OLGU SUNUMU / *CASE REPORT*

Rectus Sheath Hematoma After Prophylactic Subcutaneous Enoxaparin Treatment in a COVID-19 Patient

Bir COVID-19 Hastasında Profilaktik Subkutan Enoksaparin Tedavisi Sonrası Rektus Kılıf Hematomu

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ABSTRACT

COVID-19 is a disease that causes microvascular thrombosis with respiratory failure. Anticoagulant treatments sometimes cause life-threatening gastrointestinal, intracranial, and abdominal bleeding. A 68-year-old male patient was admitted to the infectious diseases service because the COVID-19 PCR-RT test performed in the emergency department was positive and it was compatible with COVID-19 pneumonia on thoracic tomography. Prophylactic subcutaneous enoxaparin treatment was initiated considering that the patient would have a high risk of microvascular thrombosis due to hypertension and coronary artery disease. On the 10th day of his treatment, the patient whose general condition was deteriorated and had severe abdominal pain, hemoglobin was 6.4 mg/dl in the hemoglobin examination performed for diagnosis, and a diagnosis of hematoma spreading to the pelvis starting from the rectus sheath of 15×11×14 cm was made in abdominal tomography.

Key words: *COVID-19; hematoma; enoxaparinsodium; computed tomography*

ÖZET

COVID-19, solunum yetmezliği ile birlikte mikrovasküler tromboza neden olan bir hastalıktır. Antikoagülan tedaviler bazen yaşamı tehdit eden gastrointestinal, intrakraniyal ve abdominal kanamaya neden olur. 68 yaşındaki erkek hasta, acil serviste yapılan COVID-19 PCR-RT testinin pozitif olması ve toraks tomografisinde COVID-19 pnömonisi ile uyumlu olması nedeniyle enfeksiyon hastalıkları servisine kabul edildi. Hastanın hipertansiyon ve koroner arter hastalığına bağlı mikrovasküler tromboz riskinin yüksek olacağı düşünülerek profilaktik subkutan enoksaparin tedavisi başlandı. Tedavisinin 10. gününde, genel durumu kötüleşen ve şiddetli karın ağrısı gelişmesi üzerine, tanı amaçlı olarak bakılan hemoglobin incelemesinde hemoglobin 6,4 mg/dl, ve batın tomografisinde ise rektus kılıfından başlayarak pelvise yayılan 15×11×14 cm abadlı hematom tespit edilmesi üzerine rektus kılıf hematomu tanısı konuldu.

Anahtar kelimeler: *COVID-19; hematom; enoksaparinsodyum; bilgisaraylı tomografi*

Introduction

COVID-19 is a highly fatal disease that causes 34 million cases and 1 million deaths in the world[1,2]. COVID-19 is a disease that causes microvascular thrombosis with respiratory failure[3]. It is thought that the formation of microvascular thrombosis in COVID-19 disease is caused by the increase in hypercoagulability caused by proinflammatory cytokines such as interleukin-6 (IL-6), tumor necrosis alpha (TNF-alpha), and other atherosclerotic changes[4]. Prophylactic anticoagulant treatment due to increased hypercoagulability reduces the risk of ischemia and pathologies related to microvascular thrombosis in patients with COVID-19[5]. Rectus sheath hematoma is a rare complication and is usually seen after trauma or due to anticoagulant therapy[6]. Rectus sheath hematomas have a mortality rate of 4%[7]. Cases of rectus sheath hematoma due to low molecular weight heparin have been reported in the literature, although it is not very common[8]. As far as we know in our case, we present a case of rectus sheath hematoma that developed on the 10th day of subcutaneous enoxaparin treatment, which was initiated prophylactically while receiving COVID-19 treatment. We would like to emphasize that it is very important that anticoagulant treatment and potentially fatal bleeding after treatment in COVID-19 patients require very close follow-up.

Case Presentation

The 68-year-old male patient had hypertension and coronary artery disease. The patient had been using

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100 mg/day acetylsalicylic acid and ramipril/hydrochlorothiazide (10/12.5 mg) for five years. Fever of 38.6° C that started in the last five days, pulse 102/min, respiratory rate 21/min, blood pressure 146/92 mm Hg, and oxygen saturation measurement by pulse oximetry was 79%.

