

Spontaneous Muscle Hematoma in Patients with COVID-19: Experience of 3 Cases

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Received: 02 Mar 2021

Accepted: 22 Mar 2021

Published: 28 Mar 2021

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Keywords:

COVID-19; Spontaneous muscle hematoma

Citation:

Morovic M. Spontaneous Muscle Hematoma in Patients with COVID-19: Experience of 3 Cases. *Ann Clin Med Case Rep.* 2021; V6(8): 1-5.

1. Abstract

The overall bleeding complication rate in patients receiving anticoagulation, whether in COVID-19 or non-COVID-19 patients is low, only slightly higher in critically ill patients and those receiving a therapeutic dose of anticoagulants. Among bleeding complications, spontaneous muscle hematomas (SMH) are particularly uncommon, often overlooked or misdiagnosed.

We present three COVID-19 positive patients with significant co-morbidities, treated with low molecular weight heparin (LMWH), who, during the course of the disease, suffered a sudden abdominal pain diagnosed as SMH; two patients died.

It is our opinion that every new main symptom in COVID-19 must be urgently diagnostically differentiated, because life-threatening conditions multifactorial induced, like bleeding, could happen at any time during the course of the disease.

2. Introduction

Spontaneous muscle hematomas (SMH) are uncommon, easily overlooked but potentially life-threatening conditions, from time to time described in literature, mostly as case reports [1-3]. A few cases were also described in coronavirus disease 2019 (COVID-19) patients [4, 5]. The most common risk factor among these patients was anticoagulant (AC) treatment, followed by elderly age, trauma, muscular exertion and various co-morbidities [1-7]. Since anticoagulation is one of the mainstay in the treatment of COVID-19 patients and since at present there is no consensus

on whether to treat with prophylactic or therapeutic doses of low molecular weight heparin (LMWH), a risk of thrombotic and/or haemorrhagic events remains still high in numerous patients [8, 9]. We report our newest experience in the management of three patients with COVID-19 diagnosed as SMH.

3. Case Reports

Clinical characteristics of the three COVID-19 patients with spontaneous muscle hematoma are shown on the (Table 1).

3.1. Case 1

The first case was an 83-year old man with a history of arterial hypertension, paroxysmal atrial fibrillation on chronic anticoagulant therapy with rivaroxaban, with dual chamber pacemaker and prostatic and bladder cancer. He was presented with fever, dyspnea, fatigue, O₂ saturation decreased to 87% on room air and with crackles in the lower lung lobes bilaterally. The PCR test on severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) was positive two days prior to his admission. Blood investigations revealed a total leucocyte count of 4.1×10⁹/L (normal 3.4-9.7) with 10.3% lymphocytes, haemoglobin 109 g/L (normal 138-175), C-reactive protein (CRP) 18.1 mg/L (normal<3), procalcitonin (PCT) 0.74 ng/ml (normal <0.5), interleukin-6 (IL-6) 32.6 pg/ml (normal <7.0), fibrinogen 4.1 g/L (normal 1.8-3.5), creatinine 142 mmol/l (normal 64-104), blood urea nitrogen (BUN) 16 mmol/L (normal 2.8-8.3), D-dimer 1.75 mg/L (normal <0.5). The Chest X ray revealed an area of increased density peripheral in the middle right

lobe. The patient was treated with oxygen, dexamethasone, remdesivir, ceftriaxone and gastroprotection, observing a good clinical response and decrease of inflammatory markers; AC therapy was enoxaparin in therapeutic dose (8000 U BID). On the 10th day of hospitalization, he complained suddenly of abdominal pain. The clinical examination revealed a palpable and painful suprapubic mass. Ultrasound (US) of the abdomen showed a heterogenous mass in the lower abdomen and pelvis, with hydronephrosis on the right of grade 4. Computed tomography (CT) scan of the abdomen and pelvis showed right muscle rectus hematoma of 18×11×17cm (ApxCCxLL), without active bleeding and with compression on the bladder and right hydronephrosis (Figure 1). Control laboratory tests showed a decrease of hemoglobin to 74 g/L and a deterioration in glomerular filtration rate with creatinin 376 mmol/l. The patient became anuric with parameters of hemodynamic instability and was immediately transferred to the ICU. Despite optimal medical care and resuscitation measures, the patient died on the 10th day of hospitalization.

