International Medical Case Reports Journal

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CASE REPORT

A Rare Case of COVID-19-Induced Acute Exacerbation of Oral Dermatitis Herpetiformis in a Geriatric Patient

Amira Shafuria[1], Irna Sufiawati[2], Hermin Aminah Usman[3]

[1]Oral Medicine Residency Program, Faculty of Dentistry, Padjadjaran University, Bandung, Indonesia; [2]Department of Oral Medicine, Faculty of Dentistry, Padjadjaran University, Bandung, Indonesia; [3]Department of Anatomical Pathology, Faculty of Medicine, Padjadjaran University/Dr. Hasan Sadikin General Hospital, Bandung, Indonesia

Correspondence: Irna Sufiawati, Email irna.sufiawati@fkg.unpad.ac.id

Introduction: Dermatitis herpetiformis (DH) is an autoimmune vesiculobullous disease associated with celiac enteropathy. The clinical manifestation of DH is the occurrence of a papulovesicular rash on the skin. Oral mucosal involvement in DH is very rare. This study aimed to describe the impact of COVID-19 on the acute exacerbation of oral dermatitis herpetiformis.

Case Report: A 74-year-old woman was referred to the Oral Medicine Department with a chief complaint of the blisters on the skin for a week and ulcers in the oral cavity appeared two days ago. Extraoral examination revealed crusts on the neck and extremities. The lips appeared dry and desquamative. Intraoral examination revealed erosive lesions covered with a white-yellowish plaques on the right and left sides of the buccal mucosa, an ulcer with a diameter of 0.5 cm, and purpura hemorrhagic on left buccal mucosa and right lateral border of the tongue. Histopathological examination of the skin lesion revealed a subepithelial blister with eosinophils and neutrophil cells. The definitive diagnosis of dermatitis herpetiformis was made. She was given 5 mg intravenous dexamethasone, cetirizine 10 mg, and clindamycin 300 mg by the dermatologist. We gave hyaluronic acid 0.025% mouthwash for oral ulcers and petroleum jelly for the lips. The oral lesions had significant improvement after 4 weeks of treatment. Two months later, the patient experienced acute exacerbation after being infected with COVID-19 (anti-SARS-CoV-2 IgG S-RBD >40,000 AU/mL). The oral lesions healed after a month of treatment.

Conclusion: COVID-19 can trigger the acute exacerbation of dermatitis herpetiformis. SARS-CoV-2 causes an immune dysregulation and hypersensitivity reaction.

Keywords: COVID-19, dermatitis herpetiformis, geriatric patient

Introduction

Dermatitis herpetiformis (DH) is an autoimmune vesiculobullous disease that was first proposed by Louis Dühring in 1884. DH is a chronic and recurrent disease caused by hypersensitivity to gluten. The predisposing factor for DH is genetic involving Human Leukocyte Antigens (HLAs) DQ2 and DQ8. DH can occur at any age, but most cases occur in young adults between 15 and 40 years of age. Men are more dominant in the ratio of 3:2 compared to women.[1,2] DH lesions in males are generally found in the mouth and genitals.[3]

Dermatitis herpetiformis is a rare vesiculobullous dermatitis and is more common in Scandinavian countries and the United Kingdom. Studies conducted in Finland show that the prevalence of DH is 10.4 per 100,000 population. A higher incidence of DH has been recorded in Ireland and predominance in Caucasians compared to Asians or African Americans.[4] The prevalence of DH in Caucasians is 10 per 100,000 population.[3]

The clinical manifestation of DH is the occurrence of a papulovesicular rash on the skin. The lesions are often located on the elbows, extensor surfaces of the forearms, knees and buttocks. The rash are polymorphic, which include plaques, papules, erythematous, and vesicles. Large bullae are rarely found in the clinical manifestations of DH.[1] These lesions will produce hyperpigmentation and hypopigmentation. Other manifestations include severe burning and itching.[5]

Received: 16 December 2022
Accepted: 24 February 2023
Published: 9 March 2023

Involvement of the oral mucosa in dermatitis herpetiformis is extremely rare and occurs in only 9.6–10% of patients.[6] Schuerman et al first reported oral lesions of dermatitis herpetiformis in 1966. Fraser et al classified oral lesions of dermatitis herpetiformis into four types, including erythematous, pseudo-vesicular, purpuric, and erosive types. Fraser described that the oral lesions of dermatitis herpetiformis showed a typical clinical and histopathological picture.[7]

Since the COVID-19 pandemic occurred, there have been several concerns regarding the impact of COVID-19 infection on autoimmune diseases, one of which is autoimmune bullous disease (AIBD). Patients with COVID-19 experience multiorgan failure caused by a cytokine storm. Cytokine storm generates inflammatory cells such as IL-1B, IL-17, and TNF-α which results in organ damage in the lungs and liver. Several studies suggest that cytokines associated with COVID-19 may also be involved in patients with bullous pemphigoid.[8,9] This case report aims to describe the impact of COVID-19 infection on acute exacerbations of oral lesions of dermatitis herpetiformis.

