

The algorithm of dental treatment in patients before and after organ transplantation

Schemat postępowania stomatologicznego przed transplantacją narządową i po niej

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Abstract

The vascularized organs transplantation has become an effective method of treating patients with end-stage organ failure. However, prolonged immunosuppressive therapy causes many side effects, which are reflected in the state of the oral cavity. Infections in transplant recipients represent the most common postoperative complication. The development of infection is dependent on pathogenic microorganisms as bacteria, fungi and viruses, including CMV, EBV, HPV, HIV. To reduce the potential for serious problems in the oral cavity occurring after organ transplantation, each patient should be subjected to a thorough dental inspection and treated by physicians in specialized medical centers. The role of a dentist should involve the evaluation before and after transplantation according to specialized algorithm of dental treatment. The information concerning the presence of infection outbreaks and pathologic lesions in the oral cavity is an important signal for transplant physician to perform extended diagnostic testing, as well as to modify the immunosuppressive therapy.

Key words: oral cavity, viral infections, dental treatment, transplant recipients, organ transplantations

Słowa kluczowe: jamy ustna, zakażenia wirusowe, leczenie stomatologiczne, biorcy przeszczepów, transplantacja narządów

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The transplantation of vascularized organs has become an effective method of treating patients with end-stage organ failure. Transplanted organs, as foreign antigens, require the constant use of immunosuppressive drugs to protect them against rejection in the recipient organism. This medicine, which is taken for life, causes many side effects, which are reflected in the state of oral cavity. Among those we can include: increased periodontitis and tooth caries, increased incidence of oral mucous membrane lesions as a result of high susceptibility to fungal, bacterial and viral infections, gingival overgrowth, xerostomia and increased susceptibility to developing cancer.

Infections in transplant recipients represent the most common postoperative complication. The source of infection can be endogenous flora of the patient, viruses in latency state, transplanted organs, the hospital environment. The majority of infections occur during 4–6 months after transplantation, when the immune system is highly suppressed.¹

The development of an infection is dependent on pathogenic microorganisms, doses of immunosuppressive drugs and their use of time, coexisting diseases, metabolic disorders and immunomodulatory virus infections (CMV, EBV, HPV, HCV, HIV).² The characteristic feature of infections in organ transplant patients is a significantly reduced inflammatory response and a low symptomatic clinical course, causing difficulties in rapid diagnosis, generalization of infection, often reinfections as well as considerable resistance to pharmacology treatment.³

Few studies provide clear dental procedures in this patient population and they also do not draw enough attention to the most common illnesses that can be observed by dentists in the oral cavity of organ transplant recipients. It should be noted that the oral cavity is one of the main sources of infection in people with impaired immunity.

To reduce the potential for serious post-transplant problems in the oral cavity, each patient should be subjected to a thorough dental inspection and treated by physicians in specialized medical centers. The role of the dentist should include the assessment of the patient's teeth before transplantation and after transplantation, with particular emphasis on the elimination of oral sources of infection. The role of a dentist should involve 2 phases: The evaluation before transplantation and subsequently the evaluation after transplantation.

Evaluation before transplantation

Chronic renal failure with the passing of time demands external blood filtering techniques, such as dialysis or hemodialysis which prolong the patient's life until a kidney transplantation, but unfortunately leads to many pathological lesions in the oral cavity. The patient should be under special medical care including specialist dental care until organ transplantation.

Chronic renal failure and dialysis results in the exacerbation of dental caries indices, erosions on the palatal and lingual teeth surfaces, aggressive periodontitis, dry mouth and xerostomia, pathological changes in the soft tissues such as erosions and ulcerations, increased frequency of non-healing bacterial, fungal, protozoan and viral infections.^{4–7}

A wide range of oral lesions have their origin in reduced salivary secretion, increased pH and buffer systems deficiency. In patients undergoing hemodialysis, the major problem is also renal osteodystrophy, which contributes to tooth loss leading to stomatognathic system disorders.^{7,8}

Early procedures of dental evaluation in this group of patients allow for the introduction of an appropriate treatment plan before organ transplantation.⁹

The algorithm of dental treatment in patients under hemodialysis

Before organ transplantation, the dentist should first of all conduct a thorough medical and dental interview. Then, it is necessary to perform a physical examination according to conventional protocol. Panoramic radiography supplemented by periapical radiographs or CBCT – cone-beam computed tomographic imaging should be done.⁹ Finally, the dentist is obliged to establish the individual treatment plan for the patient and qualify the teeth for extraction. The teeth should be extracted in the following cases: teeth with nonvital pulp or pulpless; teeth exhibiting improper endodontic treatment, particularly multirooted teeth; teeth with chronic periapical inflammation; teeth after improper resection; teeth with deep periodontal pockets and bone defects; partially and totally retained teeth.

