

Does COVID-19 increase the incidence of spontaneous rectus sheath hematoma?

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ABSTRACT

BACKGROUND: The COVID-19 pandemic started to affect Turkey in March 2020. In this study, we retrospectively investigated spontaneous rectus sheath hematoma (S-RSH) in patients with COVID-19 presenting with acute abdominal pain during the ongoing pandemic.

METHODS: The demographic characteristics, laboratory findings, length of hospital stay, and treatment processes of COVID-19 cases with S-RSH detected between March and December 2020 were recorded. The rectus sheath hematoma diagnosis of the patients was made using abdominal computed tomography, and the patients were followed up. Low-molecular-weight heparin treatment, which was initiated upon admission, was continued during the follow-up.

RESULTS: S-RSH was detected in 13 out of 220 patients with COVID-19 who were referred to general surgery for consultation due to acute abdominal pain. The mean age of these patients was 78±13 years, and the female-to-male ratio was 1.6. Mechanical ventilation support was applied to three patients, all of whom were followed up in the intensive care unit. Two patients died for reasons independent of rectus sheath hematoma during their treatment. Among the laboratory findings, the activated partial thromboplastin time (aPTT) values did not deviate from the normal range. While there was no correlation between the international normalized ratio (INR) and aPTT ($p>0.01$), a significant correlation was found between INR and interleukin-6 (IL-6) ($p<0.002$). None of the patients required surgical or endovascular interventional radiology procedures.

CONCLUSION: In the literature, the incidence of S-RSH in patients presenting with acute abdominal pain is 1.8%. However, in our series, this rate was approximately 3 times higher. Our patients' normal INR and aPTT values suggest that coagulopathy was mostly secondary to endothelial damage. In addition, the significantly higher IL-6 values ($p<0.002$) indicate the development of vasculitis along with the acute inflammatory process. S-RSH can be more commonly explained the high severity of vasculitis and endothelial damage due to viral infection.

Keywords: Coagulopathy; COVID-19; rectus sheath hematoma.

INTRODUCTION

This novel coronavirus (severe acute respiratory syndrome coronavirus 2 [SARS-CoV-2]) causing pneumonia and acute respiratory distress syndrome was reported to quickly spread from Wuhan, Hubei Province of China across the world.^[1] The World Health Organization (WHO) officially named the disease caused by this virus "COVID-19" and declared it a

global pandemic in 2020. The most common symptoms are fever, cough, tiredness, sore throat, diarrhea, headache, and loss of taste or smell. It is predicted that COVID-19 may also cause a severe inflammatory condition that results in hemostasis disorders. It is stated that this inflammation causes coagulopathy and vasculopathy associated with COVID-19.^[2,3] This coagulopathy may lead to massive thrombosis or spontaneous bleeding together with vasculopathy. Spontaneous

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bleeding manifests with separate symptoms in each anatomical region.^[4] Some of the bleeding occurs in the rectus sheath in the abdominal wall and results in hematoma.

In Turkey, the first case of COVID-19 was reported at the beginning of March 2020. A high rate of spontaneous rectus sheath hematoma (S-RSH) was observed among the patients hospitalized for the treatment of COVID-19 and referred to the general surgery clinic for consultation due to acute abdominal pain.

This case series analysis aims to investigate incidence and clinical features of S-RSH causing acute abdomen in patients hospitalized due to COVID-19. It is also our aim to determine the correlation between international normalized ratio (INR) and other laboratory values.

MATERIALS AND METHODS

Ethical approval was obtained for this study from the Ethics Committee of Ankara City Hospital (IRB Number: E1-21-1617). In addition, we received permission from the Turkish Ministry of Health Scientific Research Commission and Ethics Committee for this study (2021-03-03T19-18-41). The records were reviewed for the patients hospitalized in Ankara City Hospital due to COVID-19 infection between March 2020 and December 2020 and referred to the general surgery clinic for consultation due to acute abdominal pain.

