

CASE REPORT



***Peptococcus* sp. associated with necrotizing ulcerative gingivitis in a child with leukemia undergoing chemotherapy: A case report**

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Received 15 March 2021;
Accepted 20 April 2021

doi: 10.15713/ins.ijmocr.164

How to cite the article:

Sufiawati I, Lefaan YFM. *Peptococcus* sp. associated with necrotizing ulcerative gingivitis in a child with leukemia undergoing chemotherapy: A case report. Int J Med Dent Case Rep 2021;8:1-4.

Abstract

Leukemia patients undergoing chemotherapy are at greater risk of developing necrotizing ulcerative gingivitis (NUG) due to an increase of the colonization of the oral microbiota, but *Peptococcus* sp. infrequently causes NUG. The aim of this case report is to describe the occurrence of NUG associated with *Peptococcus* sp. in children with leukemia undergoing chemotherapy and its successful treatment. An 11-year-old boy with leukemia, febrile neutropenic, marasmus, and anemia was referred to Oral Medicine Clinic, with a chief complaint of painful ulceration in the oral cavity. He underwent the 8th cycle chemotherapy and received a combination of ceftazidime and gentamicin injection. Extraoral examination revealed exfoliative of the lips and fissure at the oral commissure. Intraoral examination showed white plaques on the oral mucosa that can be scraped off, leaving behind the erythematous area, bleeding and gingival edema, and irregular ulcers covered by gray-white necrotic membranes on the lower gingiva. Blood workup revealed pancytopenia. Oral microbiological examination showed *Peptococcus* sp. He was diagnosed with acute pseudomembranous candidiasis, angular cheilitis, and NUG. The oral treatment includes nystatin oral suspension, 2% miconazole nitrate, and irrigation with 1.5% hydrogen peroxide followed by a rinse with normal saline. Oral lesions showed significant improvement after a week of treatment. *Peptococcus* sp. plays a role on the occurrence of NUG. Early detection, timely and appropriate treatment of NUG in childhood leukemia undergoing chemotherapy are critical to prevent possible serious complications.

Keywords: Chemotherapy, childhood leukemia, necrotizing ulcerative gingivitis, *Peptococcus* sp.

Introduction

Leukemia is a type of blood malignancy in the mesenchymal (myeloid and lymphoid).^[1,2] Chemotherapy is a therapy for malignancy that has cytotoxic effects on non-cancerous bodies, which results in changes in anatomy and body conditions.^[3,4] Oral manifestations appear in 65% of patients with leukemia and are more common in patients with myeloid leukemia than other types of leukemia, with a percentage of 40% myeloid leukemia and 23% lymphoid leukemia.^[1]

In healthy individuals, bacteria that colonize the oral cavity do not cause problems, but in patient with leukemia undergoing chemotherapy, these bacterial can become pathogen due to imbalance homeostasis between host defense and bacterial that damage the epithelium and connective tissue by releasing endotoxins. Necrotizing ulcerative gingivitis (NUG) is one of the oral manifestations seen in patients with leukemia which

can develop into Noma if not treated immediately.^[1] NUG is a disease in gingiva caused by bacteria due to impaired immune response. It is characterized by necrosis of gingival tissue and has distinctive signs and symptoms of partial loss of the interdental papilla (punch out), gingival bleeding, and pain.^[5-7]

Vincent and Plaut in 1890 found that *fusiform-spirochete* bacteria played a role in the etiology of NUG.^[6] Boras *et al.* (2019) reported that *Stenotrophomonas maltophilia* and *Enterobacter faecalis* are oral pathogens in patients with acute myeloid leukemia (AML) and cause ulcer neutropenia on the gingiva.^[5] Previous studies have been published claiming that oral bacteria such as *Fusarium moniliforme*, *Capnocytophaga ochracea*, and *Streptococcus mitis* are bacteria that cause NUG in patients with granulocytopenia.^[5] Villafuerte *et al.* (2018), in their fundamental survey, reported that patients with malignant growth undergoing chemotherapy expanded the quantity of Gram-negative microorganisms such as the Enterobacteriaceae

family and Gram-positive *streptococcus* which can cause ulceration in the oral cavity.^[4]