Bilateral breathing sounds in the lower lobes of the lungs had rales and crepitations on physical examination. In his laboratory, hemoglobin 11.8 g/dL (14.1–17.8), white blood cell (WBC) 5.32×10^3 (3.91–10.9 $x10^3$), thrombocyte 153×103 (152–383×10^3), neutrophil 72.5% (40–74%), lymphocyte 11.9% (%) 17–47), absolute lymphocyte count 0.8×10^3µL (1.21–3.77×10^3 µL), serum reactive protein (crp) 48.2 mg/L (0–5 mg/L), D-dimer 1590 mgL (0–500 mgL, procalcitonin 0.193 ng/ml (0–0.05 ng/ml), fibrinogen 506 mg/dL (200–400 mg/dL), INR: 1.09 (08.1.2) (Table 1).

Table 1. *Laboratory results of the COVID-19 patient on the 1st day of treatment and the 10th-day of treatment when hematoma develops*

Laboratory results	1. Day	10. Day
Hemoglobin (g/dL) (14.1–17.8)	11.8	6.4 **
White blood cell $\times10^3$ (3.91–10.9)	5.32	4.58
Platelet $\times10^3$ (152–383)	153	132
% Neutrophil (% 40–74)	72.5	75.6
% Lymphocyte (% 17–47)	11.9	9.7
Absolute lymphocyte count $\times10^3$µL ($1.21–3.77\times10^3$µL)	0.8	0.6
CRP mg/L (0–5)	48.2	54.7
D-dimer mg/L (0–500)	1590	1684
Procalcitonin ng/ml (0–0.05)	0.193	0.254
Fibrinogen mg/dL (200–400)	506	624
Ferritin µg/L (30–400)	459	584
INR	1.09	1.11
S/D ABP mmHg	146/92	72/44
Pao_2/Fio_2 ratio	302	289
GFR (ml/dk/1.73 m^2)	79	62

** On the 10th day, a severe decrease in hemoglobin is observed.
CRP, C-reactive protein; GFR, glomerular filtration rate; INR, international normalized ratio; S/D ABP, systolic/diastolic arterial blood pressure.

More prominent peripherally located diffuse ground glass densities were observed in all lobes, lower lobes, and subpleural areas of both lungs in the thoracic tomography of the patient, and were found to be compatible with COVID -19 pneumonia (Figure 1). Favipiravir 2×1600 mg loading and 2×600 mg maintenance therapy, levofloxacin, 5 lt/min oxygen therapy with a nasal cannula, subcutaneous 60 mg/day enoxaparin, acetylcysteine 900 mg/day treatment was started for COVID-19 treatment. Acetylsalicylic acid and ramipril/hydrochlorothiazide (10/12.5 mg) were continued. Daily saturation and vital signs of the patient were followed closely. Sudden onset of severe abdominal pain, nausea, vomiting, blood pressure 72/44 mmHg, and pulse: 118/min. on the 10th day of the patient's treatment. Increased sensitivity in the abdomen was observed in the physical examination of the patient. The skin and mucous membranes in the body had an anemia appearance. Hemoglobin was found to be 6.4 g/dL in the hemogram of the patient. Unenhanced abdominal tomography was performed. A hematoma measuring 15×11×14 cm starting from the rectus sheath and continuing to the pelvic region was detected (Figure 2). The patient was transferred to the intensive care unit. Anticoagulant treatment of the patient was discontinued and intravenous fluid therapy was started at 3000 ml/day, 4 units of erythrocyte suspension and 2 units of fresh frozen plasma treatment were given. After the patient stayed in the intensive care unit for 7 days, a control abdominal tomography was performed because the Hb was 10.5 g/dL and the condition was stable. No invasive procedure was performed on the patient as the hematoma shrank to 10x11x10 cm, but a conservative treatment was applied. Our case was transferred to the normal infection service again. A written consent form was obtained from our patient to write the case.

Discussion

One of the most important causes of mortality in COVID-19 patients is venous thromboembolism and disseminated intravascular coagulopathy (DIC)[9]. COVID-19 is a disease that causes microvascular thrombosis together with respiratory failure[3]. It is thought that the formation of microvascular thrombosis in COVID-19 disease is caused by the increase in hypercoagulability caused by proinflammatory cytokines such as interleukin-6 (IL-6), tumor necrosis alpha (TNF-alpha), and other atherosclerotic changes[4]. Proinflammatory cytokines released in COVID-19 infection are among the leading factors in

Figure 1. *Thoracic tomography shows consolidated areas of peripherally located diffuse ground glass density and crazy paving findings, which are evident in the lower lobe basal segments in both lungs.*