Patients' demographic data (name, surname, age, gender, identity numbers, and registration numbers), laboratory findings (INR, activated partial thromboplastin time [aPTT], ferritin, interleukin-6 (IL-6), C-reactive protein (CRP), white blood count (WBC), and hematocrit (Hct) values), comorbidities, size of the lesions in abdominal computed tomography (CT) scans, length of hospital stay, and medical treatments were obtained from the hospital automation system and recorded. Since the effect of COVID-19 infection on S-RSH has been explored after the analyses, the prevalence of S-RSH cases with other etiological reasons described in the literature was compared with the frequency in our series.

Statistical Analysis

The statistical analysis was performed using SPSS for Windows, version 17.0 software (SPSS Inc., Chicago, IL, USA). Descriptive statistics were presented as mean and standard deviation. To identify the correlation between INR, and other laboratory variables were analyzed using the Pearson correlation coefficients, and $p < 0.01$ was considered statistically significant.

RESULTS

S-RSH was detected on the abdominal CT scans in 13 of 220 patients who were followed up for COVID-19 infection with acute abdominal pain (Fig. 1). Table 1 lists the demograph-

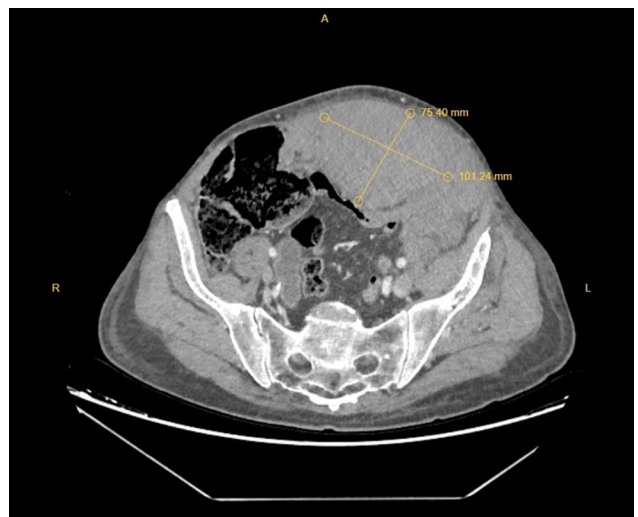


Figure 1. Axial computed tomography image of the abdomen pelvis with the diameter measurements of the left rectus sheath hematoma.

ic information and laboratory findings of the patients with S-RSH. Eight of the 13 patients with S-RSH were female, and the mean age of the all patients was 78.07 SD 13.46 (mean SD). All patients had at least one comorbidity in addition to COVID-19-related pneumonia. In addition, one patient had metastatic cervix cancer; another had metastatic breast cancer, and two patients had pulmonary tuberculosis sequelae (Table 2).

All the patients were followed up in the intensive care unit while only three patients were supported by mechanical ventilation through orotracheal intubation. One of whom received mechanical ventilation support ceased as a result of sub-instrumental bleeding and another as a result of pulmonary embolism. The mean hematoma volume was 597 mm³. Eleven patients with a mean hospital stay of 34 days were discharged after medical treatment (Table 2).

Chest CT scan performed at admission showed bilateral ground-glass opacities and sub-segmental consolidations mostly located in the peripheral zone. Other imaging features included linear opacities, crazy-paving pattern, reverse halo sign, and subsegmental vessel enlargement.

Only two of the patients were receiving anti-coagulant (Coumadin) treatment due to a cerebrovascular event and atrial fibrillation before admission. After hospitalization, the anticoagulant treatments of both patients were discontinued, and prophylactic low-molecular-weight heparin (LMWH) was initiated at the time of admission as in all the remaining cases. LMWH doses were modified according to the clinical course and diagnosis of micro- or macro-pulmonary thromboembolic incidents. LMWH treatment was continued without interruption after the diagnosis of S-RSH, and the patients received LMWH until discharge. On discharge, oral acetylsalicylic acid was prescribed and drug use was recommended for 10 days.