Peptococcus sp. together is an obligate anaerobic Gram-positive coccus, with other Gram-positive and Gram-negative bacterial can stimulates macrophages and gingival fibroblasts to produce tumor necrosis factor- α and interleukin-6.^[6] Immune stimulation by bacterial DNA from subgingival contributes to periodontal pathogenesis.^[6] *Peptococcus* sp. infrequently found as a bacterium that causes NUG.

The purpose of this case report is to describe necrotizing ulcerative associated with *Peptococcus* sp. in a child with leukemia undergoing chemotherapy and its successful treatment.

Case Report

An 11-year-old boy with acute myeloblastic leukemia (AML) was referred from the Paediatric Department with the diagnosis of AML, febrile neutropenic, marasmus, and anemia, with chief complaints of white plaques and painful ulceration in the oral cavity. He underwent the 8th cycle chemotherapy. He received a combination of 1 mg ceftazidime injection 3 times a day and 140 mg gentamicin injection once a day.

A complete blood count (CBC) result was shown in Table 1. Extraoral examination revealed vermilion border of the lips was dry and exfoliative and fissure at the oral commissure [Figure 1a]. Intraoral examination showed that gingiva was edema and tend to bleed, and irregular ulcers covered in gray-white necrotic membranes in the region 41 to 33 with the mobility of the teeth [Figure 1b]. We also found white plaques on the oral mucosa that can be scraped off, leaving behind erythematous area [Figure 1c]. Oral hygiene was poor.

The patient was diagnosed with NUG, acute pseudomembranous candidiasis, angular cheilitis, and periodontitis acute. The patient was treated with nystatin drops,

Table 1: The results of a complete blood count test

Hematology	Result	Normal
Hemoglobin (g/dl)	7.4 _L	11.5–13.5
Hematocrit (%)	20.6 _L	34.0–40.0
Red blood cell (10 ⁶ /ml)	2.56 _L	3.9–5.3
White blood cell (10 ³ / μ L)	0.88 _L	5.5–15.5
Platelets (10 ³ / μ L)	56 _L	150–450
MCV (fL)	80.5	75–87
MCH (Pg)	28.9	24–30
MCHC (%)	35.9	31–37
Eosinophil	0	0–4
Rod neutrophil (%)	2 _L	3–5
Segmented neutrophil (%)	28 _L	27–55
Lymphocyte (%)	32	36–52
Monocyte (%)	4	308
Blast (%)	28	43

H: High, L: Low, MCV: Mean cell volume, MCH: Mean cell hemoglobin, MCHC: Mean cell hemoglobin concentration

povidone-iodine mouthwash, and multivitamin. Irrigation using 1.5% hydrogen peroxide (H₂O₂) then rinsed using 0.9% NaCl was done once a day until the necrotic ulceration healing. The mother was also instructed to improve the patient's oral hygiene. Oral microbiological examination was planned to support the diagnosis of NUG.

After a week follow-up, the painful lesions and taste disorder were disappeared, and the patient was able to eat. Intraoral examination showed a significant improvement of NUG [Figure 1d-f]. The results of microbiological examinations found unchained coccus bacteria, negative indole test, and positive metronidazole test indicating *Peptococcus* sp. [Figure 2]. The patient was still instructed to improve his oral hygiene and to continue povidone-iodine mouthwash.

