Case Report

ANATOLIAN CURRENT MEDICAL

DOI: 10.38053/acmj.930047

Anatolian Curr Med J 2021; 3(3); 259-261

Mortal disseminated intravascular coagulopathy and cutaneous involvement in a COVID-19-positive patient: a case report

Muharrem Bayrak, Kenan Çadırcı

Health Sciences University, Erzurum Regional Training and Research Hospital, Department of Internal Medicine, Erzurum, Turkey

Cite this article as: Bayrak M, Çadırcı K. Mortal disseminated intravascular coagulopathy and cutaneous involvement in a COVID-19-positive patient: a case report. Anatolian Curr Med J 2021; 3(3); 259-261.

ABSTRACT

Coronavirus 2019 disease (COVID-19) is a highly deadly disease that hascaused 77 million cases and 1.6 million deaths worldwide. Many cutaneous manifestations are seen withCOVID-19. Cutaneous pathologies, such as vascular endothelial damage, prothrombotic conditions, haemorrhagic cutaneous lesions, vasculitis, disseminated intravascular coagulopathy (DIC), ecchymotic skin lesions, purpura and dry gangrene, are seen in patients with COVID-19. While our 84-year-old male patient was being treated for COVID-19-related pneumonia in the infection ward, DIC developed on the ninthday of his treatment and widespread petechia, purpura, ecchymosis, necrosis, gangrene and bullous skin lesions were observed onhis left arm related to this. Here, we aimed to present a case of DIC that developed as a complication of a COVID-19 infection and hada mortal course with cutaneous involvement, to the literature.

Keywords: DIC, coronavirus-19, cutaneous involvement, infection, mortality.

INTRODUCTION

Coronavirus 2019 disease (COVID-19) is a highly fatal disease that has caused over 77 million cases and 1.6 million deaths worldwide (1). COVID-19 causes microvascular thromboses as well as respiratory problems in patients (2). A D-dimer elevation with a COVID-19 infection is associated with coagulopathy from theinfection. D-dimer occurs after the degradation of stabilized fibril polymers by the plasmin and leads to coagulation. D-dimer elevations are associated with a prognosis in a COVID-19 infection other than coagulopathy (3). At the onset of a COVID-19 infection, disturbances in coagulation tests do not usually lead to active bleeding. Changes in coagulation can result in sepsis-induced coagulopathy or DIC over time (4). The exaggerated inflammation that occurs in host cells with a COVID-19 infection can also lead to DIC (5). An exaggerated inflammation triggered in the host cell after an infection leads to the activation of pro-inflammatory cytokines and causes consumption coagulopathy. While DIC develops in only 0.6% of survivors, there is a 71.4% development rate in those who died of a COVID-19 infection (6). Previous studies have reported that pathologies, such as cutaneous involvement, vasculitis, livedo reticularis, and multiorgan failure, may be observed with the development of DIC in a COVID-19 infection (7,8).

In our case, we aimed to contribute to the literature by presenting the development of mortal complications and associated cutaneous involvement with DIC and multiorgan failure in a patient undergoing treatment with COVID-19 lung involvement.

CASE

An 84-year-old male patient presented with coronary artery disease and hypertension for the past 12 years. He had been taking various medications, including metoprolol (50 mg/day), ramipril/hydrochlorothiazide (5–12.5mg) and acetylsalicylic acid (81 mg/day). A fever, which started duringthe previousthree days, was 38.3°C. Thepatientalsohadapulseof94beats/minute,arespiratory rate of 23 breaths/minute, a blood pressure of 136/94 mmHg and an oxygen saturation, measured by pulse oximetry, of 91%. A physical examination of the patient revealed crepitations and rales in respiratory sounds in the middle lobes of both lungs. Laboratory findings on