3.2. Case 2

The second case was an 89-year-old man with a history of arterial hypertension, dyslipidemia, coronary artery bypass grafting,

gastric ulcer and ischemic cardiomyopathy. He was presented to our department on the 14th day of mild COVID-19 symptoms (diagnosed by PCR test) after experiencing a sudden onset of shortness of breath. At admission, the patient was oriented, afebrile and severely dyspnoeic, with rate of breathing 25/min, O₂ saturation decreased to 80% on room air and he received immediately a high oxygen therapy. The blood investigations revealed a total leucocyte count of 12.5×10⁹/L, hemoglobin 165 g/L, CRP 69.6 mg/L, fibrinogen 5.5 g/L, creatinine 117 μmol/L, D-dimer 2.88mg/L. The chest X-ray revealed a non-homogenous opacification in the left upper lobe, enlarged heart silhouette with left sided pleural effusion. The patient was put briefly on a high-flow nasal cannula (HFNC) and oxygen saturation was maintained satisfactory (92% on room air). Additionally, he received dexamethasone, ceftriaxone and AC with enoxaparin in therapeutic dose (6000 U BID). On the 4th day of hospitalization, he started to complain of severe pain in the right lumbar region with the signs of local peritonism. The CT scan of the abdomen revealed multiple collections from 14 HU to 45 HU in the right retroperitoneal space, with edema of psoas, quadratus lumborum and iliopsoas muscles, which extended to the right lateral thoracic wall and around the right liver lobe (Figure 2).

