 1-2 mm are present at the edge of the main ulcer. If untreated, infection may disseminate to other sites. These ulcers may develop at the nonkeratinized sites, or develop at keratinized sites such as the hard palate, dorsum of tongue, gingiva, vermillion lip, and peri-orally.[7,22,23] Morfin *et al.* detected HSV in 10% autologous and 9.2% allogenic recipients. Mucositis was present in 79% patients excreting HSV.[16] The incidence of clinically apparent HSV disease in seropositive patients not receiving prophylaxis was reported as 35-68%.[24]

Acyclovir 400-800 mg orally twice a day, or valacyclovir or famciclovir 500 mg orally twice a day is recommended prophylactically for 1-year. Treatment includes acyclovir 400 mg thrice a day, valacyclovir 1 g or famciclovir 500 mg twice a day. For acyclovir-resistant HSV, foscarnet 80-120 mg/kg/day or intravenous (IV) or topical cidofovir is given. Extensive HSV disease is treated with IV acyclovir 5-10 mg, 8 hourly.[24,25]

Epstein-Barr virus infection causes oral hairy leukoplakia (OHL) and posttransplant lymphoproliferative disorders (PTLD). OHL has prevalence of 0-13% in renal transplant patients.[19-21] The overall prevalence of PTLD in solid organ transplant recipients is <2%. Patients receiving renal allografts have the lowest frequency of PTLD (<1%). Those with hepatic and cardiac allografts have an intermediate risk (1-2%), and those receiving heart-lung allografts have the highest frequency (5%). Treatment involves antiviral medication and reducing immunosuppression. Accessible PTLD lesions are surgically excised. Other options include intervention with chemotherapy and/or radiotherapy, cytokines (interferon, IV IgG, or IL-6), anti-B cell antibodies, or mounting cellular immunotherapy against the involved cells.[26]

Cytomegalovirus infection occurs in approximately 30-75% of transplant recipients, with incidence of CMV disease between 8% and 80%, depending on the type of transplantation, immunosuppression and the donor/recipient CMV serostatus.[27] Incidence of 1.32% ulcerations was reported involving buccal mucosa, palate, tongue, and floor of the mouth.[28] Prophylactically IV gancyclovir 5 mg/kg once daily or oral valacyclovir 2 g 4 times/day is recommended. For treatment, oral valganciclovir 900 mg twice/day, IV ganciclovir 5-mg/kg 12 hourly, foscarnet 60 mg/kg IV 8 hourly, or cidofovir 5 mg/kg once weekly is recommended.[29]

Previous studies have shown that the prevalence of candidiasis is around 7.4-46.7% in renal transplant recipients. The clinical forms described are erythematous candidiasis, angular cheilitis and pseudomembranous candidiasis.[15,18,19,21] One study reported prevalence of 60% candidiasis in patients with fissured tongue. Tongue lesions with whitish coating were observed in 77% patients, atrophic glossitis (11.5%) and median rhomboid glossitis (11.5%). *Candida albicans* (85%) was the main agent responsible.[30] Fluconazole-resistant species including *Candida glabrata* (13.5%) and *Candida krusei* have emerged. Fungal lesions are treated prophylactically with 400 mg oral fluconazole daily.[31,32] Active infections are treated with a 1-week course of daily fluconazole (100- or 200-mg). Prophylactically, nystatin suspension (5 mL)[33] or lipid formulation of amphotericin B 3-5 mg/kg/day is recommended. Caspofungin, an echinocandin, (IV 50 mg/day) is also effective.[34]

DRUG-INDUCED GINGIVAL OVERGROWTH

Cyclosporine (CsA) is a potent immunosuppressant drug that is used to prevent rejection of organ transplants. CsA affects the proliferation of gingival fibroblasts and the accumulation of connective tissue extracellular matrix components. CsA inhibits collagenase gene expression and reduces collagen degradation by lowering phagocytosis and the activities of lysosomal enzymes cathepsin-B and-L in gingival fibroblasts.[35] Gingival fibroblasts respond to CsA by