Corresponding Author: Muharrem Bayrak, muhabayrak@hotmail.com

Received: 29.04.2021 **Accepted:** 15.06.2021

the first day in the ward were: haemoglobin: 12.8 g/dL (14.1–17.8); white blood cell (WBC): 8.8×10^3 ($3.91–10.9\times10^3$); platelets (PLT): 165×10^3 ($152–383\times10^3$); neutrophil: 72.8% (40%–74%); lymphocyte percentage: 17.2% (17%–47%); lymphocyte count: $1.1x10^3$ µL ($1.21–3.77\times10^3$); serum creatine: 1.52 (0.7–1.7 mg/dL); urea: 28 (9–23 mg/dL); C-reactive protein (CRP): 121.2 mg/L (0–5 mg/L); D-dimer: 765 mg/L (0–500 mg/L); procalcitonin: 0.01 ng/ml (0–0.05 ng/ml); fibrinogen: 738 mg/dL (200–400); prothrombin time (PT): 8.2 seconds (5–15); activated partial thromboplastin time (APTT): 24 seconds (22–31); international normalized ratio (INR): 1.03 (08–1.2); ferritin: 175 ng/ml (22–232); aspartate aminotransferase (AST): 16 IU/L (0–40); alanine transaminase (ALT): 19 U/L (7–40); lactate dehydrogenase (LDH): 258 U/L (230–500); and albumin: 3.9 mg/dL (3.2–4.8). In thoracic tomography, ground-glass opacities accompanied by an increased in terlobular septal thickening were observed in the middle-lower zones of both lungs (**Figure 1a**). The arterial blood gas test results were pH: 7.38; PO_2: 84.4; PCO_2: 35.9; HCO_3: 24.5; BE: -1; and SpO_2: 89. Since the COVID-19 reverse transcriptase-polymerase chain reaction (RT-PCR) test performed in our patientwas positive, the antiviral treatment included a favipiravir loading dose (2×1600 mg) followed by a maintenance dose (2×600 mg), which was administered for 10 days. Additionally, 3–4 L/min of oxygen therapy with a nasal cannula, subcutaneous enoxaparin (60 mg/day), dexamethasone (8 mg/day), acetylcysteine (900 mg/day) and levofloxacin (500 mg/day) treatments were started. Metoprolol (50 mg/day) and ramipril/hydrochlorothiazide (5–12.5 mg) were continued. Lopinavir/ritonavir, meropenem and a three-day treatment of methylprednisolone (250 mg/day) was started because of the cytokine storm and since the oxygen saturation was only 84% and the CRP was158 mg/L on the thirdday in the ward. On the sixthday in the ward, when the CRP was 167 mg/L and the oxygen saturation was 82%, tocilizumab (400 mg/day) was given intravenously for two days. On the eighthday in the ward, the patient had a sudden onset of haematuria, accompanied by petechiae and purpura on the left arm. Fresh frozen plasma and an erythrocyte suspension were given. On the ninthday, the ecchymotic lesion on the left arm became prominent in the form of necrosis and haemorrhagic bullous lesions up to the left armpit (**Figure 2a, b**). The patient's laboratory results at this point were haemoglobin: 6.2 g/dL; WBC: 24.2×10^3; PLT: 33×10^3; neutrophil: 76.8%; lymphocyte: 0.5×10^3 µL; CRP: 112.2 mg/L; D-dimer: 3,697 mg/L; procalcitonin: 4.82 ng/ml; fibrinogen: 75 mg/dL; PT: 38.9 seconds; aPTT: 152 seconds; INR: 2.08 (08–1.2); ferritin: 1,268 ng/ml; LDH: 1,126 U/L; AST: 416 IU/L; ALT: 347 U/L; albumin: 2.6 mg/dL; serum creatine: 5.7 mg/dL; urea: 162 mg/dL; and fibrin degradation products: 148 µg/ml (<10 µg/ml). The arterial blood gas test results were pH: 7.22; PO_2: 58.7; PCO_2: 35.9; HCO_3: 8.6; BE: -12; and SpO_2: 81. There were bilateral infiltrates on the posterior chest radiograph (**Figure 1b**). On the 10th day in the ward, our patient had a 24-hour urine output of 120 ml, and when metabolic acidosis, uremic encephalopathy, and creatine increased, the patient was transferred to the intensive care unit. The patient was then placed on haemodialysis with a central dialysis catheter and connected to an invasive mechanical ventilator. Arterial and venous Doppler ultrasonography for the left arm revealed echogenic thrombus images in the cephalic and basilic veins that did not respond to compression. Fresh frozen plasma, vitamin K, and erythrocyte suspension treatments were continued with heparin. Positive inotrope therapy was initiated since the arterial blood pressure of our patient was 72/35 mmHg. Unfortunately, our patient, who did not respond to medical treatments, had a cardiac arrest and was exitus on the 15th day of his follow-up in the intensive care unit.

