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Case Report

Waterhouse Friderichsen Syndrome in a Case of Staphylococcal Toxic Shock Syndrome

Devdeep Mukherjee*, Prabhas Prasun Giri, Suman Poddar*****

*Senior resident, **Assistant Professor, Department of Pediatrics, ***Assistant Professor, Department of Microbiology, Institute of Child Health, Kolkata

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ABSTRACT

Staphylococcal toxic shock syndrome (TSS) is a rare and potentially fatal multi system dysfunction. The syndrome occurs primarily due to TSS Toxin-1 (TSS-1) liberated by Staphylococcus aureus (SA). Fever with rash followed by multi organ dysfunction in the form of acute kidney injury, raised liver transaminases and refractory hypotension indicates the possible diagnosis of a TSS, more commonly by Staphylococcus. Here, a 7 year old boy presented with all the features of toxic shock syndrome, developed hyponatremia, hyperkalemia, refractory hypoglycaemia and hypotension and succumbed within 12 hours of admission and ultimately was diagnosed to be a case of Staphylococcal toxic shock syndrome due to MSSA with Waterhouse Friderichsen Syndrome (WFS).

Keywords: Methicillin sensitive Staphylococcus aureus (MSSA), Toxic Shock Syndrome (TSS), Waterhouse Friderichsen Syndrome (WFS).

Introduction

WFS, also called as hemorrhagic adrenalitis, usually occurs following fulminant meningococcal sepsis. However there are reports of this occurring following severe infection with haemolytic Streptococci, Pneumococci, Mycobacterium tuberculosis, Escherichia coli[1] and Hemophilus influenza[2]. WFS characterised by fever, rash, coagulopathy, rapidly spreading petechial rash, refractory hypotension and adrenal haemorrhage, occurring following infection with Methicillin sensitive Staphylococcus aureus (MSSA) is extremely rare. Here we report a 7 years male child with WFS following infection with MSSA.

Case Report

7 years male child was admitted at night (3 A.M) with a history of high grade fever and vomiting for 4 days (max 103 F) with a generalised erythematous macular rash from day 3 of fever. He was initially treated with paracetamol and oral antibiotics prior to admission.

On admission, he was febrile (103.4 F) with petechiae around ankle of both feet. Child had a Glasgow coma score 12/15. Kernigs and Brudzinskis neck signs were positive. He was showing early features of encephalopathy and had not passed urine since the last 12 hours. He had a heart rate of 163/min and a blood pressure of 53/27 mm of Hg (mean 36). Respiratory rate was 22/min and oxygen saturation was 92 % in room air. He had a capillary refill time of 5 seconds with feeble peripheral pulses. Capillary blood glucose was 32mg/dl. Auscultation of chest revealed crepitations on both sides. Abdomen was tender to touch, but peristalsis sounds were audible. Liver was 4 cm palpable below the right costal margin and spleen was 3 cm palpable along its axis. He had pallor but no icterus. There was generalised lymphadenopathy.

Initial management involved providing oxygen. Intra venous cannula was inserted and blood sent for culture and routine investigations followed by fluid boluses at 20 ml/kg. A bolus of dextrose (2ml/kg of 25% dextrose) was also given. After two boluses at 20 ml/kg, the blood pressure was 70/39 (mean 49) mm of Hg (non invasive blood pressure, NIBP), which was still less than the desired mean of 60 to 65 mm of Hg. Initial blood reports showed haemoglobin of 7.8 gm/dl with normocytic, normochromic anemia. Total leucocyte count of 20,850/ cumm (neutrophil 80 %, lymphocyte

Correspondence
Prabhas Prasun Giri, Assistant Professor Of Pediatrics
Institute Of Child Health, Kolkata, Phone +919051958420,
E-mail: dr.prabhas@yahoo.co.in

17%), platelet - 40,000 /cumm. Other reports are shown in table 1. Chest X ray showed necrotising pneumonia involving both lung fields. Patient was started on Ceftriaxone and Clindamycin keeping the possibility of staphylococcal TSS. Two more fluid boluses were administered followed by Dopamine infusion at 10ug/kg/min by securing a central venous line. By early morning (5 A.M), the mean blood pressure had risen to 67 mm of Hg (NIBP). heart rate was 112/min. Urine output was 1.4 ml/kg/hour. Peripheral pulses were better palpable.Sensorium was also improved ans SPO2 was around 96% with 4 litres of O2 with face mask but ypoglycaemia was persisting, despite increasing glucose infusion rate to 8 mg/kg/min. Hyponatremia was corrected with 3% sodium chloride. Due to the proplonged Prothrombin time, Vitamin K was also given.