Case Presentation

A 74-year-old woman was referred from the Department of Dermatology and Venereology to the Department of Oral Medicine Dr. Hasan Sadikin Hospital, Bandung. The patient has been hospitalized for 4 days and has been given dexamethasone 5 mg intravenously, cetirizine 10 mg tablets, and clindamycin tablets 300 mg. Based on the anamnesis, blisters on the skin that felt burning, sore, and itchy first appeared 1 week ago. Complaints of the painful canker sores in the oral cavity began to appear 2 days ago. The patient experienced of intense pain during the day. She has no medical history of any systemic disease and does not take any medication. Extraoral examination revealed a symmetrical face and the regional lymph nodes were not palpable and painless. She had multiple crusts on the neck, buttocks, and upper and lower extremities (Figure 1).

Intraoral examination showed erosion covered by a yellowish white layer on the right and left buccal mucosa, haemorrhagic purpura on the right and left buccal mucosa and right lateral tongue, an ulcer with a diameter of 0.5 cm on the left lateral border of the tongue, and the root remnants of 12, 14, 15, 16, 17, 26, 27, 33, 34, 35, and 36 teeth (Figure 2). Hematology tests revealed increased values of leukocytes (15.93 x 10^3/μL), eosinophils (6%), and segmental neutrophils (77%). A skin biopsy of the lesion on the left thigh was performed to establish a definitive diagnosis. The results of histopathological examination showed a formation of a subepidermal blister containing eosinophil and neutrophil cells (Figure 3).

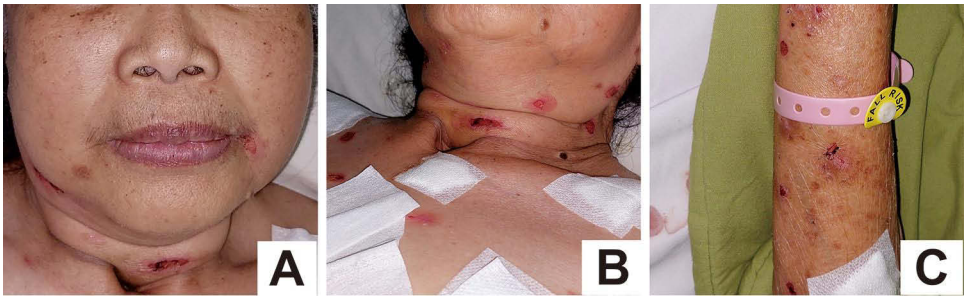

Figure 1 Extraoral features at the first visit. Multiple crusts on the neck, buttocks, and upper and lower extremities (**A**–**C**).

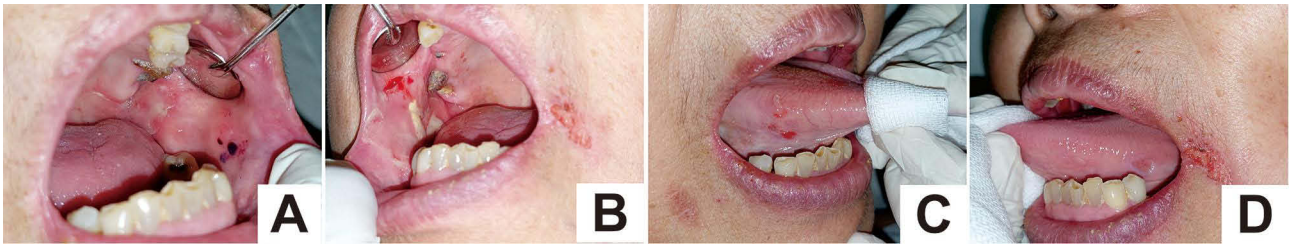

Figure 2 Intraoral features at the first visit. A yellowish white layer on the right and left buccal mucosa (**A** and **B**). Hemorrhagic purpura on the right and left buccal mucosa and right lateral tongue (**B** and **C**). An ulcer with a diameter of 0.5 cm on the left lateral border of the tongue (**D**).

