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COVID-19-Associated Retroperitoneal Hemorrhage: Same Complication, Two Different Types of Treatment

COVID-19 İlişkili Retroperitoneal Kanama: Aynı Komplikasyon, İki Farklı Tedavi

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Abstract

One of the reasons for the high mortality in COVID-19 patients is the increased risk of disseminated intravascular coagulation (DIC) and venous thromboembolism. For this reason, the use of anticoagulant treatments has become widespread. One of the rare complications of anticoagulant therapy is retroperitoneal hemorrhage. These hemorrhagies require immediate intervention. Retroperitoneal hemorrhage should be kept in mind among the many complications that develop in the patient who was followed up during the pandemic period. For this purpose, we present 2 cases who developed spontaneous retroperitoneal bleeding while clinically recovering under COVID-19 treatment.

Keywords: COVID-19, coronavirus, retroperitoneal hemorrhage, retroperitoneal hematoma, retroperitoneum

Öz

COVID-19 hastalarında yüksek mortalitenin nedenlerinden biri, yaygın intravasküler pıhtılaşma ve venöz tromboembolizm riskinin artmasıdır. Bu nedenle antikoagülan tedavilerin kullanımı yaygınlaşmıştır. Antikoagülan tedavinin nadir rastlanılan komplikasyonlarından biri de retroperitoneal kanamadır. Bu kanamalar acil müdahale gerektirir. Pandemi döneminde takip edilen hastada gelişen birçok komplikasyon arasında retroperitoneal kanama akılda tutulmalıdır. Bu amaçla COVID-19 tedavisi altında klinik olarak iyileşmekte iken spontan retroperitoneal kanama gelişen 2 olguyu sunuyoruz.

Anahtar kelimeler: COVID-19, koronavirüs, retroperitoneal kanama, retroperitoneal hematom, retroperiton

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Introduction

Spontaneous retroperioneal hematoma is a very rare, serious clinical condition defined as bleeding into the retroperiotenal area without associated trauma or surgical intervention [1]. The most important causes are anticoagulants, vascular diseases and renal tumors [2]. When the event occurs, the general condition of the patient may deteriorate due to weakness, flank pain, and hypotension requiring immediate intervention. In addition, hematoma can cause symptoms due to local compression on adjacent organs [3]. Although anticoagulants are useful in pulmonary embolism, stroke and deep vein thrombosis, they can cause bleeding in any part of the body [4].

Increased risk of disseminated intravascular coagulation (DIC) and venous thromboembolism are two of the leading causes of death in COVID-19 patients. Increase in D-dimer levels is often a herald of this situation [4]. The most important reason leading to multiple organ failure and death is hypercoagulability causing microvascular thrombus which is treated with antithrombotics such as heparin [5].

Anticoagulants are useful at therapeutic doses, but their common use increases the likelihood of spontaneous bleeding. While the probability of bleeding associated with anticoagulants is 4.8-8%, this rate has been reported as 3.5% in terms of major bleeding. Several cases of fatal retroperitoneal bleeding in COVID-19 patients receiving prophylactic or therapeutic doses of anticoagulant therapy have been previously reported in the literature [6–9].

Most cases are self-limited and resolve with cessation of anticoagulation and conservative treatment. The success rate of conservative treatment is dependent on the occurrence of these hematomas in confined spaces surrounded by adjacent structures [10]. In some cases, especially if there is a delay in diagnosis also non-adjacent vessels may rupture. And in such cases, the mortality rate is high [4]. In these special cases where persistent bleeding or hemodynamic instability despite conservative treatment occurs, transcatheter arterial embolization (TAE) may be required. Surgical treatment is applied in rare cases.

Herein, we describe two cases of life-threatening retroperitoneal hemorrhage developed during the clinical course of COVID-19. In both cases, respiratory distress caused by COVID-19 was improving when they developed retroperitoneal hemorrhage. Moreover, the patients were taking anticoagulants to prevent thrombosis. One of our patients recovered with TAE and the other with conservative treatment. Both of our patients were followed up without the need for intensive care, and were discharged.

Case 1

A 77-year-old woman without chronic disease was hospitalized because of severe respiratory distress and fever. Real-time reverse transcription polymerase chain reaction (RT-PCR) test performed to detect COVID-19 disease yielded positive results, and thorax computed tomography (CT) showed bilateral diffuse pulmonary infiltrates. The laboratory results at admission were as follows: ferritin, 1744 mcg/L (n: 23-336); procalcitonin, 0.45 ng/mL (n: <0.5); D-dimer , 0.42 mcg/mL (n: <0.5), and C-reactive protein (CRP), 118 mg/L (n: 0.3-10). Her platelet counts (n: 150-570 × 103/mcL), hemoglobin (Hgb) (n: 11.5-17.3 g/dL), and creatinine (0.74 mg/dL; n: 0.7-1.2) levels were within normal limits.

