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Case report and literature review

Large abdominal hematoma with hemorrhagic shock in a covid-19 patient

[1,2]Daciana N. Chirila, [1,2]Calin Ionescu, [3,4]Mihaela D. Chirila, [1,2]Tudor R. Pop

[1] Clinical Municipal Hospital, Cluj-Napoca, Romania; [2] Department of Surgery, "Iuliu Haţieganu" University of Medicine and Pharmacy, Cluj-Napoca, Romania; [3] „Dr. Gavril Curteanu" Clinic Municipal Hospital, Oradea, România; [4] Department of Medical Disciplines, Faculty of Medicine and Pharmacy, University of Oradea, Romania.

Abstract. The Covid-19 virus infection was constituted into a pandemic in the last two years and it is a very serious problem worldwide, with tens of million cases and deaths all over the world. Most patients have only mild symptoms, but some patients develop severe complications within a short time after infection, such as adult respiratory syndrome (ARDS) or disseminated intravascular coagulation (DIC), the sepsis being followed by organ failure, and death. Among the leading causes of death were the cardio-respiratory problems, most of them related to procoagulation issues. Many patients with SARS-CoV-2 pneumonia developed deep vein thrombosis, even when they have been receiving antithrombotic prophylaxis. There were also cases with hemorrhagic accidents encountered all over the world, part of them necessitating surgical interventions. We present the clinical case of a man, diagnosed with covid-19 infection, which presented suddenly abdominal pain and later on a hemorrhagic shock due to rupture of a branch of an internal artery, because of an overdose of oral anticoagulation. The patient underwent surgical treatment.

Key Words: Covid-19 virus infection, coagulation problems, hemorrhagic events

Corresponding Author: C. Ionescu, email: ionescu.calin@umfcluj.ro

Introduction

The medical treatment for patients diagnosed with a Covid-19 infection comprises an anticoagulant therapy because their pneumonia was associated with a hypercoagulable and also inflammatory status. Even if the great majority of patients developed thrombotic conditions, hemorrhagic complications are also reported. We present the case of a patient already diagnosed with SARS-Cov-2 (severe acute respiratory syndrome coronavirus 2), admitted with abdominal pain, dizziness, extreme fatigue and pallor. An abdominal-pelvic CT examination with contrast revealed massive intraperitoneal hematoma due to a rupture of a branch of the left hepatic artery.

The clinical case

A 68 years old male, confirmed with Covid-19 disease 11 days earlier, was admitted in the emergency unit because of a severe form of an acute viral Covid-19 pneumopathy. The symptomatology started 18 days earlier. The patient was previously diagnosed with chronic ischemic cardiopathy, chronic atrial fibrillation, NYHA II heart failure, benign prostatic hypertrophy, chronic glomerulopathy, nephrotic syndrome, chronic renal failure. Because of atrial fibrillation the patient followed a chronic treatment with acenocoumarol.

On admission in the hospital the patient presented a hemorrhagic shock. We had a suspicion of an anticoagulant overdose, because of an INR= 4.75; blood group AII Rh+. The patient showed for 3-4 hours the signs of an acute hemorrhagic event with pallor, sweating, thirst, postural imbalance, and a light form of abdominal pain. The abdominal-perineal computed tomography (CT scan) showed Fig. 1: in front of the gastric antrum, the first and the second parts of the duodenum, a seemingly closed, inhomogeneous collection of 57/88/70 mm PA/ LL/CC (Fig. 2) showing active extravasation of the contrast substance on the acquisitions made (Fig. 3); the collection was extended to the gallbladder, was multilocular, with liquid-liquid levels inside, and with the adjacent omental fat infiltrated; there was an anatomical variant with the common hepatic artery originated in the superior mesenteric artery; the proper hepatic artery and the left hepatic artery were in contact with the described collection, and at the level of the left hepatic artery there was an active extravasation of the contrast substance (Fig. 4); it was described the existence of intraperitoneal collection in medium quantity, with paralytic densities (approx. 25 UH), visible in perihepatic, around the spleen, in the left paracolic recess, at the level of the recto-bladder space, as well as between the ileal loops (but in smaller quantity at this level); on late acquisition, extravasation of the intraperitoneal contrast product at the perihepatic level was observed; there was no pneumoperitoneum; the prostate was inhomogeneous, with millimeter calcifications of median lobe and increased transverse axis of 50mm; there were some calcified atheromatous plaques in the abdominal aorta and its emergent; bilateral inguinal hernia with fat content, 75mm diameter on the right and 43mm diameter on the left; incipient dorsal-lumbar spondylarthrosis changes.

