Transient oral cavity and skin complications after mucositis preventing therapy (palifermin) in a patient after allogeneic PBSCT. Case history

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Abstract

Purpose: The aim of this study was to assess the state of oral mucosa in a patient after allo-PBSCT who has received palifermin, a recombinant human keratinocyte growth factor.

Material and methods: A 19-year-old male was treated in the Department of Haematology of the Medical University in Warsaw due to the AML. Conditional chemotherapy was applied, according to the BuCy 4 + ATG regimen and allogeneic haematopoietic cells transplantation from an unrelated donor. He was receiving palifermin intravenously for 3 consecutive days immediately before the initiation of conditioning therapy and after allogeneic PBSCT. On day +3 the oral mucous membrane was pale and swollen, with linea alba visible on cheeks. Superficial glossitis and viral pharyngitis were noted. Beginning with day +5/+6 proliferative gingivitis was observed. On day +9 gingival contour was altered and the gingiva covered nearly completely tooth crowns of all teeth. The gingiva were whitened, as if covered by thick epithelium. Slight gingival hyperplasia was still observed on day +24. Since day +4/+5 skin rash coexisted, spreading over hairy head skin, face, dorsum and chest. Disseminated papulopustular (acne-like) lesions were observed, some of them related to the hair follicles. Skin changes were present till day +15.

Conclusions: Palifermin is an efficient pharmaceutical in mucositis prevention in patients after allogeneic PBSC transplantation. Transient complication of hyperplastic gingivitis with a concomitant skin eczema of a papulopustular nature arose.

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Introduction

Mucositis (the inflammation of oral mucosa) is a frequent adverse events of haematopoietic stem cell transplantation (HSCT). Oral mucous membrane damage is the result of the applied conditioning treatment, i.e. chemotherapy and/or total body irradiation, infections developing as a result of neutropenia and agranulocytosis, as well as teeth injuries [1]. Mucositis is one of the earliest adverse events and arises between 5 and 7 days after the conditional therapy. It is also one of the most devastating. It occurs when cancer treatment destroys the rapidly dividing epithelial cells, particularly in the oral cavity, leaving the mucosal tissue opened to ulceration and infection. Clinically mucositis is characterized by pain, swelling and erythema. Erosions, ulcerations and splits, excessive or decreased saliva secretion and spontaneous bleeding can also occur [1,2]. All these symptoms lead to discomfort, make solid, and often even fluid food ingestion impossible, frequently imposing parenteral nutrition and narcotic analgesics administration. At the same time the damaged oral mucosa with a concurrent neutropenia constitutes a prospective port of entry for life-threatening infections [3,4]. Mucositis affects about 60 to 100 percent of patients after haematopoietic stem cells transplantation [5]. It plays a crucial role in the pathogenesis of post-transplantation complications. It correlates with an increased perioperative mortality rate, longer hospitalization period and the increase of treatment costs.

In 1995 Amgen submitted a Biologics License Application for palifermin, a recombinant human keratinocyte growth factor. Keratinocyte growth factor is a 28-kD, heparin-binding member of the family of fibroblast growth factors that was originally isolated from pulmonary fibroblasts as a protein (FGF-7) with keratinocyte-stimulating activity. Palifermin (recombinant human keratinocyte growth factor) is an N-terminal, truncated version of endogenous keratinocyte growth factor with biologic