Table 1. Basic demographic and laboratory findings of the patients

Patient number	Age	Sex	INR (0.8–1.2)	aPTT (21–32 sec)	Ferritin (22–322 µg/L)	CRP (0–0.005 g/L)	IL-6 (0–3.4 pg/mL)	Leukocyte (3.600–10.500 /ml)	Hct (35–45.5%)	Steroid doses	Steroid time
1	82.0	M	1.14	22.9	915.0	0.1363	25.7	25.06	28.1	80 mg/d	15
2	92.0	F	1.11	38.2	252.0	0.1520	22.5	8.83	26.5	80 mg/d	18
3	83.0	F	2.37	38.1	362.0	0.0102	22.5	5.21	36.8	40 mg/d	15
4	65.0	F	1.24	30.1	222.0	0.0053	17.8	3.26	25.6	80 mg/d	40
5	67.0	F	0.88	21.0	433.0	0.0097	2.8	10.57	29.9	40 mg/d	15
6	43.0	F	1.75	32.9	1603.8	0.0596	36.3	4.49	25.6	40 mg/d	21
7	88.0	M	1.20	30.4	788.0	0.0597	18.4	4.30	32.0	80 mg/d	13
8	80.0	F	1.03	22.2	1584.6	0.1296	25.7	4.25	35.6	80 mg/d	10
9	83.0	M	1.16	23.5	707.0	0.0646	19.7	8.51	31.3	80 mg/d	17
10	80.0	M	1.46	24.2	752.0	0.1359	94.4	9.56	39.0	80 mg/d	39
11	93.0	M	1.31	33.9	848.5	0.1940	99.0	6.14	27.9	80 mg/d	13
12	74.0	F	1.30	21.0	210.0	0.0960	84.6	2.46	24.0	80 mg/d	19
13	85.0	F	3.46	37.5	257.7	0.0568	236.0	11.19	34.8	40 mg/d	14
Total											
Mean	78.0	F/M	1.49	28.915	687.3	0.0854	54.2	7986.92	30.5	69.1	19.13
Median	82.0	8/5	1.24	30.100	707.0	0.0646	25.7	6140.00	29.9	80	15
Minimum	43.0	1.6	0.88	21.0	210.0	0.0053	2.8	2.46	24.0	40	10
Maximum	93.0		3.46	38.2	1603.8	0.1940	236.0	25.06	39.0	80	40
SD	13.46		0.7010	6.7499	476.6652	0.0604	63.2	5885.57	4.81	19.7	9.46

INR: International normalized ratio; aPTT: Activated partial thromboplastin time; CRP: C-reactive protein; IL-6: İnterleukin-6; Hct: Hematocrit; F: Female; M: Male; SD: Standard deviation.

Steroid treatment was applied to all patients at varying doses according to the clinical course. While nine of the patients used 80 mg/day prednisolone IV for the periods specified in Table 1, four of them were administered 40 mg prednisolone IV for the specified periods. Except for two patients who died, the dose was halved within the duration of use and prednisolone treatment was terminated. For COVID-19 treatment, all patients were given favipiravir (2×1600 mg/day on the 1st day, followed by 2×600 mg/day for 10 days) as well as oral hydroxychloroquine (200 mg twice a day for 10 days). Prophylactic therapy was administered to all cases, and antibiotic treatment for therapeutic purposes was a prophetic therapy which was applied to all cases, and antibiotic treatment only for one patient for therapeutic purposes.

The abdominal CT images of all patients referred to the general surgery clinic due to acute abdominal pain were evaluated, and furthermore, ultrasonography was used as the first choice in all patients for diagnosis. Patients pre-diagnosed with ultrasonography were confirmed by abdominal CT. Hematoma volume was detected by abdominal CT. Renal functions were evaluated by blood tests in all patients, which proved that none of them had any impaired renal function values. No complications were reported to develop in terms of the use

of contrast material. In the case that kidney functions were not suitable for contrast agent, evaluation with color Doppler USG was taken into consideration. All patients were followed up clinically after the diagnosis of S-RSH, and LMWH treatments were not discontinued. At the time of diagnosis, the mean and median INR values of the patients were 1.49 and 1.24, respectively. The aPTT values did not deviate from the normal range (Table 1). Even though there was no correlation between INR and aPTT (p>0.01), a significant correlation was found between INR and IL-6 (p<0.002) (Table 3).