Discussion

The diagnosis of AML in patients was made by the identification of abnormal hematopoietic cells in peripheral blood and bone marrow. A peripheral blood smear reveals a change in the number and appearance of blast cells. Children are more affected by acute

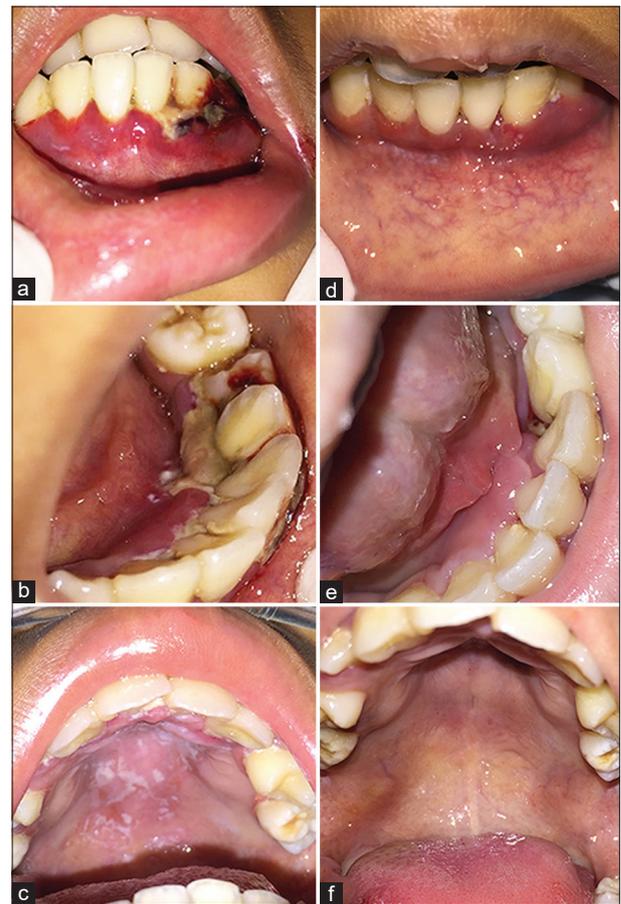


Figure 1: (a-c) Clinical features at the first visit showed irregular ulcers covered by gray-white necrotic membranes on the lower gingiva and white plaques on the palate; (d-f) The oral lesion showed significant improvement after a week follow-up

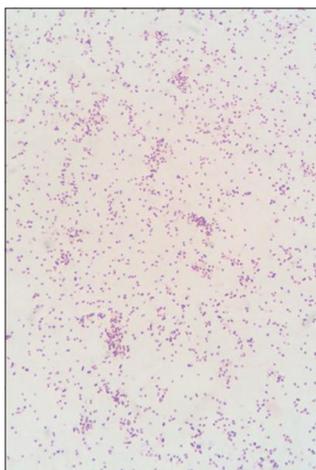


Figure 2: Gram staining examination found anaerobic Gram-positive cocci bacteria indicating *Peptococcus* sp.

leukemia than chronic leukemia.^[1,8] Manifestations of leukemia in the oral cavity include leukemia infiltration, gingival bleeding, oral ulceration, and bacterial, viral, and fungal infection.^[9,10] Oral manifestation often found in a patient with AML than in other types of leukemia.^[1,3]

A CBC shows the occurrence of pancytopenia where there is a decrease in hemoglobin, hematocrit, erythrocytes, platelets, stem neutrophils, neutrophil segments, and monocytes level due to the accumulation of blast cells.^[3,11] Pancytopenia causes changes in mucosal homeostasis as a barrier, causing oral microbiota to become a pathogen and stimulates pro-inflammatory cytokine production.^[10] These immunosuppressive conditions result in the formation of oral bacterial colonization, especially in the gingival sulcus.^[3]