The chest CT revealed bilateral pulmonary, alveolar infiltrates with a "matte glass" appearance, with mixed, peripheral and central distribution, accompanied by septal thickening - changes

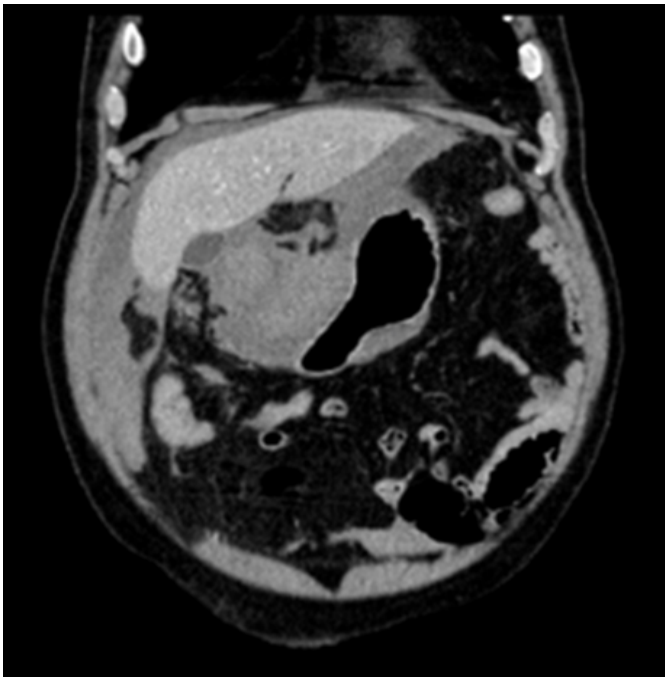

Fig. 1. Axial section in native CT scan showing a massive mass situated in front of the stomach, occupying the subhepatic region.

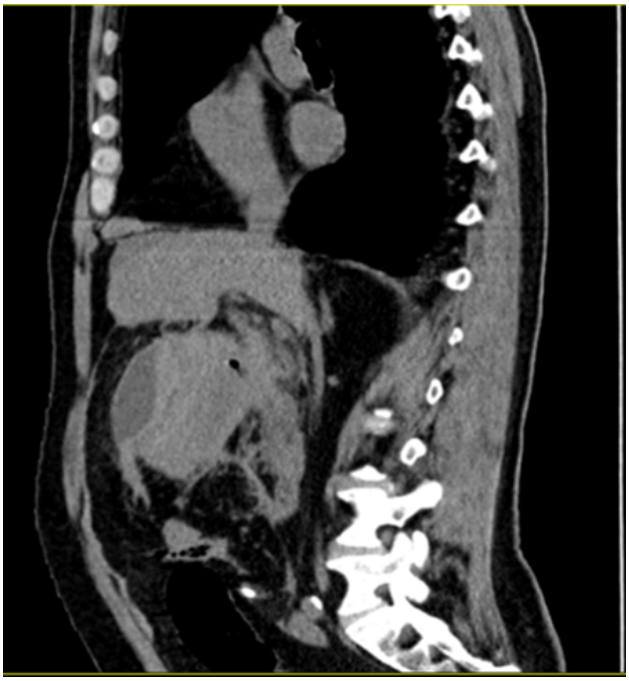

Fig. 2. A sagittal section of the CT scan reveals the hematoma which pushed back the stomach, creating a mass effect

