ORIGINAL RESEARCH

Spontaneous Hemoperitoneum in women with Coagulation Abnormalities

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ABSTRACT

Background: Spontaneous Hemoperitoneum (SH) presenting as acute abdomen is a life-threatening event that can occur in absence of trauma in patients on chronic anticoagulation or in those with inherited coagulopathies. The present study aims to describe patient characteristics, etiology, clinical course, important considerations in management and outcomes in women with acute abdomen due to SH with background coagulopathy. **Methods**: Clinical course of six non-pregnant women admitted for acute abdomen due to SH of gynaecological or unknown origin with coagulation abnormalities was retrospectively reviewed. **Results**: All six patients presented with hemodynamic collapse and coagulation dysregulation either due to chronic anticoagulants use or DIC-like picture as a sequelae of severe COVID 19 disease. Emergent surgical intervention was needed in all but one patient, who responded to conservative management. Intensive resuscitation and rapid emergency correction and reversal of coagulopathy was essential in all cases especially prior to surgery. Ovulatory or corpus luteal bleeding was identified in 2 patients and ruptured right ovarian hemorrhagic cyst was found in one, while no cause for SH could be identified in rest. Two patients died due to associated severe coronavirus disease while all others had stable post-resuscitation and post-operative course. **Conclusion**: SH secondary to coagulation abnormalities can be catastrophic. Prompt clinical and CT guided evaluation of acute abdomen should be done in those with background coagulopathy of any cause with fatal SH kept as an important differential diagnosis. Emergency reversal of anticoagulation and definitive management should be undertaken with multidisciplinary collaboration.

Keywords: Spontaneous hemoperitoneum, coagulopathy, anticoagulation, COVID 19, Corpus Luteal Bleeding

INTRODUCTION

Spontaneous Hemoperitoneum (SH) presenting as acute abdomen is an exceedingly rare but life-threatening event described as bleeding into the peritoneal cavity in the absence of trauma [1]. Heralded by the signs of acute intraperitoneal bleeding, SHrequires prompt attention to institute potentiallifesaving measures[2].

Patients on chronic anticoagulation are known to have a risk of major hemorrhage as high as 7% at one year [3], and recurrent episodes of SH have been reported in this subset of patients. In addition, SH may result from inheritedblood dyscrasias. Evolving literature on COVID-19 disease also documentshemorrhagic complications due to the associated DIC-like picture as a sequela of severe coronavirus disease.

The present paper reports the clinical courseand management of six cases of SH in women with coagulation abnormalitieswho had varied presentations and operative findings.Protocols for rapid emergency reversal of anticoagulants for emergent surgery are also discussed. To the best of our knowledge, one case discussed within the seriesdescribingcorpus luteal bleeding leading to SH in COVID-19 disease is a first in the present literature.

METHODS

Case files from the year 2019 to 2022 were retrospectively reviewed.The eligibility criterionwas SH of pelvic or unknown origin in non-pregnant women presenting with acute abdomen and associated coagulation abnormalities. The study was approved by the Institutional Human Ethics Committee (Reference Letter No.CMCH/IEC/2021/29/18). Since data was collected retrospectively, informed consent was taken from patients during follow-up visits or family members who were given the power of attorney for health care in case of demise.

CASE DESCRIPTIONS

CASE 1

A 28 year old nulligravida with prosthetic mitral valve in situ, presented to emergency in shock (BP: 80/40 mm Hg Pulse: 140 per minute), and abdominal distention. She was on oral anticoagulant (Acenocoumarol 2mg), last titrated 1 month prior. Her INR at presentation was 7 and hemoglobin was 5 gm/dL. LMP was 16 days back. An urgent CT scan revealed a massive hemoperitoneum of unknown origin (Figure 1). Suspecting ovulation-related bleeding in the background of coagulopathy, an immediate exploratory laparotomy was performed. The source of bleeding was identified to be the corpus luteum (ruptured left corpus luteal cyst) intraoperatively (Figure 2). 2.5 liters of blood was drained. She received 3 units of Packed Red Blood Cells (PRBC), 16 units of Fresh Frozen Plasma (FFP), 10 units of Single Donor Platelets (SDP). Post-operative course was uneventful. Patient was put on oral desogestrel.