The child suddenly began to deteriorate thereafter. There was a sudden onset of tachyarrythmia (184/min) and tachypnea from 6:30 A.M. He was ventilated, and arterial line was established and central venous pressure and arterial blood pressure were monitored. Owing to refractory hypotension, adrenaline, noradrenaline and vasopressin were sequentially started. Ultrasonography revealed areas of central echogenicity within the adrenals, suggestive of bilateral adrenal hemorrhage.

Table 1: Laboratory data of the patient with Waterhouse Frederichsens syndrome

	Day 1 (2A.M)	Day 1 (9 A.M)
C reactive protein	242.2	
Urea	43	
Creatinine	1.7	1.5
Sodium	114	117
Potassium	5.2	6.8
Calcium	6.2	7.1
Alanine aminotransferase	2132	
Aspartate aminotransferase	1874	
Lactate dehydrogenase	4332	
Creatinine Kinase	1170	
Prothrombin time	38 seconds	
Activated thromboplastin time	86 seconds	
pH	7.2	6.98
pCO2 (mm of Hg)	37	72
pO2 (mm of Hg)	85	32
HCO3 – (mmol/litre)	21	12
Base excess	-5	-18
urine	protein 2+, RBC 2+	

Stress dose hydrocortisone was administered. Purpura fulminans involving the calf muscle area of left leg appeared. Antibiotics were upgraded to Meropenem and Vancomycin considering severe sepsis. Fresh frozen plasma was transfused because of coagulopathy and Investigations repeated (Table 1). However the boy succumbed in the afternoon.

Antemortem blood and Mini BALcultures had growth of MSSA (>105 /colony forming unit) which was sensitive to Linezolid, Vancomycin, Teicoplanin & aminoglycosides and was resistant to Quinolones, Erythromycin & Clindamycin (inducible). The sensitivity was performed as per CLSI guidelines, 2014. Testing of toxins and genetic analysis could not be done due to economic constrains.

On evaluation, he had septicemia, pneumonia, coagulopathy, deranged transaminases, dyselectrolytemia, refractory hypoglycemia and adrenal hemorrhage suggestive of WFS.

Discussion

Rupert Waterhouse in 1911 described WFS, characterised by petechial rash, coagulopathy, cardiovascular collapse and bilateral adrenal hemorrhage. WFS is commonly attributed to meningoccemia. Friderichsen has in 1955 demonstrated Stapylococcus aureus in a patient with WFS[3]. However it is extremely uncommon and has recently been demonstrated in 3 children from Chicago who were followed up with post mortem examination[4]. 2 patients had methicillin resistant staphylococcus aureus (MRSA) and the other had MSSA. We were similarly able to isolate MSSA from blood and BAL for our index case.

Staphylococcal TSS is known to cause high morbidity by causing septic shock, acute kidney injury, necrotising pneumonia, pulmonary edema and multi organ failure ultimately leading to high mortality. Our proband was fulfilling the criteria of staphylococcal TSS as laid down by CDC[5]. Our patient had septic shock which was refractory to all inotropes and the child ultimately developed multi organ failure. The mortality rate in severe invasive staphylococcal sepsis was as high as 8.6% in a pediatric intensive care unit compared to the overall mortality rate of 6%[6].

Staphylococcal TSS is also known to cause petechiae and purpura fulminans (PF) as we saw in our patient. Out of the 5 patients in this report[7], 4 had MSSA like our patient. Our child developed PF rapidly overnight and also had petechiae over foot and palate.

It is often proposed that any severe sepsis may lead to disseminated intravascular coagulation, ultimately contributing to adrenal hemorrhage, thereby leading to WFS. Our patient had a rapid deterioration leading to WFS and had many features which made us initially consider this to be meningococcal sepsis. He had a short history of fever, sepsis parameters were positive and he had leucocytosis, unlike the children in Chicago who had leucopenia[4]. He also had refractory hypoglycemia, hypotension, hyponatremia, hyperkalemia and metabolic acidosis which could not be corrected even after vigorous management with large doses of hydrocortisone. Serum cortisol levels could not be measured.

Recent evidence suggests a rise in community acquired Staphylococcal TSS following MRSA and MSSA by producing superantigens (panton valentine leucocidin, staphylococcal enterotoxin B and C and toxic shock syndrome toxin 1)[8,9,10]. Identification of genomic strains and toxins produced (which we could not do for our patient) will go a long way in formulating the approach to such patients. Literature available suggests an equal production of toxins by MRSA and MSSA[11].

There are few articles in the literature on MSSA causing WFS[4]. Consideration should be given in treating all suspected invasive staphylococcal infections with refractory shock and hypoglycemia aggressively with stress dose of hydrocortisone (50mg/meter square) and appropriate antibiotics in order to possibly reduce the risk of mortality associated with it.

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