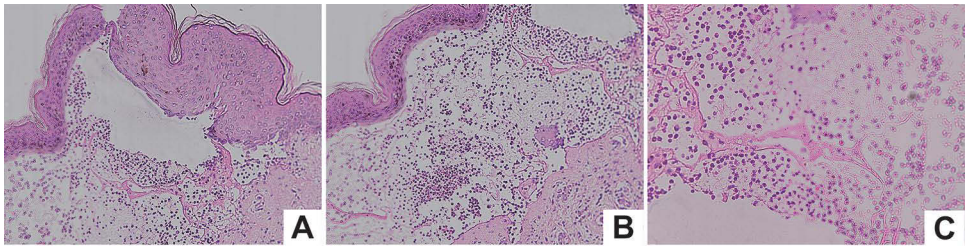

Figure 3 Histopathological examination showed a subepidermal blister containing eosinophil cells and neutrophil cells (**A**–**C**).

Based on anamnesis, clinical examination, and appropriate investigations, the definitive diagnosis was oral lesions associated with dermatitis herpetiformis with a differential diagnosis of pemphigoid bullosa and linear IgA dermatoses. Additional diagnoses were exfoliative cheilitis, chronic traumatic ulcer on the left lateral border of the tongue, chronic apical periodontitis et causa the root remnants of 12, 14, 15, 16.17, 26, 27, 33, 34, 35, 36, and generalized chronic marginal gingivitis. The therapies provided by the Department of Oral Medicine including 0.025% hyaluronic acid mouthwash and petroleum jelly. Patients were instructed to brush their teeth regularly, not consume gluten-containing foods, rinse their mouths using 0.025% hyaluronic acid mouthwash three times a day, and apply petroleum jelly to moisturize the lips. Patients are also advised to do scaling and extraction of the tooth remnants of the upper and lower teeth. The prognosis of this case is good.

The oral lesions showed significant improvement at the second visit, 10 days after treatment (Figure 4). Erosive lesions in the oral cavity began to heal. She felt no pain at all and had no difficulties in eating solid foods. The patient uses 0.025% hyaluronic acid mouthwash and petroleum jelly regularly.

The patient was being infected with COVID-19 two months later and was treated in the COVID-19 isolation room at the Hasan Sadikin General Hospital in Bandung for 1 week. She experienced the typical symptoms of COVID-19 (fever, muscle aches, and shortness of breath) and decreased oxygen saturation (87.3%). Acute exacerbations of dermatitis herpetiformis lesions on the skin and perioral occurred after the patient was infected with COVID-19. Extraoral examination revealed crusts on the perioral, erosive lesions covered by white-yellowish plaque on the vermillion border of the upper lip (Figure 5). Laboratory tests revealed anti-SARS-CoV-2 IgG S-RBD values (>40,000 AU/mL), eosinophils (6%), total eosinophils (0.50 x 10^3/µL), C-reactive protein (2 mg/dl), quantitative D-dimer (3.72 µg/mL) during hospitalization. Chest X-ray image depicted a ground-glass appearance from the mid to the lower right lung (Figure 6). The patient was diagnosed with right bronchopneumonia.

The intraoral lesions healed after a month of the treatment (Figure 7). The patient admitted that she has avoided foods containing gluten and routinely uses medicines provided by the Department of Oral Medicine. There were no adverse events or unwanted reactions from the drugs that she had been consumed. Follow-up therapy from the Department of Dermatology and Venereology includes methylprednisolone tablets (24 mg/day), cetirizine 10 mg tablets, and ranitidine 150 mg tablets. The patient was approved and written informed consent of this case including the images, and the institution has also approved for publication. This case had complied with the Declaration of Helsinki.

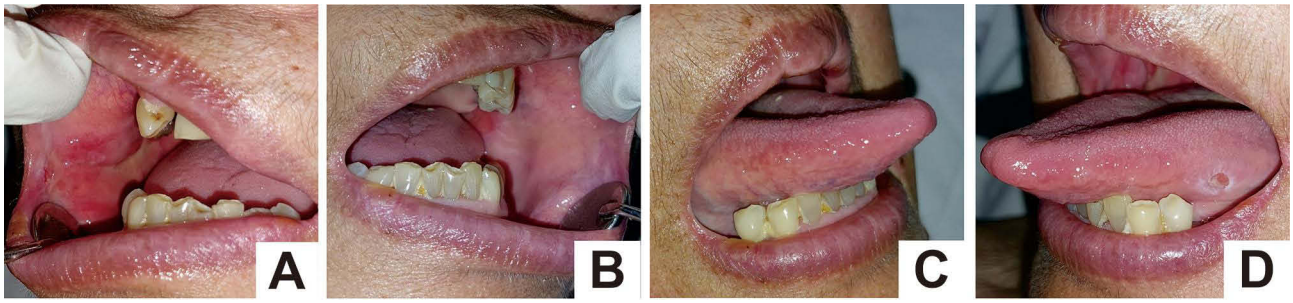

Figure 4 Intraoral features at the second visit, 10 days of treatment. The oral lesions showed significant improvement (**A**–**D**).