Figure 1. **Patient RD on day +9 after PBSCT**

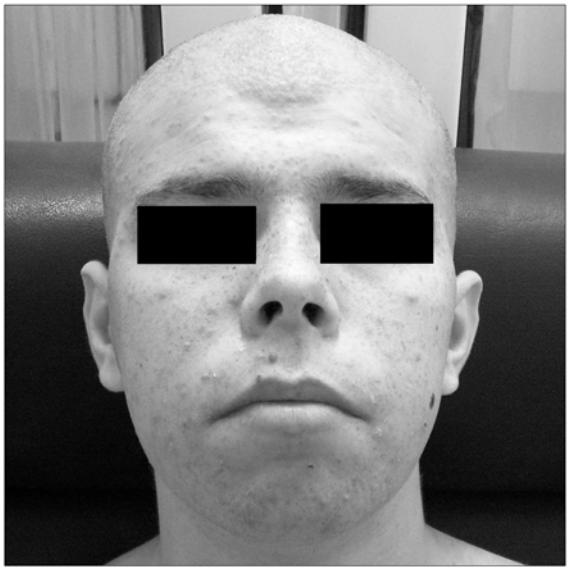


Figure 2. **Patient RD on day +9 after PBSCT**

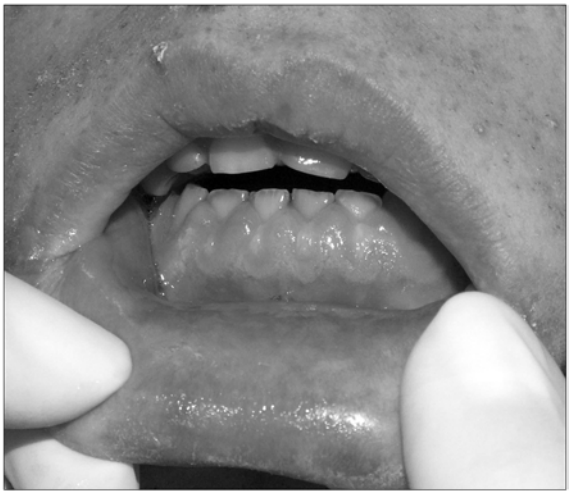
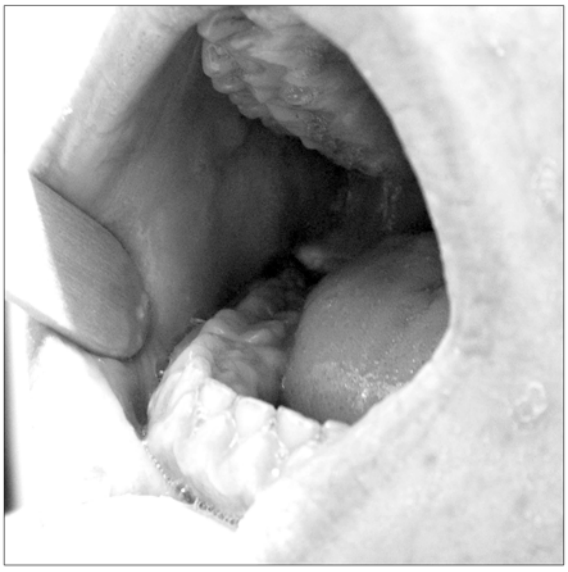


Figure 3. **Patient RD on day +9 after PBSCT**



activity similar to that of the native protein, but with increased stability [6]. Recently, palifermin (Kepivance [Amgen ,US]) was approved as the first cytokine shown to decrease the incidence and duration of severe oral mucositis in patients with haematologic malignancies receiving myeloyoxic theraphy requiring haematopoetic stem cell support [7-9].

Purpose

The aim of this study was to assess the state of oral mucosa in a patient after PBSC allotransplantation who has received palifermin, a recombinant human keratinocyte growth factor.

Material and methods

A 19-year-old male was treated in the Department of Haematology of the Medical University in Warsaw due to the AML with M2 according to FAB. Conditional chemotherapy was applied, according to the BuCy 4 + ATG regimen (busulfan 4 mg/kg/d on days -9 through -6; cyclofosfamide 50 mg/kg/d on days -5 through -2; ATG 10 mg/kg/d on days -3 through -1) and allogeneic haematopoietic cells transplantation from an unrelated donor. He was receiving palifermin (60 microg/kg/d) intravenously for three consecutive days immediately before the initiation of conditioning therapy (on days -13, -12, -11) and after allogeneic PBSCT (on days +3, +4, +5). The clinical assessment of oral mucous membrane state was performed every third day. Pathologic eruptions presenting on the oral mucous membrane were noted. Mucositis was assessed according to the WHO scale. The patients assessed the subjective pain feeling in the 10-point scale.

On day +3 the oral mucous membrane was pale and swollen, with linea alba visible on cheeks. Superficial glossitis and viral pharyngitis were noted. Beginning with day +5/+6 proliferative gingivitis was observed. On day +9 gingival contour was altered and the gingiva covered nearly completely tooth crowns of all teeth. The gingiva were whitened, as if covered by thick epithelium (*Fig. 1-4*). Slight gingival hyperplasia was still observed on day +24 (*Fig. 5,6*). During the forming of gingival hyperplasia the patient had a subjective "membrane growing" sensation with tingling and itching. He reported an oral cavity pain score of 0 in the 10-point pain scale. No mucositis was present (WHO scale = 0). Since day +4/+5 skin rash coexisted, spreading over hairy head skin, face, dorsum and chest. Disseminated papulopustular (acne-like) lesions were observed. Some of them were related to the hair follicles. Skin changes were present till day +15. Neutropenic fever was noted on day +6 (absolute leucocytosis 0.1 G/L). On day +19 after the transplantation the WBC regeneration reaching > 1 000/μl, comprising 0.5/μl neutrophils, was noted. CSA (Neoral, Sandium) in dose of 5 mg/kg body weight on day –1 and 3 mg/kg in the intravenous infusion starting on day 0; Mtx (metotrexat) 15 mg/m^2 on day +1 and 10 mg/m^2 on days +3 and +6 were administered as a prophylaxis