It is recommended to improve damaged prosthetic restorations and treat inflammatory lesions on the mucous membrane in patients. Professional scaling and root planning must be performed. It is required to educate patients on proper oral hygiene methods such as appropriate brushing methods, use of dental floss, rinse of oral cavity with the mouthwashes containing fluoride and anti-inflammatory agents and proper eating habits. Dental appointment every 3 month is necessary.

Evaluation after organ transplantation

The algorithm of dental treatment in organ transplant recipients

The potential source of an outbreak of infection in the mouth are teeth with nonvital pulp, lack of pulp, teeth that have received improper endodontic treat-

ment, teeth after pulpotomy; teeth with chronic periapical inflammation; teeth after improper resection, hemisection, premolarisation; partially retained teeth with recurrent soft tissue infections; totally retained teeth with suspicion of primordial cyst; periodontal disease coexisting with periodontal pockets and bone defects; peri-implantitis; ulcers and other pathological conditions within the oral mucosa.

In these groups of patients treatment planning is not intended to identify an individual pathology, but to provide an overall assessment of the potentially affected sites, taking into account the overall condition of the patient. It is important to detect early pathological changes in the oral cavity.

Treatment immediately after transplantation

Dental treatment during this period should be performed only in acute cases.¹⁰ During this period, the possibility of rejecting the transplanted organ is very high. In this phase of treatment the patient should regularly control his oral hygiene at home.

Treatment in the stable phase after transplantation

During the stable phase, the patient should execute routine dental checks aimed to eliminate the first signs of a potential pathology. It is recommended to have a dental check-up every month for the first 6 months after transplantation, then every 3 months. The patient should maintain proper oral hygiene that includes correct method of brushing, use of dental floss and mouthwashes containing fluoride and anti-inflammatory agents. The introduction of proper eating habits is also recommended.¹¹ Radiological control containing dental panoramic X-rays should be carried out once a year for an accurate diagnosis. In the stable phase after transplantation the oral sanitation includes professional scaling and root planning in antibiotic cover and treating dental caries. The gangrenous roots and multiple roots teeth with improper endodontic treatment should be extracted in antibiotic cover.⁹ Intraosseous implants with visible evidence of infection should be removed and the diagnosis and treatment of lesions on the mucous membrane is required.

The issue concerning extraction of endodontically treated teeth remains a matter of much controversy. There is a consensus that the dentinal tubules of root canal treated teeth can be a niche for pathogenic agents that could be the cause of focal infections. If the general condition of the patient is good, the transplanted organ shows steady progress, and the patient has full dental arches and very good oral hygiene, it is possible to leave the roots with proper endodontic treatment and annual radiological control.

Infections and pathological lesions in oral cavity in patients after organ grafting

Bacterial infections

The most often isolated bacteria in organ recipients are *Staphylococcus aureus* (35%), bacteria from *Enterococcus* family (*E. coli*, *E. faecalis*, *E. faecium* – 30%), as well as *Actinomyces odontolyticus*, *Streptococcus viridans* isolated from blood and cerebrospinal fluid, as a cause of sepsis. An increased total amount of microorganisms and the growth of anaerobic bacteria are noted in the patients' saliva. Bacterial infections in the oral cavity can be manifested as a local inflammation, erosions, ulcers with various intensity depending on patient immunological condition.³ A case of liver abscess caused by *Porphyromonas gingivalis* concerning the patient treated with kidney transplantation was described in literature. Patients treated with organ transplantation display the occurrence of hairy tongue and acute necrotic – ulcerative gingivitis more often than the healthy population. The principal factor influencing ecological changes and interactions between different groups of microorganisms inhabiting in oral cavity might be the modification of its pH, which is 5.0–5.5 in this group of patients. A poor diet, bad hygienic habits, metabolic disorders and drugs affect changes in acidity of the environment of oral cavity.¹²

Viral infections

Viral infections may be due to the reactivation of latent infection, viral transmission and acquisition of a transplanted organ after transplantation. The most often diagnosed viruses are: CMV, EBV, HPV, HSV, HZV, HHV.^{6,8}

Cytomegalovirus (CMV)

Cytomegalovirus causes mainly systemic infections, which may resemble flu-like symptoms. It manifests in oral cavity as large, white and yellow necrotic lesions, clearly demarcated, difficult to separate from the foundation, mainly localized on the tongue, cheeks, floor of the mouth.¹³ The virus has some oncogenic potential. It was isolated from non-homogenic proliferation leukoplakia lesion (53%) and from squamous cell cancers.^{2, 13–15}

Herpes Simplex Virus (HSV)

Organ recipients have a high frequency of virus incidence, reaching 50–66%. The lesions in the oral cavity are displayed as many confluent vesicles. When they burst, painful erosions and ulcers remain. They appear mostly on palate, lips, gingiva and tongue.²

Papillomaviruses (HPV)