increasing IL-6 secretion, which enhances collagen and glycosaminoglycan synthesis. CsA synergizes with IL-1β to further up-regulate IL-6 secretion.[36] CsA also regulates the transcription of transforming growth factor-β_1 which decreases the proteolytic activity of gingival fibroblasts.[37] Although the dose dependency is not clearly established, an initial threshold serum concentration is required to initiate gingival overgrowth (GO). Furthermore, GO has been reported in patients taking CsA within 3 months or more.[36] Various studies by Spolidorio *et al.*,[20] Ellis *et al.*,[38] Ghafari *et al.*[39] have shown CsA-induced GO in transplant recipients. The mandibular anterior, followed by maxillary anterior buccal areas are mostly affected.[39] The reported prevalence of CsA-induced GO in transplant recipients is 8-100%.[37] Tacrolimus-induced GO ranges from 0% to 30%, whereas in sirolimus-based regimens is 20.8%.[40]

Tacrolimus has been used as an alternative to CsA because of the comparatively decreased prevalence and severity of GO. The mean dosage of CsA was 10 mg kg/body weight/day and that of tacrolimus 1.0 mg/kg/body weight/day.[20,38] Adjunctive agents like prednisone, azathioprine, and calcium channel blockers influence the occurrence and severity of GO.[40] A cross-sectional study demonstrated that the prevalence of GO was of 60.0% for CsA, 28.9% for tacrolimus, and 15.6% for sirolimus groups. After 44 months follow-up, occurrence of GO decreased (CsA 34.8%, tacrolimus 12.9%, and sirolimus 0.0%).[40,41] Proper oral hygiene measures may reduce the degree of GO. Azithromycin (500 mg/day) is used to treat GO because it blocks CsA-induced cell proliferation and collagen synthesis.[35]

ORAL MUCOSITIS

Oral mucositis (OM) is characterized by mucosal damage ranging from mild inflammation to extensive ulceration, which affects the oral cavity. According to Lalla *et al.*, pathogenesis of mucositis involves five steps:[42]

a. Initiation of tissue injury by generation of reactive oxygen species
b. Upregulation of pro-inflammatory cytokines like tumor necrosis factors-α through generation of messenger signals
c. Signaling and amplification, which activates molecular pathways that amplify mucosal injury
d. Ulceration and inflammation
e. Healing characterized by epithelial proliferation, cellular and tissue differentiation restoring the integrity of the epithelium.

The incidence reported from 75% to 100% after myelo-ablative conditioning regimens, peaks between posttransplant days 6-12 and resolves by day 14-18. It mostly affects nonkeratinized mucosa, such as ventral and lateral surface of tongue, floor of mouth, soft palate, buccal and labial mucosa.[2,43] OM may be caused by cytotoxic drugs used to prevent GVHD. These drugs reduce the regenerative capacity of the oral mucosa, thereby increasing the risk of bacteremia due to *Streptococci viridans* and coagulase-negative staphylococci, or fungemia and virus infection.[2,31,44] Other symptoms include complete loss of taste (34%), altered taste, pain, sores, sensitive mouth, and development of thick mucus, causing difficulty in speech and mastication.[45] The regimens causing most severe type involves methotrexate[43,46] and high-dose melphalan (HDM) and HDM/total body irradiation (TBI), while the least toxic are cyclophosphamide-carmustine and cyclophosphamide-etoposide-carmustine.[47] The World Health Organization (WHO) scale of OM[48] is shown in Table 4.

Management of OM involves pain control, nutritional support, and oral decontamination, palliation of dry mouth, control bleeding, and therapeutic interventions. The Multinational Association of Supportive Care in Cancer and the International Society for Oral Oncology guidelines recommend the use of standardized oral care protocol including using a soft toothbrush, flossing, and nonmedicated rinses. Treatment includes saline mouth-rinses, ice chips, and topical anesthetic mouth-rinses (2% viscous lidocaine with diphenhydramine).[42,49] Palifermin (recombinant form of human keratinocyte growth factor) 60 μg/kg/day is recommended for 3 days before conditioning

Table 4: WHO scale for oral mucositis[48]

0	1	2	3	4
None	Soreness with or without erythema	Erythema, ulcers, and patient can swallow solid food	Ulcers with extensive erythema and patient cannot swallow solid food	Mucositis to the extent that alimentation is not possible