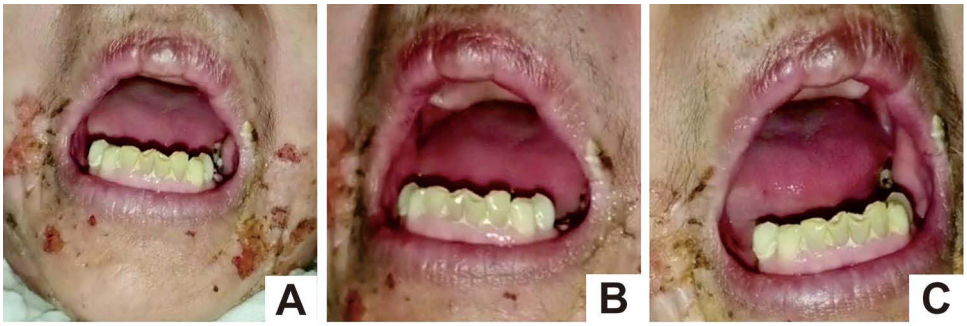

Figure 5 Acute exacerbation of dermatitis herpetiformis lesions after exposure to COVID-19 infection two months later. There was crusting on the perioral and an erosive lesion covered by a white-yellowish plaque on the vermillion border of the upper lip (**A**–**C**).

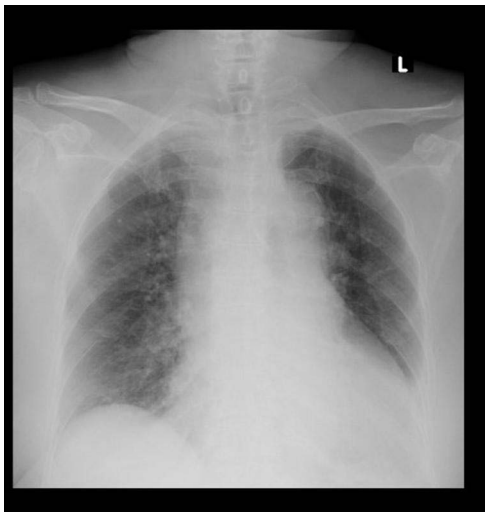

Figure 6 A chest x-ray image showed a ground glass appearance from the mid to the bottom of the right lung.

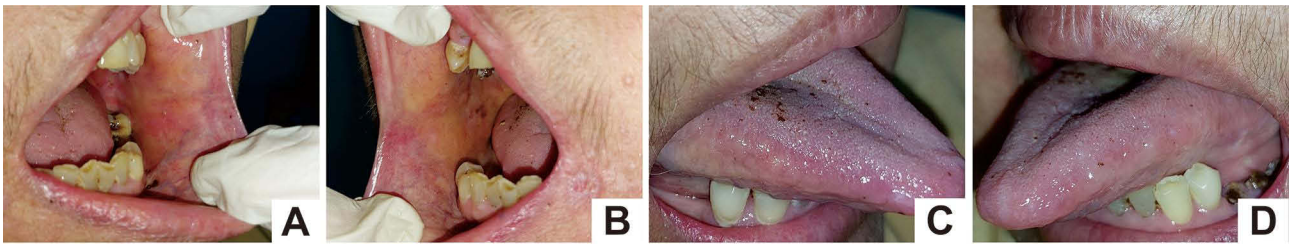

Figure 7 The oral lesions healed after a month of treatment (**A**–**D**).

Discussion

Dermatitis herpetiformis (DH) is a mucocutaneous manifestation of celiac disease (CD), in which the gluten triggers an itchy, blistering rash in genetically susceptible individuals. The etiology of DH is multifactorial with strong genetic and autoimmune influences.[10] The pathophysiology of DH involves a complex set of autoimmune factors such as genetic and environmental predisposition.[3] Human leucocytes antigen (HLA) DQ2 or DQ8 is a predisposing factor for DH.[11] DH and CD are autoantibody responses to tissue transglutaminase (TG) 2 in serum and small intestinal mucosa.[12]

The diagnosis of DH is established based on clinical, histological and serological examination. Histological examination of the initial DH lesion revealed the presence of neutrophil cells, neutrophil fragments, eosinophils, and fibrin in the papillary dermis. DH lesions are also characterized by the presence of IgA deposits over the papillary dermis. Direct

immunofluorescence is the gold standard for the diagnosis of DH, with a sensitivity of 90–95% and a specificity of 95–100%. The direct immunofluorescence shows the presence of IgA deposits in the form of granules in the papilla area in the mucous lining of the oral cavity.[6,13]