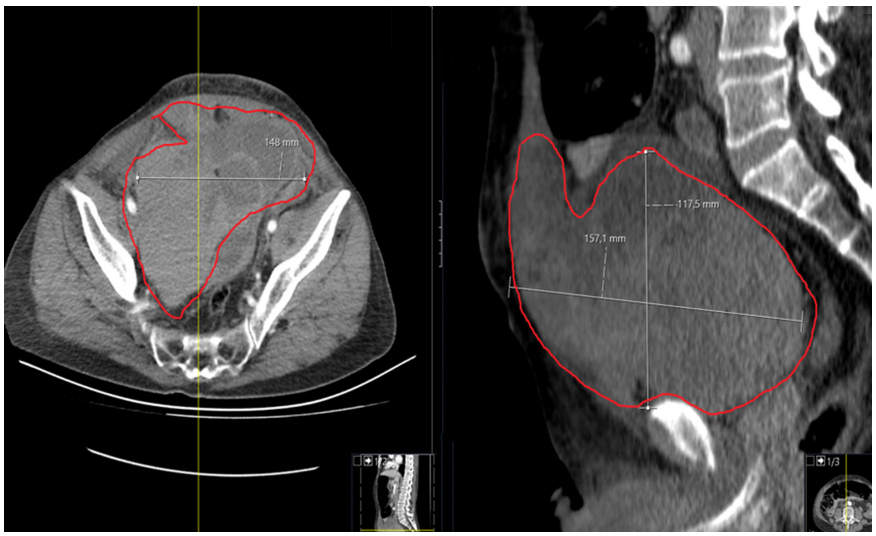

Figure 2. *15×11×14 cm hematoma image starting from the rectus sheath and extending to the pelvis and compressing the bladder on abdominal tomography.*

the development of DIC[10]. Prophylactic anticoagulant therapy is used to prevent microvascular complications in COVID-19 infection. Our case was also using subcutaneous enoxaparin 60 mg and 100 mg acetylsalicylic acid. Gastrointestinal and intracranial bleeding associated with prophylactic anticoagulant treatment has been reported in patients with COVID 19[11,12]. To the best of our knowledge, rectus sheath hemorrhage due to subcutaneous enoxaparin has not been reported in COVID-19 infection in the literature. Patel et al[13]. reported a 10×17×24 cm psoas muscle hematoma in a 69-year-old male patient with COVID-19. According to the classification of rectus sheath hematoma in our case, it was classified as Type 3 because of the presence of blood in the peritoneum and prevesical space and the hematocrit being affected and in the literature[14]. Peripherally located ground-glass opacities, consolidated areas, reticular pattern, Crazy Paving findings are observed in thorax tomography in COVID-19 pneumonia. In our case, prevalent tomography findings consistent with the literature were observed in thorax tomography[15].

Subcutaneous enoxaparin treatment was used as prophylactic and hematoma developed on the 20th day of treatment in this case. 60 mg of enoxaparin and 100 mg of acetylsalicylic acid were used in our case, whereas 81 mg of acetylsalicylic acid and 40 mg of enoxaparin were used in the case of Patel et al.[13] We think that earlier

hematoma in our case is due to differences in drug doses, clinical and genetic differences in patients, and the fact that COVID infection causes different systemic symptoms and signs in each patient. While D-dimer was 1590 mg/L in our case, it was measured as 570 mg/L in the other case. Highness in both patients was a common feature in both patients. D-dimer height was an important factor for the initiation of prophylactic anticoagulants in our case. In the 126 case series of Cherry et al.[6], which is the largest case series of rectus sheath hematoma in the literature, Median age 73 and 81 (64%) of the patients with female rectus sheath hematoma, 87 (69%) patients used at least one anticoagulant treatment, while 30 (24%) used anticoagulant and antiplatelet therapy together. The age of the patient and the development of rectus sheath hematoma secondary to anticoagulant treatment were similar in our case, while the fact that our patient being male was different.

As a result, in COVID-19 patients, as in our case, anticoagulant therapy is used prophylactically in the existence of additional risk factors such as hypertension, coronary artery disease, as well as a serious infection (viral pneumonia, etc.), CRP, and high D-dimer and also against the risk of microvascular thrombosis due to proinflammatory cytokine release in COVID-19 infection. Anticoagulant therapy was used because of many risk factors in our case, and secondary rectus sheath hematoma developed as a complication in this treatment. We think that we contribute to the literature with the fact that our case was the first reported rectus sheath hematoma as far as we know in COVID-19 patients, and also by drawing attention to the fact that subcutaneous enoxaparin treatment, which is widely used in the treatment of COVID-19 in the world, will be a serious bleeding complication, and by reporting that patient monitoring and treatment can be performed with non-invasive conservative methods in case of a hematoma that may develop.

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Authors' Contribution

All authors (MB, KÇ and MK) contributed equally to this manuscript and approved the final manuscript.

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