WHO: World health organization.

treatment and posttransplant.[50] It reduces the severity, incidence and duration of OM WHO grades 2-4.[51] Cryotherapy is suggested in patients receiving HDM.[50] Studies have shown that low-level laser therapy significantly reduces OM Grades 3 and 4.[52,53]

GRAFT-VERSUS-HOST-DISEASE

The graft-versus-host reaction is a multisystem immunologic consequence of grafting immunocompetent cells from one person to an immunodeficient host.[54] About 40-70% of patients develop acute GVHD (aGVHD) or chronic GVHD (cGVHD) after undergoing allogeneic BMT. The development of GVHD occurs under three conditions: The graft must contain immunologically competent cells; the recipient must express tissue antigens that are different from those of the donor, and the recipient must be incapable of rejecting the graft owing to tolerance, lack of recognition or immunosuppression.[55] Previously, aGVHD occurred <100 days after stem cell infusion whereas cGVHD occurred after 100 days. However, a clear distinction between the two is no longer valid in the era of reduced-intensity conditioning regimens transplantation. Therefore, GVHD is defined as acute or chronic based on its clinical presentation rather than the timing of development.[2]

Oral manifestations are observed in about 80% of patients with extensive cGVHD. The 2005 National Institutes of Health (NIH) consensus working group for diagnosis and staging of cGVHD standardized the criteria for the diagnosis of oral cGVHD. Lichenoid lesions commonly affect all mucosal surfaces with predominant reticular and papular forms; tongue lesions usually are plaque-like. These can be associated with hyperkeratotic leukoplakias. Ulcerative lesions are uncommon, covered by a grayish-yellow pseudomembrane surrounded by erythema and is localized mainly in the buccal mucosa, palate and dorsal part of the tongue. Oral GVHD can involve any site. Xerostomia, decreased salivary immunoglobulins and increased candidal infections, angular cheilitis and rampant caries are also reported. Blockage of salivary ducts can lead to mucocele formation involving palate and lips. Sclerotic fibrosis of the perioral tissue causes restricted mouth opening presenting as ”purse-string” mouth causing candidal infection and malnutrition. Other morbidities include muscle wasting and cramping and decreased joint range-of-motion.[2,55-57]

The NIH Consensus Conference Ancillary Guidelines and clinical experience recommend oral dexamethasone solution (0.5 mg/5 mL) for initial therapy. Clobetasol 0.05% solution, budesonide mouthwash (3 mg/10 mL), and tacrolimus 0.1% solution are recommended. For focal lesions, high potency (fluocinonide 0.05%) and ultra-potent (clobetasol 0.05%) gels can be applied directly to the mucosa. Tacrolimus ointment (0.1%) is the treatment of choice for lip lesions. Refractory painful ulcerative lesions require intralesional corticosteroids.[33,58] Phototherapy using psoralen (0.3 mg/kg body weight) can be given orally 1 h before ultraviolet light A treatment.[59]

MALIGNANCY

The incidence of malignancy ranges from 2.3% to 31% posttransplant. The most frequent oral cancer is lip cancer, making up to 1.5-8% of all *de novo* neoplasms.[18] Almost all secondary malignancies after HSCT, such as lymphoma or leukemia, arise in hematopoietic tissue. Secondary solid tumors are less common, but the incidence increase over time. Squamous cell carcinomas (SCC) are the most common solid tumor.[57,60] The incidence of epithelial dysplasia, SCC, basal cell carcinoma (BCC), Kaposi’s sarcoma has been reported to be 10% after 10 years, 40% after 20 years posttransplant.[61] Potential risk factors associated with the development of secondary cancers after HSCT include cGVHD-related inflammation, preoperative regimens, with either radio-chemotherapy or chemotherapy alone, radiation mutagenesis, conditioning regimes, immunosuppressive GVHD prophylaxis, viral infection and chronic stimulation as a result of viral antigens, antigenic stimulation from histocompatibility differences between the recipient and donor, interaction of any of these factors with a genetic predisposition, and sex and older age.[57,60,62] Other risk factors include Fanconi anemia and dyskeratosis congenita.[33]