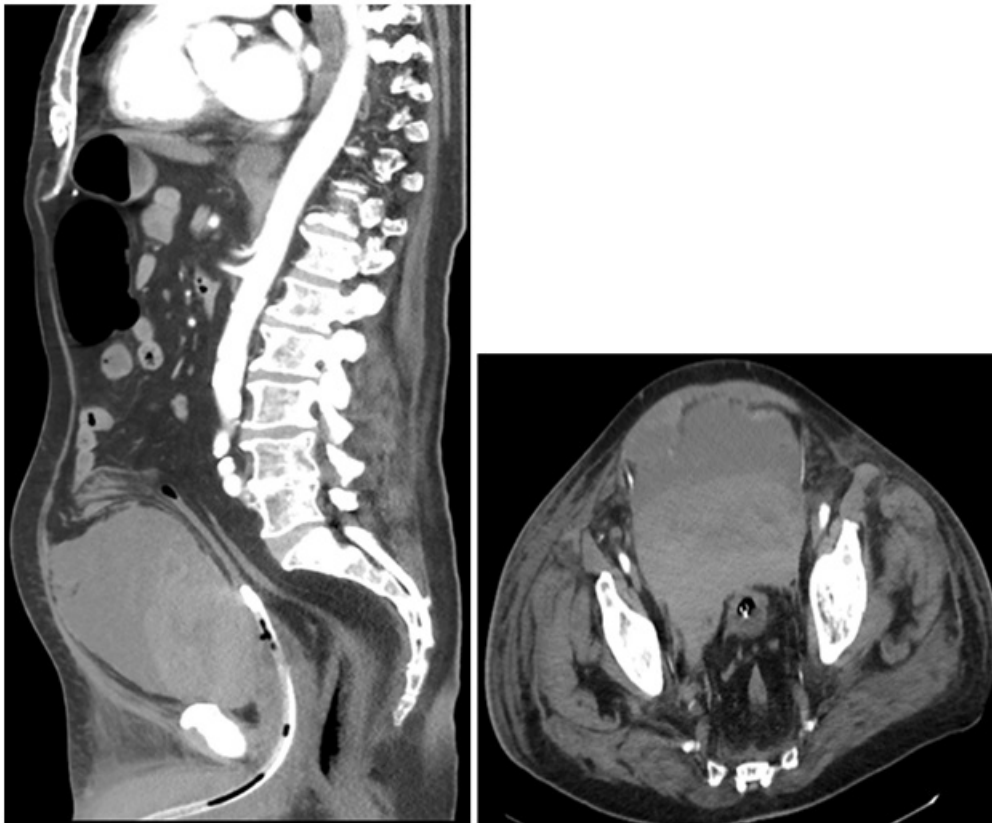


Figure 1: Abdominal CT scan, arterial phase. Large right abdominal rectus, muscle haemorrhage with hematoma in the prevesical space and extraperitoneal pelvic space. No active bleeding. A urinary catheter inserted into the bladder.

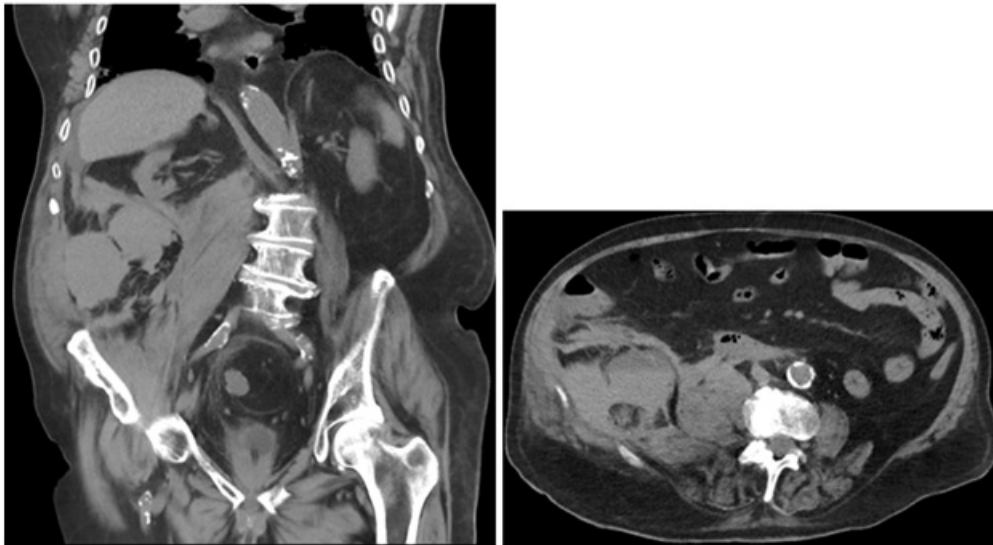


Figure 2: Large haemorrhage involving multiple right retroperitoneal compartments with haematocrit sign/effect.

Table 1: Clinical characteristics of the COVID-19 patients with spontaneous muscle hematoma

Patient No	Sex	Age	Comorbidities	-	Time (days)*	Imaging	Outcome
1	M	83	Hypertension Prostatic cancer	Therapeutic	10	US/CT	Died
2	M	89	Hypertension Ischaemic heart disease CABG	Therapeutic	4	CT	Died
3	F	53	Hypertension Renal transplant	Prophylactic	8	CT	Discharged

US, ultrasound; CT, computed tomography; CABG, coronary artery bypass graft

*Time from admission to onset of painful symptoms

The CT of the chest revealed a right pleural effusion with bilateral basal lung infiltrates. The blood tests showed a decrease of hemoglobin to 71 g/L and an increase of the total leucocyte count to $45.5 \times 10^9/L$ and creatinine to 197 mmol/L. The patient was urgently operated. Laparoscopy revealed a large blood collection in the pelvis and around the liver, which was aspirated; lumbotomy on the right showed an inflammatory retroperitoneal hematoma which was evacuated. After the operation, the patient was transferred to the ICU. He was mechanically ventilated but hemodynamically unstable and despite vasopressor and inotropic support oliguria and metabolic acidosis ensued further, the patient died on the 5th day of hospitalization.