When first detected, the mean volume of rectus hematomas was 597.010 mm³ (Table 2). When they came to the emergency room, three patients diagnosed with COVID-19 were consulted with the complaints of swelling and pain in their abdomen. The other 10 patients who were diagnosed with COVID-19 and monitored in intensive care units were diagnosed between the 5th and 9th days of the infection. S-RSH onset times were consistent with the consultation timing. According to the abdominal CT findings and clinical follow-up evaluation, hematomas either did not progress or regressed; therefore, no surgical or endovascular interventional radiology procedures were needed for these patients. The patients were followed up with ultrasonography to avoid contrast

Table 2. Hematoma size, comorbidities, abdominal CT findings, LHS and outcome of the patients

Number	LHS	Hematoma size (mm)	Hematoma volume (mm ³)	Comorbidities	Outcome
1	33	100x70x120	840.000	Coronary artery disease, benign prostatic hyperplasia, primary essential tremor	Recovery
2	37	110x70x100	770.000	Atherosclerotic cardiovascular disease, atrial flutter, heart failure	Recovery
3	30	130x50x110	715.000	Diabetes mellitus, hypertension, congestive heart failure, chronic obstructive pulmonary disease, atrial fibrillation	Recovery
4	41	80x60x40	192.000	Operated breast cancer, hypertension, diabetes mellitus, history of lung tuberculosis	Mortality
5	25	200x25x80	400.000	Goiter, varicosis	Recovery
6	40	90x35x60	189.000	Metastatic cervix cancer, nephrostomy	Recovery
7	36	150x85x60	765.000	Diabetes mellitus, dementia, Alzheimer's disease, history of cerebrovascular disease	Recovery
8	26	120x95x80	912.000	Hypertension	Recovery
9	35	135x110x60	891.000	Hypertension, heart failure, hyperlipidemia	Recovery
10	39	115x50x90	575.000	Chronic obstructive pulmonary disease, history of lung tuberculosis	Mortality
11	33	65x85x100	552.500	Alzheimer's disease, coronary artery disease	Recovery
12	39	115x95x45	491.625	Operation due to subdural hematoma one month earlier, organic mental disorder, diabetes insipidus, acute thyroiditis	Recovery
13	28	65x80x90	468.000	Chronic obstructive pulmonary disease	Recovery
Mean	34		597.010		

CT: Computed tomography; LHS: Long hospital stay.

Table 3. Correlation between INR, aPTT and IL-6

	aPTT (21–32 sec)	IL-6 (0–3.4 pg/mL)
INR (0.8–1.2)		
Pearson's correlation	0.605	0.767
Sig. (2-tailed)	0.029	0.002
Number	13	13

INR: International normalized ratio; aPTT: Activated partial thromboplastin time; IL-6: Interleukin-6. P<0.01=significant.

material side effects. At the same time, control abdominal CT was not performed because the general condition of the patients did not deteriorate during the clinical follow-up and no progress was detected by ultrasonography. For these reasons, a control abdominal CT was not taken as a criterion for discharge. During the follow-up in the hospital, no acute or late complications occurred due to S-RSH. During the follow-up in the hospital, no acute or late complications such as infection, bleeding, or acute abdomen developed due to S-RSH. No infection, bleeding, and acute abdomen due to hematoma were observed, and the patients did not report any complaints even after 1 month after their discharge, and no complications related to S-RSH were detected in the con-

trol examinations. Unfortunately, two patients ceased due to the other side effects of COVID-19, one of whom had breast cancer metastasizing to brain suffered from subarachnoid hemorrhage and died. Another patient expired due to massive pulmonary embolism. No patient had a significant decrease in Hct, which is accepted as an indicator of acute bleeding.

DISCUSSION

Although there are many articles about rectus sheath hematomas that we encounter rather frequently during the pandemic, it was our intention to draw attention to the fact that it may be related to COVID-19.^[5] S-RSH is a rare cause of acute abdominal pain, and in general, the incidence of S-RSH is reported to be 1.8% in all acute cases of abdominal pain.^[6] The rectus abdominis muscles are surrounded by a fascial sheath with the right and left sides separated by the linea alba. The upper and lower epigastric arteries run along the posterior border of these muscles within the sheath along their entire course. The rupture of these arteries or muscles causes rectus sheath hematoma.^[7] Most of the studies on the etiology of rectus sheath hematomas are retrospective, in addition to trauma, many other etiological factors are listed for the development of S-RSH, which include the use of anti-coagulant drugs, paroxysmal coughing attacks, and pregnancy

as primary factors.^[8,9] The recent studies indicate that S-RSH is more common in women than in men, and especially in elderly patients.^[10-17] In our study, S-RSH was also found to be more common in elderly and female patients.