Fig 1 CT showing massive heterogenous pelvic collection (marked with *) suggesting hemoperitoneum (Case 1)

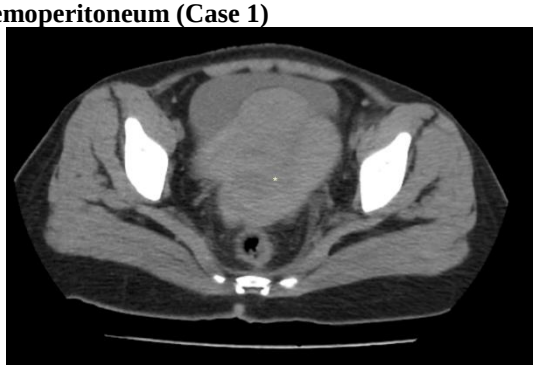
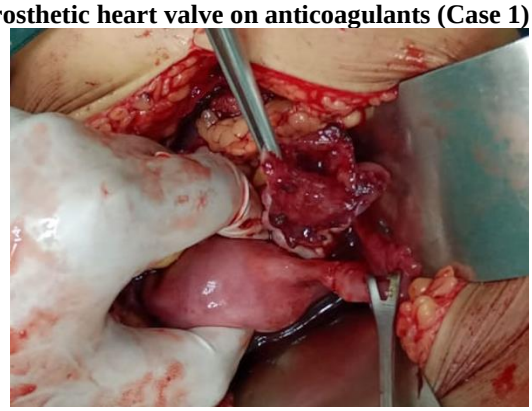


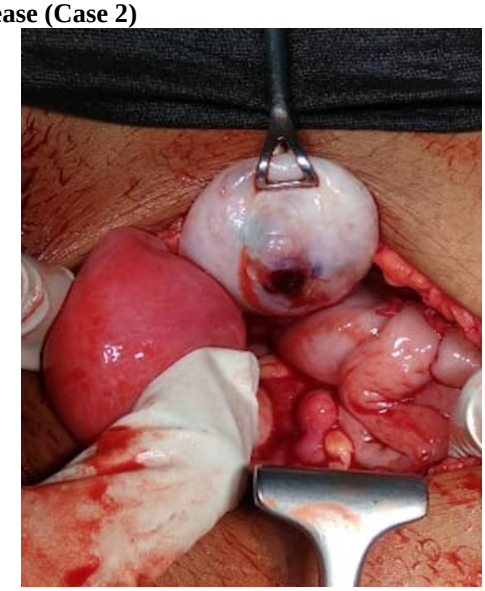
Fig2Ruptured Corpus Luteal Cyst in left ovary leading to hemoperitoneum in a patient with prosthetic heart valve on anticoagulants (Case 1)



CASE 2

A 28 years old multiparous COVID 19 positive woman with no known comorbidities was referred from a periphery hospital with severe pallor, worsening shock and gradually increasing abdominal pain and distension. She had cardiac arrest within minutes of presentation in emergency. After CPR and resuscitation, she was put on ventilatory and ionotropic support. LMP was not known. On imaging a 9*7.3*5 cm heterogenous collection was noted in the retrouterine area and moderate free fluid in the peritoneal cavity. At laparotomy, corpus luteal bleed was identified and secured (Figure 3). Immediate postoperative period was uneventful however the patient could not be weaned off the ventilator and died due to complications of COVID 19 pneumonia.

