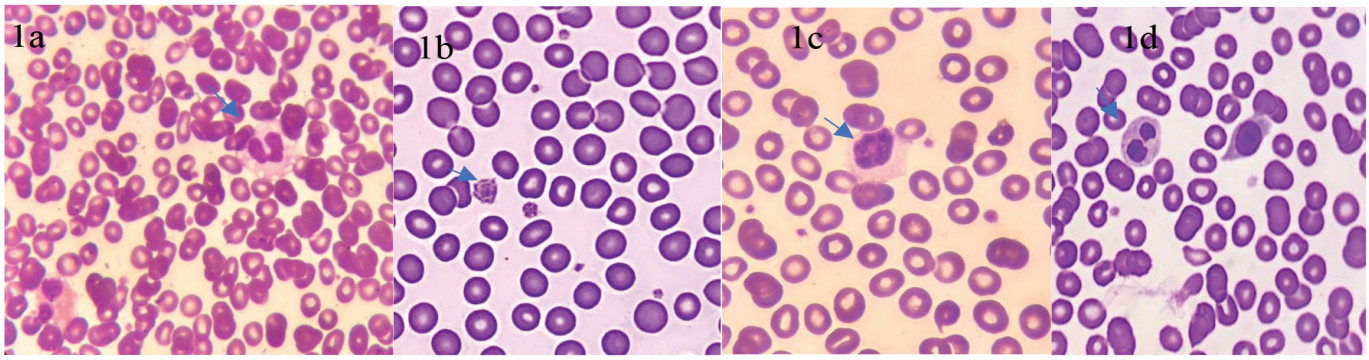

Figure 1. Blood smears of patients with COVID-19 (May-Grunwald-Giemsa): **a)** eosinophil containing multiple vacuoles; **b)** giant platelets with different sizes; **c)** circulation of a large lymphocyte; **d)** neutrophil granulocyte with marked hypogranular cytoplasm and hyposegmented nucleus.

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Hydroxychloroquine-Associated Thrombotic Thrombocytopenic Purpura

Hidroksiklorokin İlişkili Trombotik Trombositopenik Purpura

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To the Editor,

Although there have been inconsistent publications on the activity and safety of hydroxychloroquine (HQ), it is recommended by several treatment guidelines to be used for all patients with symptomatic COVID-19 disease. There were several concerns regarding the treatment-related side effects. The most important side effects include QT prolongation and visual-field defects.

A 65-year-old man with chronic obstructive pulmonary disease was admitted to the hospital with the complaints of cough and chest and back pain. Physical examination was unremarkable. Computerized tomography and angiography of the chest

revealed bilateral emphysematous changes. There were no findings suggesting venous thromboembolism. Laboratory finding were as follows: hemoglobin (Hb), 14.4 g/dL; mean corpuscular volume, 96.4 fL; lymphocyte count, 3070/µL; platelet count (PLT), 150,000/µL; prothrombin time, 14 s; and international normalized ratio, 1.0. The patient had no fever or shortness of breath. There was no previous history of travel abroad or close contact with anyone who was SARS-CoV-2-positive. A nasal swab was obtained for SARS-CoV-2 polymerase chain reaction (PCR). In the outpatient setting, HQ was started without waiting for the test results.

He was reevaluated on the third day of treatment. There was no improvement in his complaints. The SARS-CoV-2 PCR test result was negative. Laboratory results at his second admission were as follows: Hb, 10.8 g/dL; PLT, 31,000/µL; lactate dehydrogenase (LDH), 1281 U/L (upper limit of normal: <248 U/L); and creatinine, 1.7 g/dL (upper limit of normal: <1.2 mg/dL). The patient had aphasia. Cranial computerized tomography was consistent with infarction of the medial cerebral artery. He was hospitalized with the suspicion of thrombotic thrombocytopenia purpura (TTP). Direct Coombs test was negative. There were 10% schistocytes in the peripheral blood smear. Disseminated intravascular coagulation was ruled out. His PLASMIC score was 6, which indicated a high probability of TTP [1].

After a blood sample was taken for ADAMTS13 analyses, HQ was ceased and exchange plasmapheresis with 1.5 volumes was started. Methylprednisolone (1 mg/kg/day) and folic acid supplementation was commenced. The ADAMTS13 level, ADAMTS13 activity, and ADAMTS13 inhibitor levels were <0.012 (0.19-0.81) IU/ml, <0.2% (40%-100%), and 90 (<12) U/mL, respectively. On the fourth day of his admission, thrombocytopenia was improved and LDH level returned to the normal range. On day 7, plasmapheresis was discontinued.

Acute immune reactions and dose-dependent toxicity play important roles in drug-related TTP etiology. The most common drug known to be related to TTP is quinine [2]. Quinine-dependent antibodies have been shown to induce TTP through immune-mediated mechanisms by interacting with platelets and other cells. HQ belongs to the 4-aminoquinoline class and is an amine acidotropic form of quinine. There are two case reports of possible HQ-related TTP in the literature. A 64-year-old woman with rheumatoid arthritis developed TTP after 3 doses of HQ [3] and a 34-year-old woman with a diagnosis of systemic lupus erythematosus had TTP under HQ treatment [4]. However, in the latter case, the relation of HQ and TTP was suspicious. Our case is the third case of possible HQ-related TTP in the literature. The adverse drug reaction probability score was calculated as 4 and adverse drug reaction was thus assigned to the "possible" category [5] (Table 1). It may be considered that TTP may be among the rare side effects in treatment with HQ.