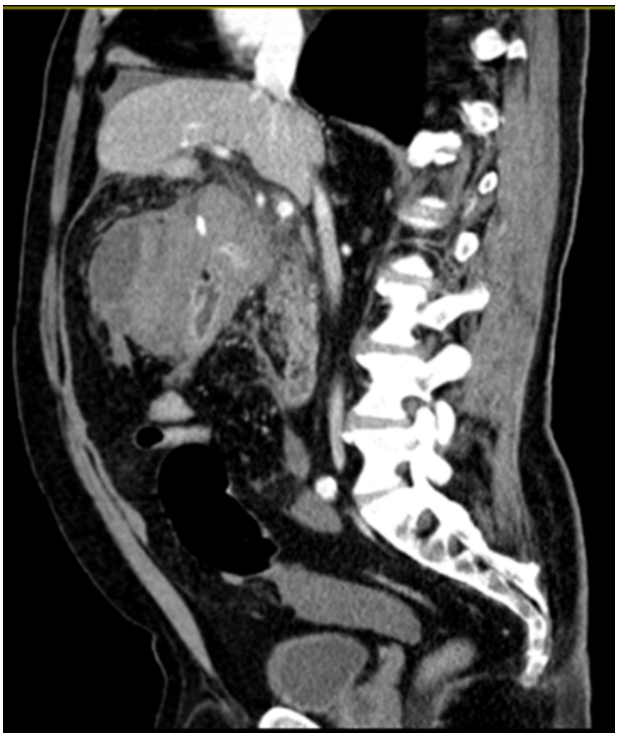

Fig. 3. Venous phase of the abdominal-pelvic CT scan.

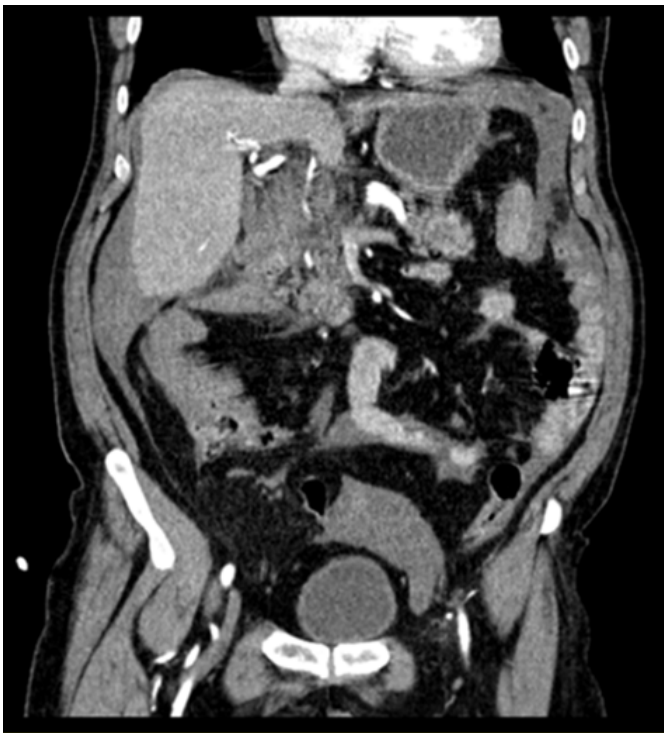

Fig. 4. The hematoma had its origin in a branch of left hepatic artery.

compatible with a pneumonia of SARS-CoV-2 etiology; the lung damage was estimated at approx.: 40-45% SRL, 40% ML, 55-60% IRL, 45% SLL and 45-50% ILL, the TSS score being 11 - being classified as severe damage; calcified lung nodules, mostly subpleural, ML, up to 7 mm in diameter (subpleural LM), with sequelae; left pleural collection in small quantity, 5mm thick; pericardial collection in small quantity, with a thickness of 10mm anterior to RV; some reactive-looking mediastinal lymph nodes; significant coronary atheromatosis.