Fig3 Corpus Luteal Bleeding causing massive hemoperitoneum in the background of coagulation dysregulation in a patient with severe COVID 19 disease (Case 2)



CASE 3

A 26 years old P2L2 woman was diagnosed to have severe COVID pneumonia and thrombosis in the hepatic vein (acute Budd Chiari Syndrome) on postnatal day 2 for which LMWH had been started outside.She was referred withsevere abdominal pain and distention since 6 hours.BP was 100/60 mm Hg and Pulse 104 per minute at presentation. CT showed moderate hemoperitoneum and confirmed thrombosis in the hepatic vein. Rapid reversal of anticoagulation and emergency laparoscopic exploration was done. Intraoperatively, 1 litre of hemoperitoneum was drained butsource of intraabdominal bleeding could not be identified. Immediate perioperative reversal of anticoagulation was adequate, however, over the course of next 4 days, coagulation parameters progressively deteriorated with thrombocytopenia, PT prolongation and raised D-Dimer (>3000ng/ml), despite intensive factor concentrate support and multiple component transfusions. She further developedcomplications of severe COVID 19 pneumonia withsystemic inflammatory response syndrome (SIRS) with multiorgan dysfunction and died on postoperative day 4. Family refused autopsy.

CASE 4

A 36 years old P2L2 woman,with prosthetic mitral valveon oral Acenocoumarol 3mg OD,presented to emergency in shock (BP 86/50 mmHg & Pulse

130/minute), severe pallor and abdominal distention. Her INR at presentation was 6.71 and hemoglobin was 4.5 gm/dl. LMP was 20 days back. Imaging revealed hemoperitoneum of unknown origin. Intraoperatively 2 litres of peritoneal blood was found but source of bleeding could not be identified. She received 6 units of PRBC and 12 units of FFP. Postoperative course was uneventful.

CASE 5

26 years old woman P1L1A3 with history ofmitral valve replacement and tricuspid valve repair done 6 years back presented with shock,severe abdominal pain andvaginal bleeding. Her INR was 11.1 with Hb% 4gm/dl and normal platelet counts. Patient was on Tab. Acenocoumarol 3mgand diuretics. LMP was 5 days back. CT revealed moderate hemoperitoneum. Patient responded to conservative management with blood and component transfusion. She was discharged on desogestrel after imaging evident resolution of hemoperitoneum.

CASE 6

33 years old female P3L3 with prosthetic mitral valve on Tab. Acenocoumarol 3mg and LMP 28 days back, presentedwith palpitations, severe abdominal pain and distension since 2 days. Ultrasound was suggestive ofcomplex right ovarian cyst of about 4.8 * 3.8cm with gross hemoperitoneum. On admission patient's hemoglobin was 6.3gm/dl and INR was not recordable. Baseline pulse was 268 per minute and ECG was suggestive of PSVT with Atrial Flutter. Sinus rhythm was achieved with Amiodarone. Intraoperatively,ruptured right ovarian hemorrhagic cyst with 2 liters of hemoperitoneum was found. Right salpingo-oophorectomy was done. Patient received a total 5 PRBC and 14 FFPs. Post-operative course was uneventful.

DISCUSSION

We encountered six cases of SH in women. All presented in shock with hemodynamic collapse and coagulation abnormalities either due to anticoagulant use or DIC-like picture as a sequela of severe COVID 19 disease.Only one responded to conservative management while emergent operative interventions were needed in the rest. SH was fatal in two patients with associated severe coronavirus disease.Post-resuscitation and post-operative course was uneventful in the rest.

Spontaneous hemoperitoneum requires high degree of suspicion and immediate attention of the treating clinician, as it can prove rapidly fatal. It typically presents with signs of acute intraperitoneal bleeding, namely abdominal pain and distention, tachycardia, and hypotension with circulatory collapse in severe cases. Acute abdominal pain is a serious diagnostic and therapeutic challenge and SH should be kept as an important differential. In women, once pregnancy is ruled out, reasons for SH can range from various gynaecological causes like corpus luteal cyst rupture, bleeding from endometriotic deposits and leiomyomas etc. to other non-gynaecological causes like spontaneous rupture of pathological liver, spleen or abdominal vasculature, and coagulopathy related causes.