Her oxygen saturation (SpO2) was 88%. Physical examination on admission revealed bilaterally decreased pulmonary breath sounds. Arterial blood pressure (150/100 mm Hg), pulse rate (95 bpm), body temperature (38°C) and respiratory rate (24/min) of the patient were measured on admission. The patient was started on favipravir (loading oral dose of 1,800 mg on day 1, followed by 400 mg twice daily for 9 days), ceftriaxone (1 g/d IV), supplemental oxygen delivered through nasal cannula and prophylactic enoxaparin (40 mg/d SC). The patient felt palpitations. On electrocardiograph (ECG) atrial fibrillation with rapid ventricular response was observed. Her D-dimer level increased to 2.47 mcg/mL (reference range <0.5). The patient was started on therapeutic dose of enoxaparin (1 mg/kg SC) due to hypercoagulation concerns. Four days later, the patient started to complain about right flank pain, and on subsequently performed CT scan of abdomen, a large retroperitoneal hemorrhage was detected. Her blood pressure and pulse rates were 100/70 mmHg and 108/min, respectively.

Hemoglobin levels dropped from 14.7 g/dL to 10.2 g/dL and then to 7.1g/dL. Hypovolemia developed due to acute bleeding. After transfusion of 2 units of packed red blood cells (pRBCs), her Hgb raised to 9.5 g/dL. All anticoagulant agents were stopped. Contrast-enhanced abdominal and pelvic CT showed areas of hematoma (10.1x7.4 cm and 9.2x5.7 cm) in the right iliopsoas muscle spreading to the retroperitoneal space with extravasation **(Figure 1)**.

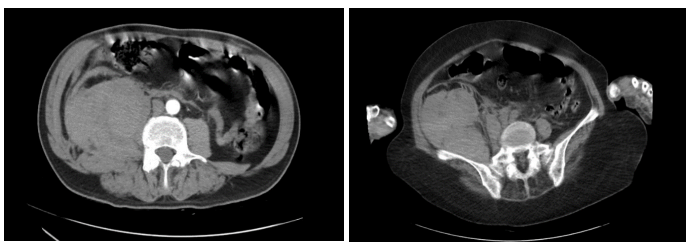

Figure 1. A 77-year-old woman; hematoma in the right retroperitoneal space was demonstrated in both abdominal and pelvic CT scans

The patient was treated conservatively, with blood transfusion. The patient was followed closely, her vital parameters and decrease in her hemoglobin values were monitored. In her new ECG, the rhythm returned to sinus rhythm. Although her D-dimer level was elevated, anticoagulant was not restarted in order to control bleeding. After one week of conservative treatment, the symptoms relieved and the retroperitoneal hematoma decreased in size.

Case 2

A 55-year-old male patient without any additional disease was admitted to the hospital with respiratory distress. The patient, whose complaints of fever and fatigue started 5 days before applying to our hospital, RT-PCR test for COVID-19 was found to be positive in another center, and favipravir treatment was started.

Admission blood pressure (145/100 mmHg), pulse rate (106 bpm), body temperature (38.1°C) and respiratory rate (26/min) of the patient whose respiratory distress was added to his complaints were as indicated. The patient was hospitalized and transferred to the intensive care unit (ICU) because of severe respiratory distress. Laboratory data on admission were as follows: hemoglobin (13.6 g/dl [n:13-18 g/dl]), white blood cell count (6890/μL [n: 4300–10800 /μL]), platelet count (202 × 103/μL [n: 150–450× 103/μL]), ferritin (2550 μg/L [n: 23-336 μg/L]), procalcitonin (0.04 ng/mL [n: <0.5 ng/mL]), D-dimer (0.51 μg/mL [n: <0.5 μg/mL]), and CRP (6.65 μg/mL [n: 0.3-10 μg/mL). His D-dimer uptrended to 0.9 ng/mL. The patient was started on daily SC doses of 40 mg prophylactic enoxaparin treatment for concern of hypercoagulable state. On the 6th day of hospitalization, the patient started to complain of abdominal pain. There was tenderness on the right lower quadrant of the abdomen on clinical examination. Vital signs at that time (heart rate, 113 bpm; blood pressure, 74/45 mm Hg; hemoglobin, 8.9 g/dL) suggested the presence of hypovolemic shock. Noncontrast CT scans of the abdomen and pelvis demonstrated a hematoma measuring 18x8 cm all along the entire length of the right psoas muscle **(Figure 2)**.