Laboratory analyses revealed leukocytosis (19.98 *10^3/µL, NV= 4-11 *10^3/µL) with neutrophilia (87.3 %, NV= 30-75%), anemia (RBC= 3.42 10^3*10^3/µl, NV= 4.5-6 10^3*10^3/µl; Hb= 10.5 g/dl, NV= 13.5-17 g/dl; Ht= 30.4 %, NV= 40-54%), thrombocytosis (422 *10^3/µL, NV= 150-400 *10^3/µL), INR (4.75, NV= 08-1.2), fibrinogen= 740.8 mg/dl (NV= 180-450 mg/dl), Ferritin= 740.6 ng/ml (NV= 30-400 ng/ml); liver cytolysis (GPT= 129 U/l, NV= 0-45 U/l; GOT 60 U/l, NV= 0-35 U/l), alkaline phosphatase= 142 U/l (NV= 53-128 U/l); GGT= 417 U/l (NV= 0-55

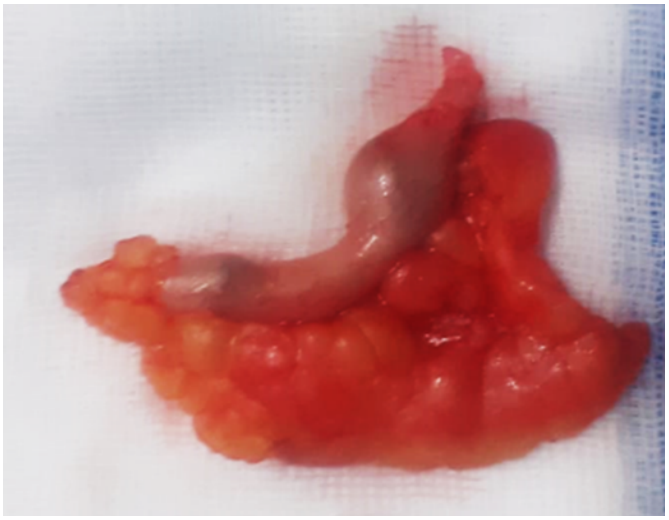

Fig. 5. The appendix with two appendicoliths inside its lumen

U/l); glycemia= 247 mg/dl; LDH= 567 U/l (NV= 0-450 U/l), hypomagnesemia.

The patient was admitted in Intensive Care Unit with a diagnosis of a hemorrhagic type of an acute surgical abdomen with hemorrhagic shock, for which the patient was quickly prepared for an emergency surgery. The emergency surgery consisted in an exploratory laparotomy through a median xipho-umbilical incision, removal of intraperitoneal clots, hematoma emptying. hemostasis of the hemorrhagic branches of the left hepatic artery. direct appendicectomy. peritoneal lavage and multiple peritoneal cavity drainage. We found dark red blood fluid in appreciable amount in the peritoneal cavity and large clots especially in the upper mesocolic floor (around the duodenum, subhepatic space, in the omental bursa, around the spleen, in the right and left parieto-colic recesses. Inside the omental bursa we did not find massive active bleeding from large arterial branches, rather oozing hemorrhage. We found also a bilateral inguinal hernia, the right one being inguinal-scrotal and the cecal appendix was about 70 mm long, and 5-6 mm in diameter, but containing two coprolites inside the lumen, one at the apex and the other at the base, the latter being large, over 1 cm in diameter. That is why we also performed a direct appendectomy (Fig. 5).

The amount of blood loss was about 2000 ml (blood collection and clots). The postoperative diagnosis was: massive hemoperitoneum through spontaneous rupturing of a branch of the left hepatic artery, vermiform appendix with obstructive coprolites inside its lumen.

In the first postoperative day the patient was conscious, cooperating, Glasgow Coma Scale (GCS) = 15, afebrile, with intermediate pupils, symmetrical, reactive to light stimulus, without neurological deficits. It presents spontaneous, efficient breathing, with O2 supplementation on the nasal cannula (4L / min), SpO2 = 96-97%, without respiratory effort, with ASTRUP oxygenation parameters that revealed a mild form of ARDS (PaO2 / FiO2 = 270) and hypocapnia, metabolic alkalosis, hypercalcemia and hyperchloremia. The patient was in chronic atrial fibrillation rhythm (110/min), with a tendency to hypertension, for which it was continued the antihypertensive treatment initiated on Intensive Care unit. The diuresis was present, without pharmacologically stimulated. The patient had a soft abdomen, mobile with respiratory movements, without pain on superficial palpation and without signs of peritoneal irritation, with clean dressings, with permeable drainage tubes with a minimal amount of sero-bloody appearance. The patient underwent hydro-electrolytic rebalancing, antibiotic, steroid anti-inflammatory, gastric protector, liver protector, antihypertensive, antitussive, eubiotic, vitamin C and analgesic therapy and also intermittent oxygen therapy through non-invasive mechanical ventilation (CPAP).