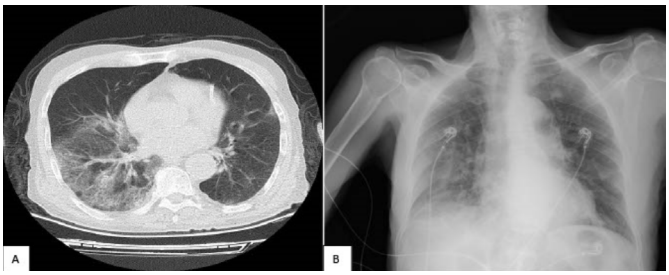

Figure 1. These radiological images show the days during which the patient was hospitalized and DIC developed.

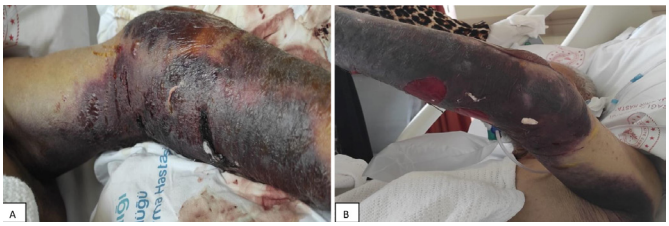

Figure 2. This figure shows the skin lesions during the period when the patient developed DIC.

DISCUSSION

Coagulation disorders, microvascular complications, DIC and thromboembolisms can be seen in cases with more severe courses of COVID-19 infection. Microthrombi, mainly in the lungs, are observed in autopsy studies (6,9). Cutaneous involvement and ecchymoses have been observed in some COVID-19 cases. Ecchymosis lesions on the skin of COVID-19 patients can occur by different mechanisms. Diffuse microvascular thrombi, perivascular neutrophilia and leukocytoclastic vasculitis were observed in skin biopsies performed with the first mechanism. In thrombogenic vasculopathy, an

accumulation of C5b-9, C4d in the complement system, and COVID-19 spike protein (S) in the microvascular area were commonly observed in the entire lesion and dermis layer. Activation in the complement system leads to damage and inflammation in microvascular endothelial cells, resulting in fibrin deposits and thrombi (7). During the second mechanism, COVID-19 enters the cell by binding to the ACE-2 receptor. ACE-2 is an effective component inthe transformation of bradykinin, which is part of the kinin-kallikrein system, and its metabolite, DABK (desArg973 the active metabolite of bradykinin). A decreased activation of ACE-2 with a COVID-19 infection may lead to an increased DABK and the formation of reactive oxygen species, increased NOX2, eNOS and an activation of the complement system, causing vasodilation, microvascular endothelial damage, multiorgan failure and ARDS. The third mechanism leads to procoagulation by activating platelets and antiphospholipid antibodies in endothelial cells by causing the antiphospholipid antibody syndrome secondary to a COVID-19 infection (7,10). In our case, we think that all three mechanisms may have beeninvolvedin the development of ecchymosis and DIC. We think that our patient with COVID-19 pneumonia had increased D-dimer, CRP level, coagulopathy and DIC formation, and with findings in the lungs and cutaneous involvement and multiorgan failure, these were serious complications of severe COVID-19 infection.

