CASE REPORT

Septic miscarriage with toxic shock syndrome and disseminated intravascular coagulation (DIC): The role of surgery, recombinant activated factor VII and intravenous immunoglobulin (IVIG)

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SUMMARY

Severe sepsis with multi-organ failure is associated with a high mortality rate. This case report highlights the challenges and modalities available in the management of a lady with refractory shock and disseminated intravascular coagulation (DIC) due to toxic shock syndrome (TSS) from genital tract sepsis. Early surgical intervention to remove the source of infection, the use of recombinant activated factor VII to treat intractable disseminated intravascular coagulation and intravenous immunoglobulin to neutralise the circulating exotoxins, have been employed and shown to drastically improve outcomes.

CASE REPORT

A 41-year-old Gravida 7 Para 6 at six weeks gestation, was admitted with sudden onset of lower abdominal pain, vomiting and vaginal bleeding for one day. Examination showed compensated shock, which rapidly became decompensated with blood pressure (BP) of 81/46 mmHg, tachycardia and fever at presentation. Vaginal examination revealed offensive vaginal discharge with products of conception (POC) seen. Bedside pelvic scan showed a thickened endometrium. Serial investigation results are summarised in Table I.

Intravenous broad-spectrum antibiotics (Ceftriaxone and Metronidazole) and fluid resuscitation were administered. Despite inotropic infusion, she continued to deteriorate with worsening hypotension and profuse per vaginal bleeding. Suction and curettage (S&C) was done under general anaesthesia with transfusion of packed cells, fresh frozen plasma and cryoprecipitate. Despite a platelet count of 38 X 10*[3]/uL, no platelet transfusion was given as there was none available in the blood bank in the hospital, which is a district specialist hospital. The nearest blood bank was three hours away.

S&C was complicated with massive haemorrhage unresponsive to uterotonics and mechanical measures including bimanual compression. Decision was made for hysterectomy for persistent bleeding and haemodynamic instability. The total blood loss at completion of surgery was 1.9 litres. Towards the end of surgery, she developed severe hypotension with systolic BP of 40-70 mmHg and diastolic BP of 18-30 mmHg despite high doses of inotropes and arterial blood gases showed severe decompensated metabolic acidosis. Antibiotics were escalated to Imipenem due to worsening septicaemic shock.

Post operatively she had persistent high-grade fever more than 40^{o}C and required high doses of inotropic support. At 24 hours post-operation, she developed supraventricular tachycardia, which failed to respond to medical treatment and synchronized cardioversion. She remained tachycardic until her sepsis improved. The gram stain for product of conception showed gram positive cocci in clusters, which was suggestive of Staphylococcus spp. She was started on intravenous Clindamycin to cover for Methicillin-resistant Staphylococcus aureus (MRSA) infection.

At 33 hours post-surgery, despite transfusion of blood products including platelets, she had refractory DIC and bled 1.2 litres from subcutaneous abdominal drains. Haemoglobin levels dropped from 11.8g/dL to 5.6g/dL with deranged coagulation profile. After ensuring the pre-requisites for administration of NovoSevenRT were met, she was given a weight-adjusted dose of NovoSevenRT.[1] Bleeding from both drains stopped within 30 minutes of administration of NovoSevenRT.

In view of refractory shock secondary to TSS, infusion of intravenous immunoglobulin (IVIG) was given at 0.5g/kg. During the first 2 hours of IVIG infusion, doses of inotropes were successfully weaned down and fever began to subside, which was evidence of marked clinical improvement. After another dose of IVIG (0.5g/kg) 24 hours later, she was afebrile, did not require any inotropic support and was extubated on Day 4 of admission. Pharmacological thromboprophylaxis was started when the platelet count was more than 100X10^{3}/uL. Unfortunately, she developed peripheral gangrene in all four limbs due to the prior use of inotropes, which required elective amputation of her right hand, left fingers and toes. She was discharged home on Day 35 and was ambulating independently.

This article was accepted: 14 August 2017
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Table I: Investigation results

	Day 1	Day 2	Day 3	Day 4	Day 5
Haemoglobin (g/dl)	10.8	5.6	10.8	10.4	
White cell count (X 10^3/uL)	10	22.5	28.5	19	
Platelet (X 10^3/uL)	38	70	32	33	
International normalised ratio	1.71	2.08	1.35		
Creatinine (µmol/L)	257	410	542	358	
Aspartate aminotransferase (U/L)	163	1485	1245	246	
Alanine aminotransferase (U/L)	65	543	570	156	
Albumin (g/L)	23	16	22	22	
Blood culture and sensitivity					No growth
POC Gram stain		Gm +ve cocci			
POC culture and sensitivity					No growth
Urine pregnancy test	Positive				

DISCUSSION

TSS is associated with multi-organ failure and a high mortality rate. The toxins released by bacteria act as superantigens, which stimulate the massive systemic production of cytokines, leading to shock. Apart from instituting life-saving measures as outlined in the surviving sepsis campaign, one of the principle treatments of intra-abdominal sepsis is the removal of the source of sepsis and thus reducing the level of cytokines.

In this case, the diagnosis of staphylococcal toxic shock syndrome was supported by the positive gram stain and presence of clinical disease as defined by all of the following: fever ≥39.9°C, rashes, desquamation, hypotension and multisystem involvement. Despite pre-operative thrombocytopenia, removal of the source of sepsis through hysterectomy was performed in view of worsening shock even with optimal medical therapy. Expedient correction of coagulopathy ameliorated difficulties in achieving haemostasis.

Even though her condition stabilised temporarily post-surgery, she deteriorated further, prompting the use of other less conventional treatments including NovoSevenRT and IVIG. NovoSevenRT is licensed for use in patients with haemophilia, congenital factor VII deficiency and Glanzmann's thrombasthenia. However, it has been used successfully in managing massive post-partum haemorrhage in the recent decade. Data available suggests that NovoSevenRT also has a potential role in DIC refractory to conventional therapy, which was also demonstrated in our case.[2,3]

IVIG works by neutralising superantigens and its role in TSS has been demonstrated in several case series and a case-controlled study.[4] It has been shown to drastically improve patients with refractory shock secondary to TSS but is contraindicated in those with congenital deficiency of Immunoglobulin A. The use of IVIG and the subsequent rapid weaning of inotropes may have prevented the woman from losing all her four limbs due to peripheral gangrene from inotrope use.[5]

CONCLUSION

Expeditious diagnosis of TSS and timely intervention to halt the disease progression may significantly reduce the mortality rate and morbidity for survivors. Until more evidence regarding the use of recombinant activated factor VII and IVIG is available, the use of these treatments should be considered in patients with refractory shock and DIC when all other methods have failed.

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