Table 1. Adverse drug reaction probability scale (Naranjo Scale).

Question	Yes	No	Do not know	Score
Are there previous conclusive reports of this reaction?	**+1**	0	0	+1
Did the adverse event appear after the drug was given?	**+2**	-1	0	+2
Did the adverse reaction improve when the drug was discontinued or a specific antagonist was given?	+1	**0**	0	**0**
Did the adverse reaction reappear upon re-administering the drug?	+2	-1	**0**	**0**
Were there other possible causes for the reaction?	**-1**	+2	0	-1
Did the adverse reaction reappear upon administration of placebo?	-1	**+1**	0	+1
Was the drug detected in the blood or other fluids in toxic concentrations?	+1	0	**0**	**0**
Was the reaction worsened upon increasing the dose? Or was the reaction lessened upon decreasing the dose?	+1	**0**	0	0
Did the patient have a similar reaction to the drug or a related agent in the past?	+1	**0**	0	0
Was the adverse event confirmed by any other objective evidence?	**+1**	0	0	+1
Total	N/A	N/A	N/A	**+4**

Drug probability category according to Naranjo scores: definite, >8; probable, 5 to 8; possible, 1 to 4; doubtful, <1.

Keywords: Hydroxychloroquine, Thrombotic thrombocytopenic purpura, Severe acute respiratory syndrome-related coronavirus

Anahtar Sözcükler: Hidroksiklorokin, Trombotik trombositopenik purpura, Ağır akut solunum sendromu ilişkili koronavirüs

Informed Consent: Informed consent was obtained from the patient.

Authorship Contributions

Data Collection or Processing: F.A., Y.Y., S.A., Ö.O., T.E.; Literature Search: F.A., F.Y., T.T., Tü.T.; Writing: F.A., F.Y., T.T.

Conflict of Interest: We confirm that there are no conflicts of interest to declare.

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Sleeve Gastrectomy in a Severe Hemophilia A Patient: One of the Very Rare Cases

Ağır Hemofili A Hastasında Sleeve Gastrektomi Operasyonu: Çok Nadir Olgulardan Biri

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To the Editor,

Obesity is becoming a problem for aging hemophilia patients. The estimated prevalence of overweight and obesity in European and North American hemophilia patients is 31% [1]. Similarly to non-hemophiliacs, excessive weight has an adverse effect on the cardiovascular system and the psychological and musculoskeletal health of hemophilia patients. Bariatric surgery is advised to be considered for patients from the general population with a body mass index (BMI) of ≥40 kg/m^2 or BMI of ≥35 kg/m^2 with comorbidities [2]. Although it is not contraindicated, there are limited data on bariatric surgery among hemophilia patients. There are only two hemophilia A patients reported in the literature who had bariatric surgery. The first one underwent a successful sleeve gastrectomy [3] and the other had mini-gastric bypass surgery [4].

A 55-year-old severe hemophilia A patient with arterial hypertension, diabetes mellitus, hyperlipidemia, obstructive sleep apnea, and morbid obesity (BMI of 42.45 kg/m^2) decided to have obesity surgery because of inconclusive efforts at losing weight and obesity-related comorbidities. He had been receiving factor VIII prophylaxis at 6000 units/week for the last few years because conventional treatment at 4500 units/week was not sufficient for his frequent joint bleedings.

According to the Hemophilia Diagnosis and Treatment Guidelines of the Turkish Society of Hematology [5], the perioperative factor VIII target was calculated as 100%. Three days before surgery, his factor VIII level was 2.3% and factor VIII inhibitor was negative. He received factor VIII at 42 units/kg preoperatively and we planned to administer 23 units/kg at the postoperative 12th hour (weight: 130 kg). At the postoperative 7th hour he had hypotension, loss of consciousness, oliguria, 13% decline in hematocrit level, and increase in creatinine and transaminase levels. At that time, activated partial thromboplastin time (aPTT) was 26.8 s (normal range: 22.5-31.3). During explorative laparotomy, approximately 500 mL of blood was drained from the abdominal cavity, but a surgical bleeding focus could not be found. Packing was performed according to damage control surgery principles. After 48 h the abdominal cavity was reopened for unpacking and no bleeding was observed. He was followed in the intensive care unit for the following 8 days with mechanical ventilation. He needed intermittent hemodialysis because of hemorrhage-related acute kidney injury. During this period, he had thrombocytopenia and prolonged prothrombin time. He had multiple erythrocyte, platelet, and fresh frozen plasma replacements due to probable disseminated intravascular coagulation. Hemorrhage from the surgical drains lessened and finally stopped. Perioperative laboratory results are summarized in Table 1.