

Lip necrosis in a patient with paroxysmal nocturnal hemoglobinuria: Can it be triggered by COVID-19?

Filiz Cebeci Kahraman Assoc. Prof.¹, Tunç Özen MD¹, Tayfun Elibol MD²

¹*Department of Dermatology, Faculty of Medicine, Istanbul Medeniyet University, Istanbul, Turkey*

²*Department of Haematology, Faculty of Medicine, Istanbul Medeniyet University, Istanbul, Turkey*

Corresponding author: Filiz Cebeci Kahraman

Address: İstanbul Medeniyet Üniversitesi, Dermatoloji Anabilim Dalı, Eğitim Mah. Dr. Erkin Cad. 34722 Kadıköy/ İstanbul, Turkey

Telephone: +902165664000-extension: 9126 **Fax:** +902165666614

E-mail: cebecifiliz@yahoo.com

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DR. FILIZ CEBECI (Orcid ID : 0000-0002-9109-3892)

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Key words: COVID-19, lip necrosis, paroxysmal nocturnal hemoglobinuria

Running Head: Lip necrosis and COVID-19 infection

Abstract

Background: CIVID-19 due to SARS-CoV-2 was first described in the city of Wuhan in China and spread around the world turning into a pandemic. COVID-19 can affect different organ systems, including the oral mucosa.

Aims: Although cutaneous involvement has been defined in association with COVID-19, the number of case reports about mucosal involvement by SARS-CoV-2 is limited. Hereby, we report a case of hemorrhagic necrosis on the lip in a patient with paroxysmal nocturnal haemoglobinuria (PNH) and COVID-19 infection and briefly discuss its possible mechanism.

Patients: The clinical features and causes of hemorrhagic necrosis on the lip in a woman are presented.

Results: In our patient, we think that PNH-associated dermal micro-occlusions caused extensive painful necrosis of the lip. Additionally, COVID-19-induced endothelial damage helped to develop exaggerated hemorrhagic necrosis.

Conclusion: This current case presentation will contribute to the literature as another case with COVID-19 triggering mucosal involvement.

Introduction

COVID-19 due to SARS-CoV-2 was first described in the city of Wuhan in China and spread around the world turning into a pandemic.¹

COVID-19 can affect different organ systems, including the oral mucosa. Although cutaneous involvement has been defined in association with COVID-19, the number of case reports about mucosal involvement by SARS-CoV-2 is limited.² Hereby, we report a case of hemorrhagic necrosis on the lip in a patient with paroxysmal nocturnal haemoglobinuria (PNH) and COVID-19 infection. COVID-19 infection seems to present features of a multisystem disease, with impairment of several organs, although initially described as a viral pneumonia. It is a new disease and currently there are limited data about the impact of underlying medical conditions such as benign haematologic diseases and whether they increase the risk for severe illness from COVID-19.

Case report

A 67-year-old female patient was admitted to the haematology department with fatigue and pancytopenia on 31 March 2020. During her follow-up, she was diagnosed with COVID-19 pneumonia based on a positive PCR result on 7 April 2020. She was transferred to a COVID-19 care unit and started to receive treatment with Lopinavir/ritonavir (LPV/r) (400/100 mg twice a day), ceftriaxone (1000 mg twice a day), and doxycycline (100 mg twice a day). As she was admitted to the hospital, a small, hemorrhagic crusted lesion was spotted on her lip and she was referred to the dermatology clinic. Her history revealed that the lip lesions started before the administration of the drugs and was present for 2 weeks but rapidly progressed within last week. There was no previous history of any drug use. The dermatological examination revealed painful, extensive, and thick-crusted hemorrhagic necrosis; which covering the lips entirely and had an appearance similar to a mass lesion (Fig. 1). The laboratory analysis revealed a leukocyte count of $3.4 \times 10^3/\mu\text{L}$, a red blood cell count of $0.57 \times 10^6/\mu\text{L}$, and a platelet count of $14.0 \times 10^3/\mu\text{L}$. Coombs-negative haemolytic anaemia (haemoglobin was 2.5 g/dl) was detected by the haematology department and the suspicion of PNH was confirmed by CD55/59 flow cytometry. Combination treatment with platelet and/ or red blood cell transfusions and eculizumab was started. The bone marrow biopsy was hypocellular. A biopsy could not be performed because the patient refused a biopsy. Therefore, the clinical suspicion of severe mucosal thrombosis with hemorrhagic

necrosis of the lip associated with PNH could not be confirmed by biopsy because of the patient's refusal. The patient's lips were treated with subcutaneous low-molecular-weight heparin and empirically by administering a topical wound healing promoting agent, the *Triticumvulgare* extract, four times a day. With the eculizumab and low-molecular-weight heparin therapy, the necrotic plaque on the lip resolved in 10 days (Fig. 2).

Discussion

Paroxysmal nocturnal haemoglobinuria (PNH) is a haematopoietic clonal stem cell disease resulting from a deficiency in glycosylphosphatidylinositol (GPI)-anchored surface proteins such as CD55 and CD59 in the cell membrane of haematopoietic stem cells. This protein deficiency almost always occurs due to mutations in the phosphatidylinositol glycan class A (PIG-A). Clinical manifestations of PNH are complex involving primarily haemolysis, cytopaenia, and a tendency for thrombosis. Venous thrombosis is seen in up to 30-40% of European patients with PNH. Thrombosis is one of the most severe complications and it can occur in unusual sites, including cutaneous vessels. In the literature, PNH associated skin lesions were reported predominantly on the lower extremity and the ear manifesting as localized or widespread petechia, hemorrhagic and necrotic bullae, and/or ulcerations in 6 cases. Two of these six cases had dermal thrombosis resulting in acute necrosis of the ear.³ Similarly; in our patient, we think that PNH-associated dermal micro-occlusions caused extensive painful necrosis of the lip. Additionally, COVID-19-induced endothelial damage helped to develop exaggerated hemorrhagic necrosis. The question here is if the patients with benign red blood cells defects like hemoglobinopathies, membranopathies, and enzymopathies are more susceptible to COVID-19 infection. Till now, there is no scientific evidence related to this issue yet but, it is well known that the presence of comorbidities such as diabetes, heart disease, pulmonary hypertension, reduced kidney and /or liver function, exacerbates the impact of the COVID-19.

Rapidly accumulating evidence shows that the pathogenesis of COVID-19 infection and complications related to it is caused by endothelial dysfunction and endotheliitis.⁴ Eventually, severe infection with COVID-19 can also precipitate lip necrosis such as acute respiratory distress syndrome and renal failure.

We have previously described the first mucosal manifestations of COVID-19.² This current case presentation will contribute to the literature as another case with COVID-19 triggering mucosal involvement.

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Figure Legends

Fig 1: before treatment of thick-crust lip hemorrhagic necrosis

Fig 2: after treatment of thick-crust lip hemorrhagic necrosis



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