

Case Report

Fatal Case of Systemic Salmonella Infection with Acute Renal Failure, Hemolytic-Uremic Syndrome and Rhabdomyolysis

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ABSTRACT

Acute renal failure (ARF) is an uncommon complication of typhoid fever. Reports of hemolytic-uremic syndrome (HUS) or rhabdomyolysis producing ARF in systemic salmonellosis are scanty in the medical literature. We report a case of a systemic salmonella infection complicated by HUS, rhabdomyolysis and ARF with a fatal outcome. A 27 year old male was transferred to the nephrology service with oliguria and rapid deterioration of renal function. He showed features of HUS and rhabdomyolysis.

Blood and stool culture grew *salmonella typhi*. Ultrasound kidneys, CT brain, virological, immunological and cerebrospinal fluid studies showed normal findings. He was treated with ciprofloxacin, cefuroxime, haemodialysis and supportive measures including ventilatory support. He died six days after admission. Delayed presentation, severity of bacteremia and toxemia could have contributed to HUS, rhabdomyolysis and fatal outcome in our patient.

KEYWORDS: acute renal failure, hemolytic uremic syndrome, rhabdomyolysis, *salmonella*

INTRODUCTION

Enteric fever is seen world wide, but acute renal failure (ARF) in this setting is a relatively rare complication^[1]. Reports of hemolytic-uremic syndrome (HUS) and rhabdomyolysis producing ARF in systemic salmonellosis are scanty in literature^[2]. We report a case of fatal ARF in a patient with enteric fever.

CASE REPORT

A 27-year-old Indian gentleman, previously in good health presented to a general hospital with oliguria and rapid deterioration of renal function. He had come as a new recruit from India, just about a month ago. His illness had started a week earlier with watery diarrhea and high fever. He was transferred to the Nephrology service from a peripheral hospital where he received intravenous crystalloid and colloid solutions. On admission, he was febrile (40 °C) with generalized muscle tenderness. His blood pressure (120/70 mmHg) and pulse rate (100/m) were normal. He showed meningism without any neurological lateralizing signs. He did not have any skin rash and systemic examination including cardiovascular and respiratory systems were normal. Optic fundi showed normal findings. His condition deteriorated rapidly, becoming drowsy and hypoxic and requiring

ventilatory support.

Laboratory investigations showed: leucopenia ($3.2 \times 10^9/l$), thrombocytopenia ($21 \times 10^9/l$) and normal hemoglobin (126 mgs/l). Repeated peripheral blood smear examination showed large number of fragmented erythrocytes suggesting microangiopathy (Fig. 1), reticulocyte count 2%, S. haptoglobin 200 mgs% and negative Coomb's test. He had low serum fibrinogen (1.21 gm/l) and high D dimer (42000 ng/ml) but prothrombin time (PT = 11 seconds), activated partial thromboplastin time (APTT = 30 seconds) and thrombin time (TT = 14 seconds) were normal. He had myoglobinuria with no significant urinary sediments and urine was sterile on culture. Serum creatinine was 1150 μ mol/l and blood urea was 50.5 mmol/l. Creatinine phosphokinase (CPK 3800 U/l) and lactic dehydrogenase (LDH 430 U/l) had increased to 58,000 U/L and 36,000 U/L respectively by day five and six. Serum bilirubin (40 mmol/L), GGT (9210 U/l), AST (76 U/l) and ALT (86 U/l) were high (Table 1). CT brain and cerebrospinal fluid study showed normal findings. Blood and stool culture grew *Salmonella typhi* sensitive to ceftriaxone. Viral studies for CMV, EBV, HSV, HBsAg, Hepatitis-A specific IgM and antihepatitis-C antibody were negative. Immunological studies including serum complements C3, C4 were normal. ANA, anti-DNA

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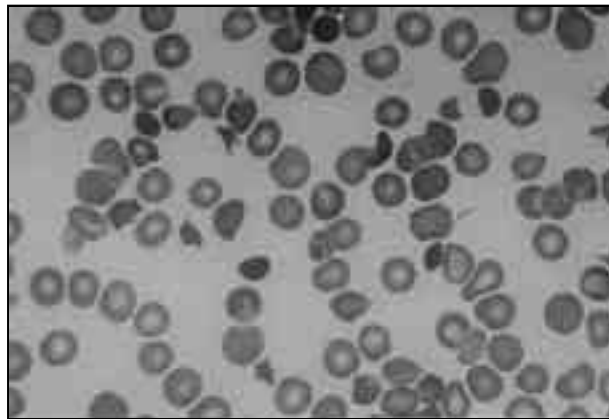


Fig. 1: Peripheral smear showing fragmented red-blood-cells

antibody, ANCA and anticardiolipin antibody were negative. Ultrasound showed normal sized kidneys with normal pelvicalyceal systems.