Autoimmune bullous disease (AIBD) can be triggered by environmental factors in genetically susceptible individuals. Viral infection is one of the environmental factors that trigger an autoimmune reaction. SARS-CoV-2 could hyper-stimulate the immune system inducing autoantibodies' synthesis and triggering autoimmune diseases. A previous report showed a case of pemphigus vulgaris which was triggered by a COVID-19 infection.[14] Another report also described 18 out of 93 AIBD patients developed AIBD flare-ups following COVID-19 infection.[8] SARS-CoV-2 causes an immune dysregulation and induces a state of hypersensitivity. There was a molecular mimicry between the virus and human proteins, where immune responses raised against SARS-CoV-2 cross-react with human protein that share peptide sequences with the virus. Cross-reactivity due to similarity between immunogenic proteins on the SARS-CoV-2 virus membrane and human extracellular molecules might be plausible trigger. The process of autoimmunity begins with the migration of CD8+ T cells to the site of infection resulting in the death of target cell and phagocytosis by macrophages. There is a natural affinity between the virus and the host antigen, which results in the identification and destruction of the autoantigen by the immune system.[14,15] Java et al also described the ability of coronaviruses to activate complement pathways and their potential involvement in disease severity.[9,16]

The onset of AIBD may be generated by an overstimulated state of the immune system. Vaccines form a substantial component of the environmental factors that affect the immune system. Vaccination against COVID-19 can trigger an exacerbation of the autoimmune bullous disease. Autoantibody production is caused by a dysfunction of regulatory T cells that trigger a humoral immune response in susceptible individuals. Cytotoxic T-cell activation can also stimulate disease exacerbation, especially in the pemphigoid group. SARS-CoV-2 vaccination is associated with a complement dysregulation which can lead to exacerbations of bullous pemphigoid and mucous membrane pemphigoid (MMP). The generation of proinflammatory cytokine and type I interferons following vaccination would induce innate and adaptive immune cell proliferation. Patients who were vaccinated in the active phase of the disease were more prone to experience post-vaccine disease exacerbation.[6,8,17]

The therapeutic strategy for patients with autoimmune bullous disease during the COVID-19 pandemic is to control the mild disease with topical or intralesional corticosteroids, dapsone, and doxycycline. Systemic steroid doses ≤10 mg/day may be continued during treatment. Doses of prednisolone >10 mg/day should be tapered off gradually to the lowest effective dose. The severity of autoimmune bullous disease should be considered in tapering the steroid dose. Significant reduction in steroid dose can lead to disease recurrence.[8]

The main therapy of DH is to avoid consuming foods that contain gluten. Suppressive therapy using dapsone at a dose of 25–100 mg per day for a short period of time can treat local symptoms and reduce the severity of skin injuries.[18] Anonkhina et al described the therapy given to patients with oral dermatitis herpetiformis lesions. Patients were advised to avoid foods containing wheat, oats, rye, barley and other grains.[5] The patient was given sulfonic drugs, vitamins B and C vitamins, lipoic acid, methionine, and folic acid. Treatment in the oral cavity includes antiseptic therapy using chlorhexidine, application of 0.025% glucocorticoid ointment, and linseed oil three times a day for 14 days.[6]

In this case report, the therapy provided by the Department of Oral Medicine included 0.025% hyaluronic acid mouthwash and petroleum jelly. Hyaluronic acid acts as an antimicrobial barrier which reduces the penetration of bacteria into the tissue. Hyaluronic acid inhibits tissue damage and accelerates wound healing by inhibiting inflammatory cells of serine proteinase.[19–21] Hyaluronic acid also degrades lysosomal enzymes such as hyaluronidase and chondroitinase, causing a wound healing effect.[22] Collela et al analyzed the mechanism of wound healing through the use of sodium hyaluronic acid. Hyaluronic acid can increase fibroblast activity by promoting re-epithelialization and wound closure.[23]

Conclusion

In this case report, COVID-19 infection can trigger an acute exacerbation of dermatitis herpetiformis. SARS-CoV-2 causes an immune dysregulation and induces hypersensitivity reaction. Dentists can collaborate with other departments in diagnosing and treating oral lesions related to dermatitis herpetiformis.

Acknowledgment

We would like to thank the patient and his family who participated kindly in this study. This study was approved by Oral Medicine Department, Faculty of Dentistry, Padjadjaran University.

Disclosure

The authors declare that they have no conflicts of interest in this work.

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