Biologically, persisted the leukocytosis with decreasing neutrophilia, lymphopenia, anemia (Hb= 8.4; Hematocrit= 25.6 %), severe inflammatory disease, fibrinogen= 1377.8 mg/dl, CRP = 266 mg/l (NV= 0-10 mg/l), NT-proBNP= 1512 pg/ml (NV= 0-125 pg/ml), troponin T-HS= 15.32 ng/l (NV= 0-14 ng/l), decreasing hepatocytolysis, total protein= 4.8 g/dl (NV= 6.4-8.3 g/dl), albumin= 28 g/l (NV= 35-52 g/l) glycemia=159 mg/dl in the second postoperative day. The 9th day after surgery the CRP was within normal values. A thoracic radiography revealed an accentuation of the bilateral interstitial lung pattern, associated with several areas of bilateral basal pulmonary veil, with a radiological covid-19 score of 6.

The patient showed a slow evolution towards improvement, and he was discharged improved in the 12th postoperative day, without fever, with normal arterial pressure and ventricular allure, with SpO_2 = 100% with 2l O2 on the nasal cannula.

The patient remained with oral anticoagulants (with INR between 2-2.50), vitamin C, Zinc, liver protector and antiH2 therapy.

The histopathology for the appendix revealed a chronic sclero-atrophic appendicitis.

Discussions

The Covid-19 infections constituted in a pandemic disease over the last two years. Many patients developed severe, average or mild type of infection. The most common problems were respiratory with development of bilateral pneumonia. Most patients have only mild symptoms, but some patients develop severe complications within a short time after infection, such as adult respiratory syndrome or disseminated intravascular coagulation, the sepsis being followed by multiple organs failure, and death (Yang et al 2020). There were described many disturbances and among them the Covid-19 infections were associated with hypercoagulation, thrombosis and inflammatory changes (Guan et al 2020). The malfunctions of the coagulation system could be associated with an uncontrolled inflammation-mediated endothelial injury, the cytokines inflammatory storm, and renin angiotensin system dysregulation (Iba et al 2019, Shi et al 2020). These patients have a hypercoagulable state with high D-dimer values (Helms et al 2020), (Breakey & Escher 2020, Tang et al 2020b). The coagulopathy in COVID-19 patients may appear because of direct viral effects, the increase in the vasoconstrictor angiotensin II, the decrease in the vasodilator angiotensin, and the sepsis-induced release of cytokines (Miesbach & Makris 2020). The thrombotic complications were encountered in 31% of the Covid-19 patients treated in ICU despite thromboprophylaxis (Klok et al 2020). The direct endothelial infection with SARS-COV-2 and the indirect damage caused by inflammation are considered to play the predominant roles in the development of COVID-19-associated coagulopathy (Iba et al 2020).

The medical treatment of hospitalized patients included an anticoagulant therapy. It was necessary to draw attention to the changes in coagulation function in COVID-19 patients on a

daily basis (Xiong et al 2020). In terms of prophylactic anticoagulation in Covid-19 patients the low molecular weight heparin (LMWH) offers a lower mortality and intubation risk compared with unfractionated heparin, and a supplementary reduction in hazard of mortality for therapeutic dosage of anticoagulants (Nadkarni et al 2020). Also, oral anticoagulant seems to be associated with better survival and lower intubation rates compared with LMWH. The incidence of venous thromboembolism in the intensive care unit of patients with severe novel coronavirus pneumonia was 25%, being related to poor prognosis. Elevated D-dimer level is a sign of excessive coagulation activation and hyperfibrinolysis. After receiving anticoagulant therapy D-dimer level can not only predict thrombosis but also monitor the effectiveness of anticoagulants (Cui et al 2020). The thrombotic disease in COVID-19 infection appear because of inflammation, hypoxia, and sometimes through pharmacotherapeutic interactions (Thachil et al 2020, Levi et al 2020, Bikdeli et al 2020). If the patients infected with Covid-19 virus do not receive thromboprophylaxis they have an increased rate of mortality, as much as 40% (Kollias et al 2020).