Figure 2.A- A 55-year-old male patient; hematoma in the right retroperitoneal space was demonstrated in both abdominal and pelvic CT scans

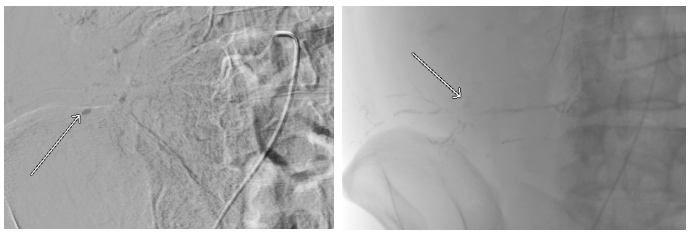

Figure 2.B- Angiography confirmed numerous sites of bleeding. Coil embolization performed achieved complete vessel obstruction and cessation of bleeding

Urgent transarterial embolization (TAE) was performed by interventional radiologists. Extravasation was identified from the right L2-L3-L4 lumbar arteries. Embolized using NBCA-lipiodol mixture. Complete embolization was achieved with no complications. After the procedure, no active contrast extravasation was observed. During his stay he received 3 units of packed red blood cells (PRBC).

Discussion

Spontaneous retroperitoneal hematoma is a well identified life-threatening condition, but its exact mechanism is not understood due to its uncommon occurrence. It is an undoubted fact that rupture of organs or vessels will cause bleeding in the retroperitoneal area without trauma or surgical intervention. Immune microangiopathy secondary to anticoagulation, intact vascular strain, and arteriosclerosis of small vessels are a few of the blamed etiologies [11]. Anticoagulation and antiplatet therapies have important roles in preventing thrombosis and thromboembolism in acute myocardial infarction, deep vein thrombosis and pulmonary embolism. Warfarin is the most commonly preferred anticoagulant agent that interferes with blood coagulation by inhibiting vitamin K epoxide reductase enzyme [3].

Due to the relationship between COVID-19 disease and thromboembolic events, anticoagulant treatment is used in all patients without contraindications in the management of hospitalized patients with COVID-19 disease in compliance with the guidelines. Spontaneous rectus sheath and retroperitoneal hematomas are rare complications of therapeutic anticoagulation and carry a mortality risk up to 20% [10]. There are few reports of these spontaneous bleeding in COVID-19 patients in the literature. With the increase use of therapeutic anticoagulation in those at high risk of thrombotic events, notifications of spontaneous bleeding cases will increase.

Asymptomatic retroperitoneal bleeding can occur. Diagnosis of this condition is mostly based on presenting symptoms and results of radiological studies [12]. Symptoms range from hip-leg pain to cardiovascular collapse and hypovolemic shock, although the Lenk triad, which includes symptoms of acute flank pain, tenderness, and internal bleeding, has been described for spontaneous retroperitoneum hematoma. Generalized weakness, headache, shortness of breath, syncope, and altered mental status are less common symptoms associated with the extent and duration of bleeding.

Therapeutic anticoagulant therapy is frequently used in patients hospitalized for COVID-19 disease, which may cause serious hemorrhagic complications. Vigilance is required in the diagnosis and management of this fatal complication. Administration of heparin at therapeutic doses may be risky in COVID-19 patients and we think that it should be administered with extreme caution. Therefore, vital signs and hemoglobin levels of these patients should be closely monitored.

The management mostly depends on the degree of bleeding and the underlying pathology. If the patient's condition is compromised or the underlying pathology is a kidney tumor, nephrectomy is recommended, but the clinical situation is much more complicated if the hematoma is associated with anticoagulant treatments [13]. It is difficult for the physician to make the decision because on one side there is a bleeding patient requiring surgical intervention, on the other hand, surgical intervention may further contribute to bleeding. In our cases, it was sufficient to remain conservative in the first case and hemodynamic stability was achieved only by transfusion. However, in the second case, TAE was required. There was no need for surgical intervention in both cases.

