Periodontal infection in cancer patients treated with high-dose chemotherapy

Abstract The infected and inflamed periodontium can act as a focus for systemic infection in neutropenic cancer patients. The incidence of these oral infections is unknown, but probably underestimated. Periodontal infections can easily be overlooked, primarily because symptoms of gingival inflammation may be minimal and the infection may be located in deeper parts of the periodontium. Assessment of a patient’s periodontal condition before the onset of profound neutropenia is critical to the diagnosis and the management of these potentially life-threatening infections. This review article is aimed at informing supportive care providers of recent insights into the pathogenesis of periodontal diseases and the role of subgingival microorganisms, with the emphasis on these infections in cancer patients treated with high-dose chemotherapy. Furthermore, a multidisciplinary approach to the management of periodontal infections and the need for future research is discussed.

Keywords Periodontal infection · Subgingival microflora · Febrile neutropenia · Oral care

Introduction

Oral and systemic infections emerging from the oral cavity are significant problems in cancer patients treated with intensive chemotherapy regimens, including hematopoietic stem cell transplant (HSCT) procedures [19]. During profound neutropenia patients are particularly at risk of developing infections caused by oral bacteria, but fungi and viruses may also play a part. A substantial number of these infections are associated with oral mucositis, which is the result of complex interaction between the toxicity of cancer chemotherapy to oral mucosal tissues, myelosuppression, and the oral microflora [48].

In addition to infections arising from ulcerated oral membranes (e.g. mucositis), there is evidence that pre-existing infections around the teeth (periodontal infections, e.g. gingivitis and periodontitis) are associated with fever and sepsis in these patients [15, 30, 34, 36, 44].

Ulcerated periodontal pocket epithelium can act as a portal of entry for translocation of microorganisms into the bloodstream [51]. In addition, inflamed and infected periodontal tissues may serve as a reservoir of endotoxin (lipopolysaccharide, LPS), pro-inflammatory cytokines, and other inflammatory mediators which may spread systemically [28].
Particularly in neutropenic cancer patients, periodontal infections can be easily overlooked or misdiagnosed, and thus their contribution to fever, bacteremia, and sepsis may be underestimated. Gingival infections can be missed because symptoms of gingival inflammation, such as redness and swelling, may be muted as a result of the lack of neutrophils. On the other hand, periodontal infections may be associated with marked gingival redness, tenderness and pain during neutropenia. Nevertheless, if such an exacerbation of gingivitis and/or periodontitis coincides with severe oral mucositis, the condition may be overlooked or incorrectly ascribed to mucositis. Furthermore, and probably most importantly, in patients with severe periodontitis the infection affects the deeper parts of the periodontium, and it should be realized that such an infection cannot be diagnosed by visual inspection.

An infectious cause is suspected but never confirmed in up to 40% of episodes of neutropenic fever [8]. It is feasible, however, that some proportion of these febrile episodes can be attributed to unrecognized periodontal infections. There is also circumstantial evidence suggesting that subgingival microorganisms and cytokines from pathologic pockets translocate into the oral cavity and may contribute to oral mucositis [5] and to lower respiratory tract infection [18, 42, 43].

Given that periodontal infections in cancer patients may cause significant morbidity and are potentially life-threatening, the present paper aims to inform supportive care providers about recent insights into the etiology and the pathogenesis of periodontal diseases. In addition, the literature on periodontal infections and their potential systemic sequelae in neutropenic cancer patients will be reviewed and recommendations for prevention, management and future research will be provided.

Fig. 1 a Healthy periodontium (A periodontal ligament, B alveolar bone, C cementum, D oral epithelium, E sulcular epithelium, F junctional epithelium, G gingival sulcus, H cement–enamel junction, I tooth enamel, J supragingival dental plaque microflora). b Established gingivitis lesion (A inflammatory cell infiltrates in gingival connective tissue, sulcular epithelium, and junctional epithelium, B gingival tissue swelling leading to increased gingival sulcus depth, C junctional epithelium at cementum enamel junction, D subgingival dental plaque microflora). c. Periodontitis lesion (A loss of connective tissue attachment, B loss of crestal alveolar bone, C apical migration of junctional epithelium, D ulceration of periodontal pocket epithelium, E inflammatory cell infiltrates in gingival connective tissues, sulcular epithelium, and junctional epithelium, F deepened periodontal pocket and pathogenic subgingival microbial flora, G cement–enamel junction). Adapted with permission from [46]

The periodontium and periodontal diseases

The tissues that support the dentition form the periodontium. These include the root cementum, the alveolar bone, the periodontal ligament that connects the teeth to the jaw, the gingiva and the alveolar mucosa (Fig. 1a). The gingiva, which can be divided into the free gingiva and the attached gingiva, is the only site of the body where the continuity of the epithelial protective lining is interrupted. One of its roles is to protect the underlying periodontal tissues against microbial invasion. In periodontally and otherwise healthy adults it is estimated that 530,000 leukocytes (predominantly neutrophils) migrate every minute from the small vessels of the subgingival plexus through the junctional epithelium into the oral cavity [37]. The protective properties of the gingival epithelium are often compromised by oral microorganisms present in dental plaque, which is a biofilm that adheres to the tooth surface at or below the gingival margin. Ma-