While the Fothergill's sign is an important part of the physical examination in differential diagnosis, a definitive diagnosis can be achieved using non-invasive examinations, such as CT.^[18]

The most common pathologies such as sarcoma, hematoma, and abscess can be considered in the differential diagnosis of abdominal wall masses. During or after the intravenous injection of contrast medium, the presence of mass signal characteristics, vascular pattern, and other elements (e.g., small intralesional calcifications) may help the radiologist to make an accurate diagnosis.^[10,19-22]

In our cases, abdominal CT imaging showed widespread enlargement, as well as heterogeneous density of the rectus abdominis muscle with a high-density or fluid-fluid level area for subacute hematoma. The absence of a contiguous mass with a vascular pattern led to the exclusion of hemorrhagic sarcoma. Since a standard treatment modality has not been reported in S-RSH, generally, the follow-up of the patients is recommended, and interventional or secondary surgical procedure is indicated as a treatment method if there are signs of active bleeding that disrupts the hematoma growth or hemodynamics.^[13-16] Rectus sheath hematomas rarely require surgical treatment except for the incidences in which hematoma enlarges and pain increases. In this case, ligation of the vessel causing the hematoma is required along with drainage of the hematoma, which is, however, seldomly encountered. As a primary course of action, conservative treatment and follow-up should be applied, and in some cases, embolization of the bleeding vessel with interventional procedures can be considered.

Spontaneous hematoma cases have been reported in patients with the COVID-19 pandemic.^[23-25] In the largest series conducted in Turkey on this subject, spontaneous hematoma was detected in 11 of 5484 patients hospitalized for COVID-19, and rectus sheath hematoma was found in two of them. It is seen that both patients were using anticoagulants before COVID.^[26]

We included 220 patients who were hospitalized due to COVID-19, who were consulted with only acute abdomen symptoms and abdominal pain. While the rate of S-RSH in all acute abdomen cases was 1.8%, we detected S-RSH in 13 (5.91%) of 220 patients, which is approximately 3 times higher the rate reported in the literature.^[6] However, the age and gender distribution of the patients in our series were consistent with the previous studies.^[6,13]

Another important feature of coagulopathy due to COVID-19 is endothelial damage in the pulmonary circulation and microcirculation in other vascular beds.^[2,3] Since SARS-CoV-2

directly infects the vascular endothelial cell by causing cellular damage and apoptosis, the antithrombotic activity of the lumen surface is also significantly reduced.^[27] Non-traumatic hematomas are called spontaneous. Systemic vasculitis due to COVID-19 is thought to cause bleeding and hematoma in the rectus muscle. In the treatment of systemic vasculitis, the use of steroids is preferred at the beginning of the treatment algorithm. In our cases, it is observed that the hematomas did not progress with the steroid treatment started after the rectus sheath hematoma was detected, and there was no need for any other intervention.

Regarding hematoma size, quite different figures are given in different series in the literature. While the mean hematoma size is given as 130×568 mm in some series;^[9] in some series, it is also given as an average of 20×40 mm.^[7] We measured the hematoma size by volume to determine the size and found the mean size to be quite large in COVID-19 patients (mean 597,000 mm³) more accurately.

In their autopsy series of COVID-19, researchers^[28] demonstrated the induction of endotheliitis, apoptosis, and pyroptosis following the direct viral infection of endothelial cells and widespread endothelial inflammation. In this postmortem analysis, it was striking that mononuclear cell was observed to have infiltrated into the vascular intima along the lumen of many vessels, suggesting that the virus may enter the human vascular system and cause vasculitis. In another study, researchers^[29] reported that the induction of immune complexes with COVID-19 and their accumulation in vascular walls caused a more severe inflammatory reaction and stated that IL-6 was the key marker indicating this process.

The normal values of INR and aPTT among the 13 patients in our series suggest that coagulopathy is mostly secondary to endothelial damage. In addition, the significantly higher IL-6 values ($p < 0.002$) indicate the development of vasculitis through an acute inflammatory process. Therefore, it is considered that steroid therapy used in the treatment of patients for acute inflammation without interruption of LMWH causes the regression of S-RSH.