The cumulative incidence of arterial and venous thromboembolism was 49% in a 2020 study (Thacil et al 2020). The already known risk factors for the development of severe symptoms in COVID-19 infection patients were: an advanced age, male sex, presence of comorbidities, especially hypertension (Zhou et al 2020).

Along with the hypercoagulability phenomenon associated to COVID-19, few cases have been reported because of hemorrhagic problems in patients with SARS-CoV-2 infection. It was mentioned also a concurrent spontaneous retroperitoneal bleeding and a massive acute deep vein thrombosis at the initial presentation of COVID-19 (Erdinc & Raina 2020). Beside pneumothorax, there were cases in which it was associated a hemothorax. It is well known as a possible complication in patients with anticoagulants the appearance of large hematoma located into the muscles (Dorgalaleh 2020, Rogani et al 2020, Singh et al 2021). Hematoma developed in patients with severe cough, as we may encounter in SARS-CoV-2 infection may produce an increased abdominal pressure, which can lead to an arterial vessel rupture, as it was already described for intercostal or gastroduodenal artery (Conti et al 2020). There were reported also other hemorrhagic events, along with an increased risk of thrombosis in patients with this viral infection, because of an increased risk of bleeding. There were patients with different bleeding manifestations: petechiae, hematochezia, intracerebral hemorrhage, neck and chest spontaneous hematoma, pectoral muscle, rectus sheath hematoma due to rupture of thoracic artery or inferior epigastric arteries in patients where we could implicate a trauma (Dorgalaleh 2020). Hematomas were discovered in Covid-19 patients usually in the limbs, thoracic wall (Shiraki et al 2021), intramuscular, and in rare cases intraperitoneal. We had in our SARS-CoV-2 infection patients several ilio-psoas hematomas in patients treated with LMWH, as it was described in other papers (Vergori et al 2021, Nakamura et al 2021), and this condition could be the factor that may cause a higher mortality rate, even up to 50% (Artzner et al 2019). Some patients were old, some of them had history of multiple falls (Shiraki et al 2021). Some hematomas were treated by emergency angiographic transcatheter embolization (Nakamura et al 2021), but in some cases was necessary a laparotomy. It was and it still is very important to monitor the potential bleeding in patients under anticoagulant therapy for an atrial fibrillation and also for Covid-19 coagulopathy. Therefore, it is recommended caution and surveillance for both thrombotic and hemorrhagic complications in patients with SARS-CoV-2 infection, especially in those treated with LMWH or at a higher hemorrhagic risk (Rogani et al 2020).

In COVID-19 critically ill patients the therapeutic-intensity anticoagulation was associated with a greater risk of major bleeding compared with standard thromboprophylaxis (Halaby et al 2021). Vasculitis and small vessel thrombosis resulting in infarct laceration and hemoperitoneum could be self-limiting events (Karki et al 2020).

There were described patients with major hemorrhages, an uncommon complication of COVID-19 infection (Palumbo et al 2020, Chan et al 2020, Sottilotta et al 2021, Ito et al 2021, Reisi-Vanani et al 2021, Knefati et al 2021). The development of hematomas has several predisposing factors, such as anticoagulant therapy, advanced age, microvascular vulnerability from atherosclerosis and microtrauma, hemodialysis (Nakamura et al 2021). Other patients developed spontaneous muscle hematomas while treated with LMWH, some of them being resorbed and other treated through arterial coil embolization (Rogani et al 2020). Other cases reported consisted in spontaneous bleeding from rupture of superior thoracic artery complicated by left pectoral muscle hematoma, a rectus sheath hematoma due to both right and left inferior epigastric arteries injury, a large left thigh hematoma (Bargellini et al 2020).