Thromboembolic events occurring in the course of COVID-19 increase mortality. For this reason, use of prophylactic and therapeutic doses of anticoagulant treatments has taken place in the treatment guidelines. Although rare, retroperitoneal

hemorrhages, which are complications related to this treatment, are life-threatening bleeding episodes. When a hemorrhage occurs, anticoagulation should be stopped immediately and, in case of need, it can be initiated again. In severe cases, department of interventional radiology should be consulted for TAE. These bleedings can be overlooked among many comorbidities encountered during intensive patient follow-up in the pandemic period. Therefore, anticoagulant therapy should be applied in selected cases and followed up carefully. We hope this case report will serve as a reminder of the risks inherent in anticoagulant therapy.

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References

[1] Melde SL. Enoxaparin-induced Retroperitoneal Hematoma. Ann Pharmacother 2003;37:822-4. https://doi.org/10.1345/aph.1C395.

[2] Daskalopoulos G, Karyotis I, Heretis I, Anezinis P, Mavromanolakis E, Delakas D. Spontaneous Perirenal Hemorrhage: A 10-year Experience at Our Institution. Int Urol Nephrol 2003;36:15–9. https://doi.org/10.1023/B:UROL.0000032680.65742.9a.

[3] Simsek A, Ozgor F, Yuksel B, Bastu E, Akbulut MF, Kucuktopcu O, et al. Spontaneous Retroperitoneal Hematoma Associated with Anticoagulation Therapy and Antiplatet Therapy: Two Centers Experiences. Arch Ital Urol Androl 2014;86:266-9. https://doi.org/10.4081/aiua.2014.4.266.

[4] Cattaneo M, Bertinato EM, Birocchi S, Brizio C, Malavolta D, Manzoni M, et al. Pulmonary Embolism or Pulmonary Thrombosis in COVID-19? Is the Recommendation to Use High-dose Heparin for Thromboprophylaxis Justified? Thromb Haemost 2020;120:1230-2. https://doi.org/10.1055/s-0040-1712097.

[5] Papageorgiou C, Jourdi G, Adjambri E, Walborn A, Patel P, Fareed J, et al. Disseminated Intravascular Coagulation: An Update on Pathogenesis, Diagnosis, and Therapeutic Strategies. Clin Appl Thromb Hemost 2018;24(9_suppl):8S-28S. https://doi.org/10.1177/1076029618806424.

[6] Nakamura H, Ouchi G, Miyagi K, Higure Y, Otsuki M, Nishiyama N. Case Report: Iliopsoas Hematoma During the Clinical Course of Severe COVID-19 in Two Male Patient. Am J Trop Med Hyg 2021;104:1018-21. https://doi.org/10.4269/ajtmh.20-1507.

[7] Ottewill C, Mulpeter R, Lee J, Shrestha G, O'Sullivan D, Subramaniam A, et al. Therapeutic Anti-coagulation in COVID-19 and the Potential Enhanced Risk of Retroperitoneal Haematoma. QJM 2021:hcab059 Online ahead of print. https://doi.org/10.1093/qjmed/hcab059.

[8] Javid A, Kazemi R, Dehghani M, Bahrami Samani H. Catastrophic Retroperitoneal Hemorrhage in COVID-19 Patients Under Anticoagulant Prophylaxis. Urol Case Rep 2021;36:101568 Online ahead of print. https://doi.org/10.1016/j.eucr.2021.101568.

[9] Scialpi M, Russo P, Piane E, Gallo E, Scalera GB. First Case of Retroperitoneal Hematoma in COVID-19. Turk J Urol. 2020;46:407-9. https://doi.org/10.5152/tud.2020.20302.

[10] González C, Penado S, Llata L, Valero C, Riancho JA. The Clinical Spectrum of Retroperitoneal Hematoma in Anticoagulated Patients. Medicine (Baltimore) 2003;82:257–62. https://doi.org/10.1097/01.md.0000085059.63483.36.

[11] Srinivasan V, Turner AG, Blackford HN. Massive Intraperitoneal Hemorrhage Associated with Renal Pathology. J Urol 1994;15:980-1. https://doi.org/10.1016/s0022-5347(17)35141-8.

[12] Mrug M, Mishra PV, Lusane HC, Cunningham JM, Alpert MA. Hemothorax and Retroperitoneal Hematoma After Anticoagulation with Enoxaparin. South Med J 2002;95:936-8. https://pubmed.ncbi.nlm.nih.gov/12190238/.

[13] Morgentaler A, Belville JS, Tumeh SS, Richie JP, Loughlin KR. Rational Approach to Evaluation and Management of Spontaneous Perirenal Hemorrhage. Surg Gynecol Obstet 1990;170:121-5. https://pubmed.ncbi.nlm.nih.gov/2300864/.