The majority of infections are latent. The viruses have a large oncogenic potential. Clinical symptoms are displayed as single or multiple warts mostly located on the gingiva, where they can coexist with gingival overgrowth associated with cyclosporine treatment, on cheeks, palate and the tongue. They are detected in precancerous lesions and in head and neck cancers.^{16–19}

Epstein-Barr Virus (EBV)

Epstein-Barr Virus is detected in 84% of recipients. EBV is often in the latency stage in lymphocytes and monocytes. Lesions in the oral cavity are displayed as multiple, red ecchymosis localized between the hard and soft palate, as ulcerative gingivitis, painful throat ulcers¹⁰, hairy leukoplakia on the lateral surfaces of the tongue with excessive keratosis and filiform papillae overgrowth also described as frotte tongue.^{2,14,20}

Fungal infections

The most frequent pathogenic fungi and dermatophytes isolated from oral mucous membranes are: *Candida albicans*, *Aspergillus fumigatus*, *Cryptococcus neoformans*, *Histoplasma capsulatum*. On the mucous membrane white and grey deposits, which can easily become separated from the substrate are observed. In infections caused by fungus *Aspergillus*, deposits are mainly black and situated on the palate and on the base of the tongue. They can infiltrate the bone tissue, causing considerable destruction of adjacent anatomical structures.

Candida albicans is the most frequently isolated yeast-like fungus in patients after transplantation (30%). The clinical picture of infection are angular cheilitis, pseudomembranous candidiasis, atrophic and hyperplastic, which in 50% of patients is associated with cellular atypia and in 40% may undergo malignant transformation. Lesions occur mainly on the tongue and palate.^{21–23}

Protozoan infections

The protozoa of the genus *Trichomonax tenax* and *Entamoeba gingivalis* in the oral cavity are observed more frequently in patients after organ transplantation.¹² Their presence correlates with periodontal diseases and gingivitis as well as with poor oral hygiene. It is believed that when the immune system is functioning properly these protozoa are saprophytic pathogens.

Gingival overgrowth

Gingival hyperplasia is most frequently observed in patients treated with cyclosporine and usually begins in the area between the dental papilla of canines and incisors in the mandible. The incidence is estimated at 30–80% of patients, mainly males. The mechanism of hypertrophy after application of CsA is still unknown. It is believed that CsA affects the fibroblasts, increasing their proliferation, as well as other extracellular factors. This suggests a significant role of dental plaque, in which CsA can accumulate. Administration of CsA with other drugs, including calcium channel blockers, can exacerbate gingival overgrowth. A significant reduction in doses of CsA or its conversion, for example to TAC, cause regression of clinical symptoms. In other cases a surgical procedure that restores the correct, aesthetic

shape of the gums is required. Gingival hyperplasia and periodontal pockets hinder proper cleaning of teeth and interdental spaces, leading to bacterial colonization.^{10, 24–27}

Xerostomia

Xerostomia, or dry mouth, is a set of symptoms caused by reduced secretion of saliva. This is a common ailment in patients after transplantation. It is believed that the cause of a significant reduction in salivary flow is post-steroid vascular fibrosis, which impairs the blood supply to the salivary glands and causes increasing loss of their proper function.²²

Precancerous lesions/tumors

The most frequently observed precancerous lesions on the oral mucosa in organ transplant recipients is homogenous leukoplakia 30%, hairy leukoplakia 13%, which has the etiologic agent of EBV virus and lichen planus. Hairy leukoplakia can transform to squamous cell carcinoma and may be the first sign of the development of post-transplant lymphoproliferative disorder (PTLD). Leukoplakia is usually located in the mucous membrane of the cheek, the floor of the mouth, on the lips. It is believed that the pathogenesis of these lesions involved additional HPV and HSV. Atrophic, erosive and ulcerative forms of lichen planus are lesions difficult to heal and that have potential for cancerous metaplasia.

Cancers of the lip are more frequently observed compared to the general population, 7 and 0.3% respectively, as well as skin cancers, which are observed 7–20 times more often compared to a population of healthy subjects.^{28–31}

Kaposi's sarcoma is frequently observed in patients infected with HIV (human immunodeficiency virus) as well as in organ transplant recipients. It is displayed as an exophytic lesion, mainly located on the gums and palate. It is believed that its etiologic agents are EBV and HHV – 8 virus.

Summary

Along with the evolution of transplantation and transplant immunology, and thus an increasing number of patients undergoing transplantation of organs and tissues, there is a growing need to implement regular dental care, both in transplant patients and in those waiting for a transplant.

It should be noted that many lesions appear first in the mouth region. Information concerning the presence of infection outbreaks in the stomatognathic system is an important signal for transplant physician to perform extended diagnostic testing, as well as to modify the immunosuppressive therapy. Patients should be diagnosed and treated in specialized centers by physicians familiar with this patient population.

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