

## Refractory Disseminated Intravascular Coagulation Following Ovarian Torsion and Rupture in a Pregnant Patient

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### Abstract

This report describes a case of a 36 year old pregnant woman presenting at 33 weeks' gestation with torsion and rupture of a malignant ovarian tumour. She undergoes an emergency laparotomy, Caesarean section and oophorectomy following which develops severe Disseminated Intravascular Coagulation (DIC) develops. Persistent blood loss warranted multiple surgical explorations, as well as, blood and blood product transfusions in excess of 100 units. Additional complications that arose included hyperkalaemia and VF cardiac arrest. The clinician should be alerted to the possibility of a deleterious coagulopathy which may be seen following a malignant ovarian tumour rupture and torsion.

**Keywords:** ovarian cancer, tumour, rupture, pregnancy, Disseminated Intravascular Coagulation, haemorrhage

**Abbreviations:** DIC- Disseminated Intravascular Coagulation, DVT - Deep vein thromboses, IABP -Invasive Arterial Blood Pressure, FFP - Fresh Frozen Plasma

### Case report

A 36 year old multiparous woman presented to the Labour Ward at 33 weeks' gestation with lower abdominal pain. She had mild asthma and her obstetric history included 2 previous normal vaginal deliveries.

At 16 weeks' gestation she was found during antenatal scanning to have a right ovarian cystic lesion measuring 59x34x50mm. This was monitored and a repeat scan at 25 weeks' showed it had increased in size to 73x55x47mm.

At 32 weeks' she was diagnosed with a DVT and was commenced on therapeutic enoxaparin (stopped two days before current presentation). (D-Dimer > 4000micrograms/L). An inferior vena cava filter was inserted. The patient declined any surgical intervention of the cystic lesion during pregnancy and an early elective Caesarean Section with surgical management of the cyst at 34 weeks' gestation was planned. She had no symptoms or signs suggestive of a PE and was not formally investigated for one prior her current presentation.

On this presentation at 33 weeks' gestation, her pain suddenly worsened with associated hypotension and evidence of foetal distress and so an emergency exploratory laparotomy was performed.

Admission haematology results: haemoglobin 10g/dL, platelets  $158 \times 10^9$  /L, INR 1.0, APTT 28.4 seconds, APTT ratio 1, fibrinogen 3g/L.

She underwent a rapid sequence induction in the supine wedged position using thiopentone and suxamethonium. She was a Grade 1 intubation and anaesthesia was maintained with oxygen/nitrous oxide/sevoflurane and muscle relaxation was

achieved with atracurium. A ruptured, torqued right ovarian mass containing an estimated one litre of altered blood was noted. At Caesarean section a live male infant was delivered. A right oophorectomy was then performed. The infant was subsequently intubated and transferred to the Neonatal Intensive Care Unit.

Oxytocin 5IU followed by a 40IU infusion over 4 hours was administered following delivery of the baby. Effective haemostats was achieved, the uterus appeared well-contracted and the patient's abdomen was closed. Surgical blood loss was estimated as 600mls (excluding blood within the ovarian mass).

Thirty minutes following completion of surgery the patient, fresh blood was noted vaginally. A HemoCue\* reading was taken as 5.9g/dL. Four units of blood and two units of FFP were transfused whilst a second laparotomy was performed. Fresh blood was noted intra-abdominally and the uterus was markedly atonic. Ergometrine 500mcg and carboprost trimethamine 250mcg were administered intramuscularly, as well as, misoprostol 800mg vaginally. A hysterectomy was performed due to the rate of bleeding and the evident haemodynamic instability.

Coagulation studies: platelets  $27 \times 10^9$ /L, INR 1.4, APTT 101.8 seconds, APTT ratio 3.6 and fibrinogen 1g/L.

A further 4 units of blood, 4 units of FFP, 1 pool of platelets and 2 units of cryoprecipitate were transfused. Factor VII was also administered on advice from the Haematologist.

An internal jugular central venous catheter was inserted and a noradrenaline infusion started. Initial attempts to insert an arterial cannula were unsuccessful as peripheral pulses were difficult to palpate. Venous blood gas readings revealed hyperkalaemia (K+ 6.4mmol/L) which was treated with sodium

bicarbonate, 10mls 10% calcium chloride and a continuous 50% dextrose and insulin infusion. Her abdomen was packed and percutaneous drains were inserted. Anaesthesia, close monitoring and resuscitation continued.

Ongoing output from drains prompted a third exploration after an hour. There was generalised oozing particularly around the bed of the resected ovary in the pouch of Douglas.