Finally, SH resulting from an unknown or undetectable cause, termed as Idiopathic Spontaneous Intraperitoneal Haemorrhage (ISIH) can be encountered. Apotentially fatal condition, itspre-operative diagnosis is difficult and rarely possible. Even with thorough surgical exploration source of hemorrhage cannot be localized in many cases.

Of the six cases in the present series, a definite source of bleeding could not be identified in three. In the remaining 3 cases, two hadmassive hemoperitoneum in the background of coagulation dysregulation due to corpus luteal bleed, and one had uncontrollable bleeding from ruptured hemorrhagic cyst. Normally, ovulation induces self-limiting bleeding of little consequence. In women with coagulation disorders, this may however trigger a massive bleeding episode leading to a clinical emergency.Enquiry about last menstrual period is valuable in this regard.Underlying coagulopathy prevents spontaneous resolution of bleeding after ovulation and corpus luteum may be distended with blood or form a hematoma. Continued hemorrhage increases the intraluminal pressure, leading to rupture and intraperitoneal bleeding. Women with a bleeding diathesis like von Willebrand's disease (VWD), haemophilia A and B, afibrinogenaemia, sitosterolaemia and factor VII, X, and XIII deficiency, and those on chronic anticoagulants are at greater risk of significant life threatening hemorrhage and recurrent rupture [4-7].

A large series by Wen-Kuang Ho et al. characterisedprofile of patients with corpus luteum hemorrhage.In their study, incidence ranged throughout the child-bearing years, with a propensity to occur in younger ages. Presentation wasduring the secretory phase of the menstrual cycle with sharp and sudden-onset pain more often on the right sideand history of recentsexual intercourse or strenuous physical activity[8]. As rupture may occur with any ovulatory cycle, thelifetime risk of recurrence in predisposed women may be considerable [4]. Ovulation suppression with progestin-only-based preparations, including depomedroxyprogesterone acetate (DMPA) and desogestrel, is an effective way to prevent recurrence. Due to inherent risk of thromboembolism with estrogen-containing preparations, use of combined oral contraceptives is not recommended in patients on anticoagulants and in those with prosthetic heart valves.

Two women in our series with associated COVID 19 infection had unsteady clinical course and died from the complications of severe systemic COVID 19 disease. Corpus luteal bleeding was identified in one while no specific cause of hemoperitoneum could be

determined in the other. Vasculitisand coagulopathy due to severe COVID 19 disease combined with hypercoagulable state of pregnancy likely resulted in thrombus formation and visceral (hepatic) infarction which consequently led to DIC and hemoperitoneum in the latter.Table 1 summarizes literature on the clinical outcomes of spontaneous intraperitoneal hemorrhagic episodes in patients with COVID 19presenting with acute abdomen.

Table 1: Clinical outcomes of spontaneous hemoperitoneum reported in patients with COVID 19 disease presenting with acute abdomen.

Authors	Patient's Age/Sex	Presentation	Imaging/Operative findings	Associated condition	Treatment	Outcome
Reisi-Vanani V et al. [9] (2021)	64/F	Symptomatic COVID at presentation; developed features of intraabdominal bleeding and associated worsening of vitals after overcoming respiratory phase		COVID 19 SARI on Enoxaparin, Aspirin	Supportive Management	Death
	65/F			COVID 19 SARI on Enoxaparin	Operative intervention (Laparotomy)	Death
	59/M			COVID 19 SARI on Enoxaparin and Warfarin	Resuscitative measures	Death
	80/M			COVID 19 SARI on Enoxaparin Aspirin and Atorvastatin		Death
Koubaissi S. et al. [10] (2021)	57/F	Symptomatic COVID at presentation; developed Hemorrhagic shock six days after starting anticoagulation	Rectus abdominus and retroperitoneal hematomas with multiple actively bleeding arteries.	COVID 19 Pneumonia on enoxaparin	Arterial Embolization	Stabilization
Karki S et al. [11] (2020)	35/M	Abdominal pain and fever	Splenic infarct with hemoperitoneum	COVID 19 SARI on LMWH	Supportive Management	Resolution on Day 7 of admission
Botezatu C. et al. [12] (2020)	77/F	Acute abdomen, Hypotension on vasopressor support	Rectus abdominus hematoma and hemoperitoneum	COVID 19 SARI on LMWH	Operative intervention (Laparotomy)	Death
Conti CB et al. [13] (2020)	72/F	Severe COVID symptoms followed by acute abdomen and hemorrhagic shock on Day 10	Pelvic blood collection (size:16×10 cm) not dissociable from the right ileo-psoas muscle	COVID 19 SARI on LMWH & venous femoral thrombosis	Arterial Embolization	Stabilization
	76/M	Severe COVID symptoms followed by acute abdomen and hemorrhagic shock on Day 7	Pelvic blood collection anterior to the left ileo-psoas muscle (size. 9×13 cm)		Arterial Embolization	Transferred to another hospital for second embolization