3.3. Case 3

A 53-year-old woman with a history of arterial hypertension, hypothyreosis, chronic cystitis and a ten years earlier kidney transplantation was presented with fever and cough, but she was eupnoic. The day before admission, she was positive on SARS-CoV-2 by PCR test. The blood test showed total leukocyte count of $9.5 \times 10^9/L$ with 8.5% lymphocytes, hemoglobin 119 g/L, CRP 16.5 mg/L, IL-6 7.8 pg/ml, fibrinogen 5.7 g/L, D-dimer 0.58 mg/L. The patient was constantly febrile and the treatment with ertapenem was started plus enoxaparin in prophylactic dose (4000 U daily); other chronic therapy with everolimus, mycophenolic acid,

prednisolon, lercanidipium and levothyroxine. On the 8th day of hospitalization, she became dyspnoeic and complained of a strong abdominal pain. The CT scan of the abdomen and pelvis showed a left rectus abdominis muscle hematoma of 35 mm (Figure 3). The CT of the chest showed bilateral ground glass opacities (GGO) and peribronchial consolidations. The blood tests revealed total leucocyte count of $3.1 \times 10^9/L$, decrease of hemoglobin to 103 g/L and increase of CRP to 143 mg/L. We continued with antimicrobials cefepime and antifungal voriconazole. The abdominal surgeon did not find an indication for surgery. The patient gradually felt better and was discharged on the 20th day of hospitalization.

4. Discussion

Thrombosis is an extensive and well-studied process in COVID-19, in contrast to bleeding, probably due to its uncommon occurrence and the less severe and/or fatal consequences.

One multi-centric prospective study showed a high rate of thrombotic complications in a cohort of 150 intensive care unit (ICU) patients of 49.3% opposite to only 2.7% of haemorrhagic complications; these bleeding complications occurred under either prophylactic or therapeutic dosing of LMWH (10). Also, a large retrospective study of the association of AC with bleeding and mortality showed that among 4,389 patients with COVID-19 only 2% had major bleeding, slightly more on therapeutic dose,

3% vs 1.7% on prophylactic dose AC. The most common site of bleeding was gastrointestinal (50.7%), followed by mucocutaneous (19.4%), bronchopulmonary (14.9%), and intracranial (6%) (11). In the above cited study of coagulation in 400 COVID-19 patients, an overall bleeding rate was of 4.8%, with a rate of 5.6% in critically ill patients; in this study the overall thrombotic complication was 9.5% [8]. It is of interest to note also a large prospective multi-centric study in 3,746 critically ill non-COVID-19

patients receiving heparin thromboprophylaxis which showed that bleeding occurred also in only 5.6 %. Time-dependent predictors in this study were prolonged activated partial thromboplastin time, lower platelet count, therapeutic heparin, antiplatelet agents, renal replacement therapy and recent surgery, while the type of pharmacologic thromboprophylaxis was not associated with bleeding; patients with bleeding showed to have a higher risk of in-hospital death [12].