Coagulation profile: platelets  $50 \times 10^9/L$ , INR 1.4, APTT 89.6 seconds, APTT ratio 3.1 seconds, fibrinogen 1.4g/dL.

A further 10 units of blood, 3 pools of platelets, 5 units of FFP and 3 units of cryoprecipitate were transfused. Sequential coagulation profiles and thromboelastography were used to guide transfusion.

During this exploration, ECG revealed a broad complex tachycardia with no palpable pulse confirming cardiac arrest likely secondary to hypovolaemia and/or hyperkalaemia. Return of spontaneous circulation was achieved after 3 cycles of continuous cardiac massage, 4 direct current shocks and adrenaline 1mg.

A femoral artery cut-down was performed and arterial cannula was inserted by a general surgeon. IABP monitoring commenced.

A fourth exploration was carried out around two hours later for ongoing blood loss. Again only generalised oozing was noted particularly from the oophrectomy site. Her abdomen was re-packed.

Coagulation profile: haemoglobin 7.4g/dL, INR 1.2, APTT 48.9 seconds, APTT ratio 1.7, fibrinogen 1.9g/dL, platelets  $94 \times 10^9/L$ .

She was transferred to the ICU eight hours from the start of the primary operation. Estimated total blood loss was 13,200mls. Transfusions continued and her abdomen was closed two days later. She received haemofiltration therapy for acute kidney injury. She recovered to her pre-morbid level with no neurological deficit before being discharged with her baby a few weeks later. In total, she was transfused 64 units of blood, 35 units of FFP, 10 pools of platelets and 11 units of cryoprecipitate. Histology of the ovarian mass revealed high grade clear cell carcinoma for which she received chemotherapy but unfortunately she died two years later.

## Discussion

The association between cancer and thromboembolism has been well established for many decades.<sup>1</sup> Ovarian cancer patients have one of the highest incidences of VTE amongst cancer patients, particularly clear cell carcinoma (CCC). One study found the incidence of thromboembolic complications to be

significantly higher in CCC when compared with other epithelial types of ovarian cancer (27.3% vs 6.8%).<sup>2</sup>

The pathological mechanism behind the hypercoagulable state induced in ovarian cancer patients appears to be largely multifaceted. A variety of procoagulant substances may be involved. Of particular interest is tissue factor (TF), a potent procoagulant found in endothelial and blood cells, as well as, in tumour cells. TF may play an important role in this hypercoagulable state through activation of the coagulation cascade.<sup>3</sup> TF is frequently over-expressed in ovarian cancer tissue and there is research suggesting it influences tumour progression.<sup>3,4</sup>

A hyperviscosity syndrome may also be seen in association with ovarian cancer which favours thrombosis and may accelerate tumour progression and metastasis. DVT is a recognised complicating factor of ovarian cancer which may adversely affect the course of the disease possibly as a component of this hyperviscosity syndrome.<sup>5,6</sup> Ovarian cancer patients are also vulnerable to developing cerebrovascular complications and carry a higher risk of developing ischaemic strokes which has a significant impact on morbidity and mortality.<sup>7</sup>

The hypercoagulable state seen in cancer patients can have a spectrum of manifestations that ranges from DIC to massive thromboembolism. DIC in these instances is usually chronic and subclinical.<sup>8</sup>

The degree of coagulopathy which was seen in this case could not be attributed solely to dilutional effects incurred through fluid resuscitation. Instead we propose the acute severe coagulopathy was a consequence of procoagulant factors inherent to neoplastic tissue, including TF, which were suddenly released into the circulation following rupture and surgery to the ovarian tumour. The overall result would be widespread activation of the clotting cascade and a consumptive coagulopathy.

This case aims to increase awareness of a refractory coagulopathy which may be seen following rupture and/or surgical resection of a malignant ovarian tumour. The presence of an ovarian cyst especially in conjunction with evidence of vascular thrombosis in pregnancy should raise suspicion for an ovarian malignancy and hence vigilance for this potential complication. Anticipation of such a severe coagulopathy and associated significant blood loss should pre-empt early establishment of invasive monitoring, ample intravenous access and ensuring quick access to blood and blood products. Bedside coagulation tests such as thromboelastography are useful guides to blood product transfusion.<sup>9</sup> Prompt mobilisation of resources, multi-disciplinary input and effective team work were crucial factors which facilitated the management of this case.

Acute, severe DIC associated with ovarian intratumoural bleed which resolves following resection of the tumour has been

reported previously.<sup>10</sup> This is the first case to the best of our knowledge occurring following ovarian cancer torsion and rupture during pregnancy.

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**Competing Interests**

None declared

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