Hasegawa *et al.*[63] in their study have reported that the incidence of secondary malignancies was 5.6% after 6.79 years posttransplant and 4.2% at 10 years posttransplant. BCC and SCC of the skin and oral cavity were common, comprising 45.7% of the malignancies. In one study, verrucous hyperplasia (12%) developed on gingiva, hard palate, and buccal mucosa. Dysplasias (19%) were present on the lower lip predominantly and tongue, presenting as

asymptomatic white or red/white (leukoplakia or erythroleukoplakia) plaques (40%), ulcerations (40%), crusting (40%), or papillary lesions (40%). Invasive carcinomas (69%) presented with pain and paresthesia (11%).[62] Minimal data exist on treatment outcomes, but secondary oral cancers are associated with higher rates of recurrence and poorer long-term survival.[33]

SALIVARY GLAND DYSFUNCTION

The prevalence of xerostomia has been reported to be significantly greater in renal transplant patients than HSCTs (1.4% vs. 0.2%).[18] Hyposalivation was reported in 40%, 53%, 31% and 26% of the HSCT recipients at pre-HSCT, 6, 12, and 24 months post-HSCT, respectively. TBI and myelo-ablative conditioning increased prevalence of hyposalivation up to 6 months post-HSCT. Opioids, immunosuppressive agents, corticosteroids, and antimicrobials contributed to hyposalivation.[64] A shift toward a lower buffer capacity and a higher amount of cariogenic microorganisms was more pronounced with TBI. Reduced salivary secretion rate has also been reported by Bågesund *et al*.[65] and Larsen *et al*.[66]

In addition to ensuring good hydration, rinses, sprays, gels and salivary stimulants (sugar-free gum/candy) can control symptoms. Sialagogue therapy includes pilocarpine (5 mg) thrice/day as initial therapy or cevimeline (30 mg) thrice/day. Topical steroids may reduce the frequency and number of superficial mucoceles. Rarely, surgical removal is indicated.[33]

EFFECTS ON DEVELOPMENT OF TOOTH

Children transplanted under the age of 12 years are at risk of developmental disturbances involving teeth and overall growth of the jaws. Dental disturbances are manifested as decreased crown size, shortened and conical roots, microdontia, or complete agenesis. Damage to jaw growth centers by conditioning regimens can lead to decreased size of jaw bones.[12] Hölttä *et al*.[67] emphasized the impact of TBI and age on HSCT children <10 years. The most frequently missing teeth were second premolars (58%), second molars (28%), first premolars (10%) and maxillary lateral incisors (4%). Tooth agenesis occurred in 62% of recipients. Dental abnormalities are caused by therapeutic insults on rapid odontogenic changes. Root stunting was reported in 27% of patients.[68] Patients aged 3.1-5.0 years presented with the most severe aberrations of the root/crown ratio (77%). More teeth were affected after TBI (85%). Disturbed root growth in permanent teeth occurred when HSCT was performed before 10 years of age.[69] Among the late dental effects, hypoplasia of enamel and/or roots occurred among patients under 18 years of age.[70]

Proper dental care and rehabilitation can improve the quality of life.[67] Patients should follow noncariogenic diet and good oral hygiene. Sodium fluoride gel (1.1%) should be applied using toothbrush or custom-fitting trays. A calcium/phosphate-based remineralizing agent can be applied just before topical fluoride.[33]

CONCLUSION

The posttransplantation period is hampered by many potential complications which can lead to morbidity and mortality. The most common complications include CsA-induced gingival enlargement, GVHD, OM, viral infections like HSV infection, and oropharyngeal candidiasis. Among the late complications, secondary malignancies are recognized, with SCC being the most common. These changes emphasize the importance of regular oral screening. Most transplant centers conduct a complete oral evaluation before transplant conditioning. The primary responsibilities of a health care professional are prevention of infections and providing instruction on oral prophylaxis and hygiene as well as direct intervention.

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How to cite this article: Nappalli D, Lingappa A. Oral manifestations in transplant patients. Dent Res J 2015;12:199-208.

Source of Support: Nil. **Conflict of Interest:** The authors of this manuscript declare that they have no conflicts of interest, real or perceived, financial or non-financial in this article.