We found few cases similar to our case in the literature. Takahashi et al. (11) reported that a 65-year-old patient with COVID-19 and pneumonia developed DIC complications. While the presence of CRP, a high D-dimer level and lung involvement in their case was similar to our case, there were additional severe cutaneous findings in our case. Novara et al. (12) reported a case of DIC and dry gangrene of the hands ofa 78-year-old patient with COVID-19 pneumonia. Our case had many similar symptoms, such as the development of DIC, an advanced age, cutaneous involvement and mortality.

CONCLUSION

In our case, we consider the lack of a skin biopsy in cutaneous involvement as a limitation of the study. In conclusion, our case was an advanced-age patient withcoronary artery disease, hypertension and high CRP and D-dimer levels, whichwere prognostic factors for a COVID-19 infection. Simultaneously, these were important predisposing factors for the development of DIC. Our aim with this case study was to contribute to the literature by presenting a DIC case, which is a mortal complication of COVID-19 infections, and its associated skin involvement.

ETHICAL DECLARATIONS

Informed Consent: Written informed consent was obtained from all participants who participated in this study.

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: The authors have no conflicts of interest to declare.

Financial Disclosure: The authors declared that this study has received no financial support.

Author Contributions: All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

REFERENCES

1. JHU, Coronavirus resource center. Medicine 2020.
2. Connors JM, Levy JH. Thromboinflammation and the hypercoagulability of COVID-19. J Thromb Haemost 2020; 18: 1559-61.
3. Asakura H, Ogawa H. COVID-19-associated coagulopathy and disseminated intravascular coagulation. Int J Hematol 2021; 113: 45-57.
4. Connors JM, Levy JH. COVID-19 and its implications for thrombosis and anticoagulation. Blood 2020; 135: 2033-40.
5. Iba T, Levy JH, Thachil J, Wada H, Levi M, Scientific and Standardization Committee on DIC of the International Society on Thrombosis and Haemostasis. The progression from coagulopathy to disseminated intravascular coagulation in representative underlying diseases. Thromb Res 2019; 179: 11-4.
6. Tang N, Li D, Wang X, Sun Z. Abnormal coagulation parameters are associated with poor prognosis in patients with novel coronavirus pneumonia. J Thromb Haemost 2020; 18: 844-7.
7. Magro C, Mulvey JJ, Berlin D, et al. Complement associated microvascular injury and thrombosis in the pathogenesis of severe COVID-19 infection: A report of five cases. Transl Res 2020; 220: 1-13.
8. Widysanto A, Wahyuni TD, Simanjuntak LH, et al. Ecchymosis in critical coronavirus disease 2019 (COVID-19) patient in Tangerang, Indonesia: a case report. J Thromb Thrombolysis 2020; 1-5.
9. Dolhnikoff M, Duarte-Neto AN, de Almeida Monteiro RA, et al. Pathological evidence of pulmonary thrombotic phenomena in severe COVID-19. J Thromb Haemost 2020; 18: 1517-9.
10. Iba T, Levy JH, Connors JM, Warkentin TE, Thachil J, Levi M. The unique characteristics of COVID-19 coagulopathy. Crit Care 2020; 24: 360.
11. Takahashi W, Yoneda T, Koba H, et al. Potential mechanisms of nafamostat therapy for severe COVID-19 pneumonia with disseminated intravascular coagulation. Int J Infect Dis 2021; 102: 529-31.
12. Novara E, Molinaro E, Benedetti I, Bonometti R, Lauritano EC, Boverio R. Severe acute dried gangrene in COVID-19 infection: a case report. Eur Rev Med Pharmacol Sci 2020; 24: 5769-71.