Studies on COVID 19 suggest activation of a distinct coagulation disorder with dynamic fluctuations in coagulation and fibrinolysis which may lead to simultaneous thromboembolic and haemorrhagic events.Proinflammatory state associated with the severe disease may induce a cytokine storm which leads to SIRS. Subsequently, endothelial damage in response to systemic vasculitis may result in vascular

leakage, thrombosis, hyperinflammation, and dysregulated vascular responses. Inappropriate activation of coagulation may lead to DIC. Anticoagulation therapy, initiated in the severe forms of the infection, further increases the risk of development of a hemorrhagic complication [14-16].

CT plays a crucial role in the diagnosis. It can localisethe source of bleeding to a specific organ, detect active hemorrhage with contrast, and provide information on time elapsed since hemorrhagic episode. A so-called hematocrit sign may be seen on CT wherein the cellular elements appear to settle down in the dependent portion of a hematoma creating a fluid level in images.This is a highly sensitive (87%) and specific sign for coagulopathic hemorrhage. In patients with normal coagulation, heterogeneous appearance of clotted blood can be distinctly appreciated [17].

Emergency reversal of anticoagulation is a critical clinical step to control coagulopathic bleeding especially when surgical intervention is indicated. Use of Vitamin K and four-factor prothrombin complex concentrate (4F-PCC) containingcoagulation factors II, VII, IX and X and endogenous inhibitor proteins C and S, is recommended for reversal in patients on Vitamin K antagonists with any major bleeding or bleeding that requires intervention [18].FFPcan also be used in resource restricted settings. For LMWH,the recommended protocol is1 mg of protamine sulfate per 1mg of LMWH up to a maximum single dose of 50 mg if LMWH was given within 8 hours and afurther second dose of 0.5 mg protamine sulfate per 1 mg units if bleeding continues. Smaller titrated doses of protamine sulfate can be given if LMWH was last administeredmore than 8 hours prior [19].In our series, all patients received FFP (10 to 20 ml/kg)and 10 mg Vitamin Kslow intravenous administration (in 25 to 50 mL normal saline over 15 to 30minutes) for reversal of anticoagulation with adequate perioperative response.

Expectant management of SHcan be undertaken carefully selected patients. Mean arterial pressure,periodic complete blood panels including hematocrit and INR, and surrogate markers for organ perfusion like urine output, serum lactate levels etc. need strict monitoring. A hemoglobin drop of ≥ 2g/dL or requiring transfusion of ≥2 units of RBCs should prompt urgent re-evaluation and intervention [20].

CONCLUSION

The present series highlights significant morbidity and possible catastrophic outcomes in patients with SH secondary to coagulation abnormalities. Prompt evaluation of any acute abdomen especially in those on anticoagulants should be done with fatal SH kept as an important differential diagnosis. CT can detect hemoperitoneum, active extravasation andunderlying cause in many cases. Emergency reversal of anticoagulation and definitive managementshould be undertaken with multidisciplinary collaboration.

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