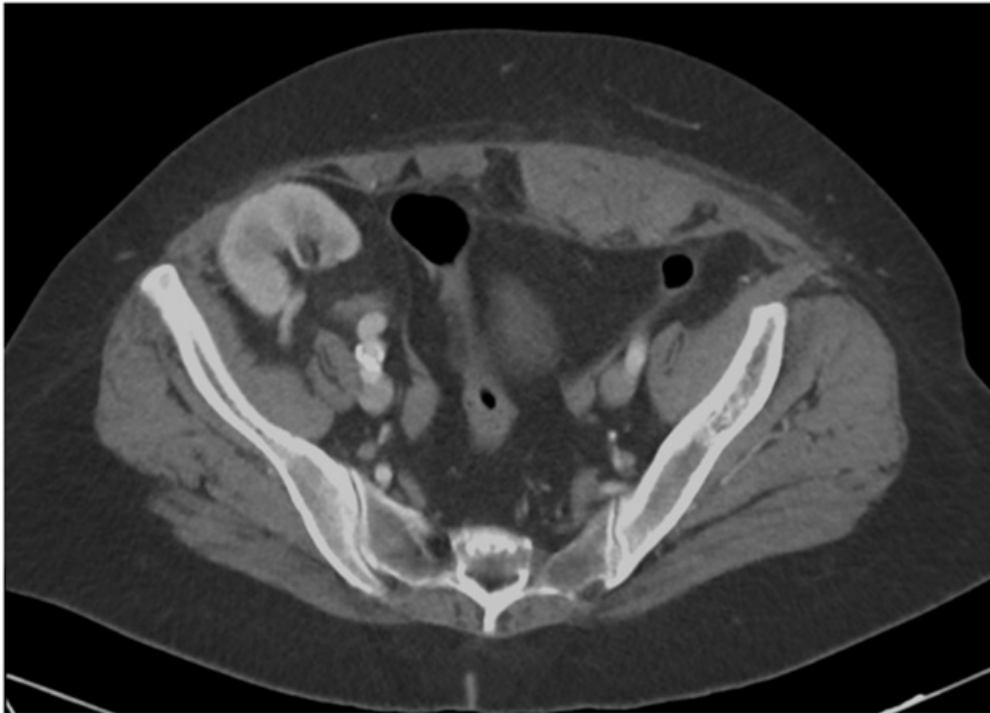


Figure 3: Abdominal CT scan, arterial phase. Left rectus abdominis muscle hematoma, confined to the abdominal wall. No active bleeding. Kidney transplant in the right iliac fossa.

In our three patients, the symptoms of bleeding episodes occurred suddenly during the hospitalization, without previously laboratory or clinical signs suggestive on the development of a haemorrhagic event; the main symptom was severe pain, abdominal and lumbar. All of them had as a main predisposing factor LMWH treatment; in addition, two elderly males had chronic cardiovascular illnesses and one of them was previously on chronic rivaroxaban treatment, while the female with a renal transplant history was on chronic immunosuppressive therapy. In all three patients, abdominal muscle hematomas were diagnosed by computed tomography (CT), in two of them the abdominal rectus muscle was affected, and in the third one the iliopsoas and psoas muscles.

The rectus abdominal muscle sheath has been recognized as the most frequent location of SMH [13, 14]; it is interesting here to mention two cases of SMH of the rectus muscle during the oral AC therapy, one on apixaban and the second on rivaroxaban [15, 16]. Iliopsoas hematoma is also an infrequent disease, with incidence ranging from 0.1% to 0.6%, which either occurred spontaneously or post traumatically but which is followed by a high mortality,

mostly related to AC therapy [17]. The clinical presentation and prognosis depend on the extension of the retroperitoneal bleeding and an urgent surgery is often necessary [18].

In our first patient, a large hematoma compressed bladder caused hydroureter which was followed by renal dysfunction and hemodynamic instability; in the second patient, the extension of muscles edema and progression of anemia indicated an operative treatment (inflamed retroperitoneal hematoma was found), which was followed by hemodynamic instability; both patients were transferred to the ICU, and, despite all conducted measures, they died. The disease course of the third patient, with a minor hematoma, vanished without further complications and finished with a good outcome. We concluded that SMH was not the cause of death in these high-risk patients, but it doubtlessly had significantly contributed to the bad outcome. In addition, COVID-19 by itself, as a disease with several mechanisms that increase the risk of bleeding, coagulation abnormalities, thrombocytopenia or platelet dysfunction and disseminated intravascular coagulation, had probably contributed to the hematoma occurrence [7, 8]. It

must be pointed out that bleeding in COVID-19, although infrequent, may occur at any time during the course of disease also in other organ systems, respiratory, central nervous, gastrointestinal and urinary [6, 19-21].

5. Conclusion

These data altogether suggest that even in conditions with low bleeding rates, like in COVID-19, clinicians should maintain a high index of suspicion of bleeding possibilities in all patients receiving anticoagulants, irrespective of the type or mode of therapy. In these cases, besides the clinical symptoms, urgent laboratory bleeding predictors and radiologic CT diagnostic could be lifesaving.

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