The overall bleeding rate of 400 patients, among them 199 critically ill, was 4.8%, with a rate of 3.1% in noncritically ill patients and 7.6% in critically ill patients. The major bleeding (WHO grade 3-4) rate was 2.3% (Al-Samkari et al 2020).

The therapeutic anticoagulation with low molecular weight heparin (LMWH) seems to be associated with a lower mortality rate of patients with severe COVID-19 infection, but they may develop a gastro-intestinal bleeding (estimated annual risk: 4.5-8%) as a complication of systemic anticoagulation (Sanku et al 2021).

Usually, the mortality rates for patients with COVID-19 intubated for respiratory failure ranged from 25% to 80% (Zhou et al 2020, Bhatraju et al 2020, Richardson et al 2020).

In Covid-19 infected patients in some studies the most common site of bleeding was gastrointestinal (50.7%), then mucocutaneous (19.4%), bronchopulmonary (14.9%), and intracranial (6%) location. The risk of bleeding is usually greater for patients with a therapeutic anticoagulant, higher for those with LMWH compared with oral anticoagulant, and higher for unfractionated heparin compared with fraction types.

Gastro-intestinal bleeding was reported as unusual cases (Sanku et al 2021, Gulen & Satar 2020, Barrett et al 2020), usually in critically ill patients (Gulen & Satar 2020). Other gastro-intestinal manifestations encountered more often were lack of appetite (78.6%), diarrhea (34%), vomiting (3.9%), and abdominal pain (1.9%) (Sanku et al 2021). A direct mucosal injury because of viral infection may produce hemorrhage, or the bleeding may appear because of the coagulopathy (Gulen & Satar, 2020). The prothrombotic changes conduct to venous thromboembolism (Sanku et al 2021), an excess in thrombin and impaired

fibrinolysis, associated also with an increasing of hyperviscosity because of hypoxia (Tang et al 2020a). It is emphasized the necessity of limitation of the anticoagulation to an appropriate indication because of the possibility to appear significant bleeding at unusual sites in COVID-19 patients upon anticoagulation, both prophylactic and therapeutic treatment (Singh et al 2021, Sanku et al 2021).

The patient consented the use of investigations and clinical data for being published under anonymity.

Conclusions

COVID-19 patients may present not only thrombosis, but also major life-threatening bleedings, especially when we use systemic anticoagulation. Usually, the rates of major bleeding were low in patients with COVID-19 infections. Our report sustains the need of active surveillance for possible hemorrhagic complications in patients with SARS-CoV-2 infection.

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Authors

•Daciana N. Chirila, Clinical Municipal Hospital, 11 Tăbăcarilor Street, postal cod: 400139, Cluj-Napoca, Romania; Department of Surgery, University of Medicine and Pharmacy,"Iuliu Haţieganu", 8 Victor Babeş Street, postal code: 400012, Cluj-Napoca, Romania. E-mail: dacianachirila@gmail.com

•Călin Ionescu, Clinical Municipal Hospital, 11 Tăbăcarilor Street, postal cod: 400139, Cluj-Napoca, Romania; Department of Surgery, University of Medicine and Pharmacy,"Iuliu Haţieganu", 8 Victor Babeş Street, postal code: 400012, Cluj-Napoca, Romania. E-mail: ionescu.calincj2002@gmail.com

•Mihaela D. Chirila, „Dr. Gavril Curteanu" Clinic Municipal Hospital, Oradea, România; Departament of Medical Disciplines, Facultaty of Medicine and Pharmacy, University of Oradea, Romania. E-mail: cristimihachirila@yahoo.com

•Tudor R. Pop, Clinical Municipal Hospital, 11 Tăbăcarilor Street, postal cod: 400139, Cluj-Napoca, Romania; Department of Surgery, University of Medicine and Pharmacy,"Iuliu Haţieganu", 8 Victor Babeş Street, postal code: 400012, Cluj-Napoca, Romania. E-mail: poptudorradu@gmail.com

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