Leukemia patient undergoing chemotherapy leading the colonization of the oral microbiota and disturb the oral homeostasis.^[3,4] A bacterial infection in gingival of leukemia patients indicates high levels of *Prevotella intermedia*, spirochetes, *Fusobacterium nucleatum*, and Gram-positive anaerobic coccus (GPAC) bacteria.^[3,12] Bacterial infection in a patient with leukemia can cause gingival or periodontal disease. More frequent are acute gingivitis and NUG.^[6] NUG is a disease in gingiva caused by bacteria due to impaired immune response, is characterized by necrosis of gingival tissue, and is present with distinctive signs and symptoms characterized by partial loss of the interdental papilla (punch out), gingival bleeding, and pain.^[5,6] The predisposing factor of NUG is influenced by many factors, including poor oral hygiene, stress, lifestyle, malnutrition, smoking, alcohol, lack of sleep, and the presence of comorbidities that reduce the immune system.^[6,7]

In this case, oral swab for the microbiological examination revealed *Peptococcus* sp. Microscopic appearance only found the presence of *Peptococcus* sp., no other anaerobic bacteria that cause NUG along with *Peptococcus* sp. This is related to the sensitivity of anaerobic bacterial isolates to oxygen.^[3,12] Preparation of anaerobic bacterial isolate collection, method of collection, transport of isolates, and special culture of anaerobic

bacteria are important things to consider in the cultivation of anaerobic bacteria.^[13]

Peptococcus sp. is an obligate anaerobic Gram-positive coccus that has a cell wall. *Peptococcus* sp. is able to produce a high-level enzyme nicotinamide adenine dinucleotide hydrogen (NADH oxygenase) which reduces oxygen.^[12,13] Classified on the basis of morphological characteristics, Clostridia species, *Peptococcaceae* family.^[13] *Peptococcus* sp. can cause an infection form into an abscess, these microbes are likewise connected with genuine diseases, for example, cerebrum abscesses, pleuropulmonary infection, necrotizing fasciitis, and other skin diseases, intra-abdominal diseases, and infection of the female genital tract.^[12,13]

GPAC is a pathogen opportunistic bacterial that is most often found in mixed infections with other anaerobic Gram-positive and Gram-negative bacteria.^[12,13] Anaerobic bacteria generally damage or destroy tissue by produce the enzyme heparinase and collagenase. In the oral cavity, *Peptococcus* colonizes with other commensal bacteria such as *F. nucleatum*, *Porphyromonas gingivalis*, and *P. intermedia* results in oral necrotizing ulceration, especially in patients with leukemia.^[3,6,12]

The vulnerability of AML patients to co-infection is a major cause of death, referring to the mutation in DNA nucleotide methyltransferase A3 (DNMT3A); this mutation causes high mortality due to infection, oral bacterial peptidyl-arginine deiminases, hydrolyzed arginine and lysine from p53, enhancer-binding protein and DNMT3A mutation leads to impaired growth hormone-stimulated, c-fos and lead tissue damage.^[14] Hence, it very important to reduce oral microflora and the possibility of food retention, or other sources of infection of the teeth that are the focus of infection that can interfere with the integrity of the oral mucosa defense, where oral microbiota is very potential to become a pathogen in immunosuppressive conditions.^[1,11]

NUG in patients shows significant improvement after treatment with hydrogen peroxide (H_2O_2). 1.5% H_2O_2 has an antibacterial effect which is able to kill bacteria and active against various forms of organisms, including bacteria, viruses, and spores. H_2O_2 can show antimicrobial effects through the release of oxygen and the pathogenic effect on Gram-positive and Gram-negative organisms.^[15,16] Dental consideration and proper oral mucosal treatment of leukemia patients previously, during, and after chemotherapy are crucial to reduce complications.^[1]

Conclusion

Peptococcus sp. colonization with other anaerobic Gram-positive bacteria has a role on the occurrence of NUG in leukemia patients undergoing chemotherapy by producing heparinase, collagenase, and other enzymes that harm or annihilate mucosa tissue.

Acknowledgments

We thank the staffs of the Department of Paediatric, Faculty of Medicine, Universitas Padjadjaran/Dr. Hasan Sadikin General Hospital for their interprofessional collaboration.

Conflicts of Interest

All authors state that there are no conflicts of interest.

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