The patient did not develop any cutaneous rashes and muscle swelling or tenderness. He was treated with intravenous ciprofloxacin 750 mgs twice a day, cefuroxime 2 gms once a day, daily hemodialysis, fresh frozen plasma, ventilation and other supportive measures. He remained toxic, febrile, oliguric and unresponsive. He died six days after admission.

DISCUSSION

Even though there is a progressive decline in the incidence of typhoid fever, it continues to occur sporadically in this country, mainly in the expatriate work force. Overseas travel and existence of reservoirs of long term carriers add to the occurrence of these cases. Unusual life threatening combination of typhoid hepatitis, rhabdomyolysis, HUS and ARF are rare in classical typhoid fever^[1-3]. This prompted us to report this case.

Haemolysis due to G6PD deficiency, chloramphenicol and septicemia have been reported to accompany enteric fever, with or without acute renal failure. Hemolytic uremic syndrome is a condition in which ARF is associated with microangiopathic hemolytic anaemia. Occurrence of HUS is frequent in Gram negative coliform enteric infections^[4]. Endotoxin produced by these organisms are known to play a pathogenetic role in HUS^[5]. Salmonella organisms producing HUS, even though rare are also reported^[6-9]. It was proposed that salmonella endotoxin could cause glomerular microangiopathy with renal intravascular coagulation, leading to features of red cell fragmentation and renal failure^[10,11].

Rhabdomyolysis and myoglobinemia can occur in severe septicaemia with high fever. Even though the exact pathogenesis is unclear, very high fever and severe septicemia with toxic state could have contributed to rhabdomyolysis in our patient

Table 1: Relevant clinical and laboratory parameters

Parameters	Day 1	Day 3	Day 6
Temperature (in °Centigrade)	41	39	38
Blood pressure in mm Hg	110/70	120/80	100/70
Urine output - ml/24 hrs	160 cc	90 cc	50 cc
WBC in 10 ⁹ /l	3.2	3.9	4.2
Hb in gms/l	126	118	120
Platelets in 10 ⁹ /l	36	30	20
Blood Urea in mmol/l	69	60	43
S. Creatinine in µmol/	1190	950	880
ALT/AST U/L	70/65	75/68	50/40
Bilirubin T/D mol/l	40/23	60/29	45/25
S. Alkaline Phosphatase U/l	130	126	116
S. Albumin gms/l	26	30	32
S. Creatinine Phosphokinase U/l	630	46,000	58,000
S. Lactodehydrogenase U/l	420	31,000	36,000S
Fibrigen mg/l	1.2	1.1	1.5
D. Dimer ng/ml	6,000	12,000	42,000

PT, APTT and TT were within normal limits

[3, 7, 8]. Rhabdomyolysis and bacteremia also could have definitely contributed to the hypermetabolic state. Polymyositis was also considered as a probability but absence of cutaneous rashes and normal immunological parameters makes it unlikely.

It is possible that HUS could have been the cause for ARF in our patient, but one cannot rule out combined insults from rhabdomyolysis and septicemia producing renal damage. A renal biopsy would have given more information but could not be done since the patient was critically ill.

Acute renal failure due to sepsis usually carries a higher mortality than ARF from other causes. Presence of added complications of HUS and rhabdomyolysis could have contributed to the unfortunate outcome in this patient. The patient was treated with daily hemodialysis and systemic alkalinisation. Continuous renal replacement therapy (CRRT) in the form of continuous arteriovenous hemodiafiltration (CAVHDF) or continuous venovenous hemodiafiltration (CVVHDF) are known to markedly improve the prognosis and outcome in such critically ill patients with acute renal failure^[12]. Hence, we recommend prompt introduction of CRRT along with antibiotics and other supportive measures in such critically ill patients.

To conclude, this case indicates that salmonella infection can present with severe complications like HUS, rhabdomyolysis and ARF. Prompt active management should be instituted in the course of illness to prevent mortality in such cases.

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