The reason for the approximately 3 times higher S-RSH rate (5.91%) detected in our COVID-19 series referred to our clinic due to acute abdomen compared to the literature (1.8%) describing other etiological causes^[6] can be explained by the very severe vasculitis and endothelial damage due to infection.

In our series, the lack of an increase in the WBC count in viral infection, except for one case, was consistent with the literature.^[30,31] Higher ferritin and CRP values were also expected as a result of COVID-19 infection.^[32]

The shortcomings of this study are the total number of cases was low and it was single centered that although it was observed frequently during the pandemic.

Conclusion

In this study, we aimed to draw attention to the possibility that S-RSH, which is normally a rare condition, can develop at a 3 times higher rate in patients with COVID-19. S-RSH was increased, especially in elderly patients, females, and those with comorbidities. A significant positive correlation was found between INR and IL-6. Considering the risk of widespread thrombosis in patients with COVID-19, anticoagulant therapy should be continued, and the adequacy of conservative treatment is to be evaluated. Since the diffuse vasculitis as a result of acute inflammatory process is considered to increase S-RSH, steroid use may make an important contribution to the treatment of these patients.

Ethics Committee Approval: This study was approved by the Ankara City Hospital Clinical Research Ethics Committee (Date: 17.03.2020, Decision No: EI/1617/2021).

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ORJİNAL ÇALIŞMA - ÖZ

COVID-19 spontan rektus kılıf hematom insidansını artırır mı?

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AMAÇ: COVID-19 pandemisi Türkiye'yi Mart 2020'de etkilemeye başladı. Bu çalışmada, devam eden pandemi sırasında akut karın ağrısı ile başvuran COVID-19 hastalarında spontan rektus kılıf hematomunu (S-RSH) geriye dönük olarak araştırdık.

GEREÇ VE YÖNTEM: Mart–Aralık 2020 tarihleri arasında S-RSH saptanan COVID-19 olgularının demografik özellikleri, laboratuvar bulguları, hastanede kalış süreleri ve tedavi süreçleri kaydedildi. Hastaların rektus kılıf hematomu tanısı tüm batın bilgisayarlı tomografisi ile konuldu ve hastalar izleme alındı. Başvuru sırasında başlanan düşük molekül ağırlıklı heparin tedavisine izlemde de devam edildi.

BULGULAR: Akut karın ağrısı nedeniyle genel cerrahiye sevk edilen 220 COVID-19 hastasının 13'ünde S-RSH tespit edildi. Bu hastaların yaş ortalaması 78±13 yıl, kadın erkek oranı 1.6 idi. Tamamı yoğun bakımda takip edilen üç hastaya mekanik ventilasyon desteği uygulandı. İki hasta tedavileri sırasında rektus kılıf hematomundan bağımsız nedenlerle öldü. Laboratuvar bulgularından aktive parsiyel tromboplastin zamanı (aPTT) değerleri normal aralıktan sapmadı. INR ile aPTT ($p>0.01$) arasında ilişki bulunmazken, INR ile interlökin-6 (IL-6) arasında anlamlı bir ilişki bulundu ($p<0.002$). Hiçbir hastada cerrahi veya endovasküler girişimsel radyoloji prosedürü gerekmedi.

TARTIŞMA: Literatürde akut karın ağrısı ile başvuran hastalarda S-RSH insidansı %1.8'dir. Ancak bizim çalışmamızda bu oran yaklaşık üç kat daha fazlaydı. Hastalarımızın normal INR ve aPTT değerleri, koagülopatinin çoğunlukla endotel hasarına sekonder olduğunu düşündürmektedir. Ek olarak, anlamlı derecede yüksek IL-6 değerleri ($p<0.002$), akut enflamatuvar süreçle birlikte vaskülit gelişimini de göstermektedir. S-RSH, daha yaygın olarak viral enfeksiyona bağlı vaskülit ve endotel hasarının yüksek ciddiyeti ile açıklanabilir.

Anahtar sözcükler: COVID-19; koagülopati; rektus kılıfı hematomu.

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