Figure 4. **Patient RD on day +9 after PBSCT**

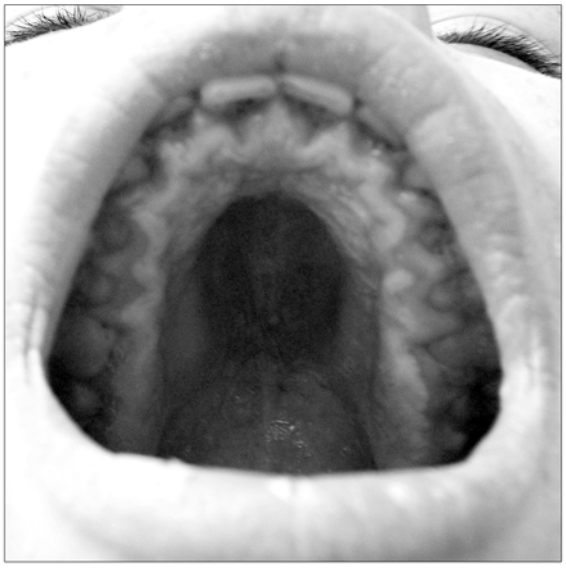


Figure 5. **Patient RD on day +19 after PBSCT**

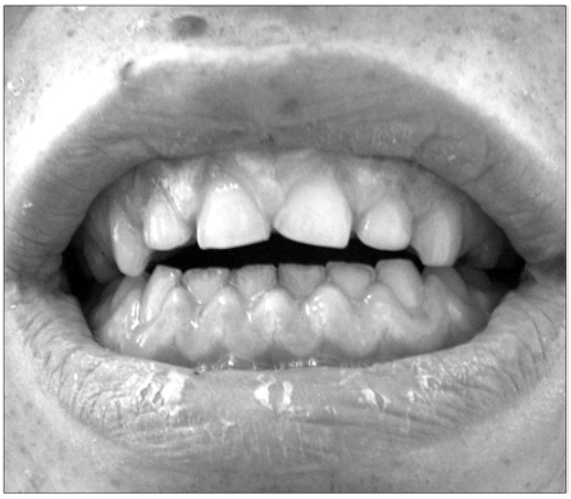
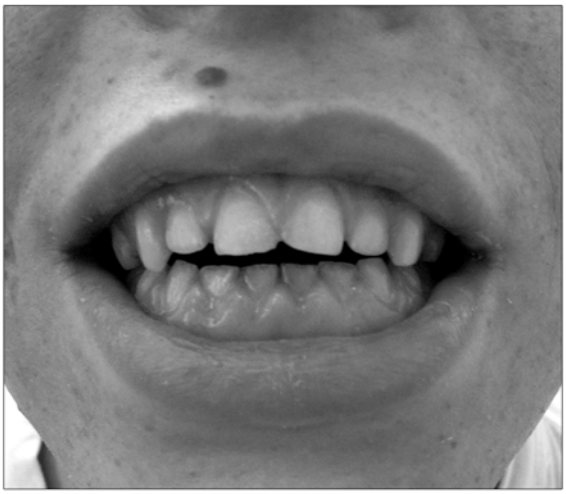


Figure 6. **Patient RD on day +21 after PBSCT**



and treatment of GHVD. On day +15 after transplantation in the postoperative treatment human immunoglobulins (IVIG) were administered in dose of 0.5 g/kg. Concomitant medications were Orungal 2x200 mg p.o., Heviran (aciclovir) 5x400 mg p.o., Tazocin 4x4.5 g i.v. on days +2 and +3, Maxipime 3 x 2.0 g i.v. on days +3 through +7, vancomycin 2 x 1 g on days +5 through +14, metronidazole 3x500 mg i.v. on days +4 through +14, Neoral 2x100 mg i.v. since day +5 and 2x150 mg since day +13, Zyrtec 1 tablet/day since day +6.

Conclusions

Palifermin is an efficient pharmaceutical in mucositis prevention in patients after allogeneic PBSC transplantation. Transient complication of hyperplastic gingivitis with a concomitant skin eczema of a papulopustular nature arose.

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