CASE REPORT

Capillary leak syndrome – A life-threatening complication rarely reported in patients with typhoid fever

Muhammad Afzal, Maria Bibi, Ayesha Afzal, Sauleha Wasif, Nayab Khaliq

Abstract

A 9-years-old girl was admitted in to a peripheral hospital with a two-week history of fever and loose stools. Despite initial treatment, her condition worsened. On arrival, she was critically ill, drowsy, lethargic, febrile, Heart Rate 108/min, Respiratory Rate 34/min and Blood Pressure 90/60 mmHg, Capillary Refill time >3 seconds and had cold peripheries. Blood Culture was sent and appropriate antibiotics started. Her condition further deteriorated, with worsening level of consciousness, oedema and abdominal distension. Serum Albumin levels were low (2 g/dL). Blood culture subsequently grew extensively drug-resistant Salmonella typhi, and antibiotic therapy was changed accordingly. She developed features consistent with capillary leak syndrome, including oliguria, rising haematocrit, and worsening oedema. Hypotension and impending shock were treated with albumin transfusion and close monitoring of vital signs and urine output. After 48 hours, her BP stabilized, with improvement in consciousness, urine output and resolution of oedema. She was discharged in stable condition after 10 days of treatment.

Keywords: capillary leak syndrome (CLS), typhoid fever.

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Introduction

Capillary leak syndrome is defined as a condition characterized by increased capillary permeability, leading to leakage of plasma from the intravascular to the interstitial compartment, resulting in hypotension, haemoconcentration, and hypoalbuminaemia.[1]

Typhoid fever, caused by Salmonella typhi, is a systemic infection transmitted predominantly through ingestion of food and water contaminated by human faeces. Clinically it presents with a wide range of symptoms and signs of varying severity including fever, abdominal pain, nausea, and vomiting etc. Timely and accurate diagnosis is very important because if untreated or improperly treated, typhoid fever may lead to life-threatening complications.[2] Common complications include intestinal perforation,[3] gastrointestinal haemorrhage, encephalopathy, meningitis,[4] pneumonia, anaemia, cholecystitis, myocarditis, hepatitis, and septic shock.

In recent years, multidrug resistant (MDR) cases have been reported with poor response to conventional antibiotics therapy and a higher risk of complications.[5] To the best of our knowledge, capillary leak syndrome (CLS) as a complication of typhoid fever has not been previously reported in our country in the medical literature.

The patient was diagnosed with CLS as a rare complication of typhoid fever, which shares many features like hypotension and end organ hypoperfusion, which are also observed in typhoid-associated septic shock. However, the pathophysiology and management of these two conditions differ significantly, as discussed later. She was treated with meticulous fluid balance and strict monitoring along with appropriate antibiotics. The patient recovered completely and was discharged in a stable condition.

This case is reported to emphasize that capillary leak syndrome (CLS), although a rare complication, can occur in typhoid fever, in addition to its more commonly recognized association with viral infections and autoimmune disorders.

Case Report

A 9-years-old girl was admitted through the Emergency Department of Quaid-e-Azam International Hospital Islamabad, on 05- 11-2024, with a 2-week history of high-grade intermittent fever and 4–5 daily episodes of loose stools, classified as type 6-7 [6] (Bristol Stool Chart) without blood or mucus. In the last 2 days, she developed generalized abdominal pain and reduced oral intake. Initially, she was managed as an outpatient, then admitted to a private hospital for 5 days, where she received IV fluids and antibiotics for suspected typhoid fever. Her clinical condition deteriorated, with persistent abdominal pain and anorexia, necessitating referral for

Department of Paediatrics, Quaid-e-Azam International Hospital, Islamabad, Pakistan.

Correspondence: Maria Bibi. **Email:** mariarazi183@gmail.com

ORCID ID: 0009-0005-0816-2201

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Table: Mean organ weights (g) and ventricle thicknesses (cm) of the study population.

Vitals	On admission	During hospital stay	On discharge
Heart Rate	108/min	105/min	100/min
Respiratory Rate	34/min	38/min	30/min
Temperature	100 F	101 F	Afebrile
Blood Pressure	90/60 mmHg	100/60 mmHg	105/65 mmHg
Oedema	Generalized oedema	Partial resolution	Complete resolution

further management. There was no past history of any significant febrile or non-febrile prolonged illness. On arrival, she was sick, drowsy, and lethargic. Vitals were as follows: Heart Rate 108/min, Respiratory Rate 34/min, Temperature 100°F, Blood Pressure 90/60 mmHg (below 50th centile) (Vitals Table). All anthropometric measures were within normal range. On general examination, she appeared pale, with generalized oedema, a dry coated tongue, cold extremities, feeble pulses, and a capillary refill time >3 sec, no rash, jaundice, or lymphadenopathy. Chest examination revealed reduced air entry and dullness at both lung bases. Abdominal examination showed distension, diffuse tenderness, and positive shifting dullness, with no evidence of organomegaly.

Initial laboratory investigations revealed anaemia Hb 8.7 g/dL (11.5-15.5), thrombocytopenia 78×10^9/L (170-450), WBC 6.55×10^9/L (5-13), Neutrophils72% (33-61), Lymphocytes 26% (28-48), and raised CRP (0.0079 g/dL (<0.0005). Liver Function Tests (LFTs) showed S/bilirubin level of 2.5mg/dl (0.2-1.0), ALT-74U/l (<42), AST-284U/l (<30), GGT- 220U/l (9-36) and ALP- 236U/l (<500). Serum albumin was low (2 g/dL (3.5-5g/dl). CXR revealed bilateral basal pleural effusion, mild to moderate ascites and no organomegaly on Abdominal Ultrasound. Blood culture was sent. She was started on antibiotics (IV Meropenem1g IV TDS, Levofloxacin250mg IV BD, IV Metronidazole300mg IV TDS) and supportive care. Urinary catheterization showed an initial urine output of 1cc/kg/hr. Over the next two days, she developed worsening oedema and ascites. Repeat CBC showed Hb 8.6 g/dL, platelets 81×10^9/L, WBC 5.60×10^9/L, Neutrophils 69%, Lymphocytes28 %, and haematocrit 48%, indicating haemoconcentration despite fluid boluses. With persistent hypotension and third spacing, capillary leak syndrome (CLS) was suspected. She received 20%(100ml) human albumin infusions three times, with improvement in blood pressure, capillary refill time, and urine output (4cc/kg/hr). Fluid restriction was implemented as per CLS guidelines[1]. Workup for autoimmune diseases (Anti-Nuclear factor), and immunodeficiency (IgA, IgG, IgM, IgE) were negative. Dengue, HIV, and COVID-19 tests were negative. Pancreatic enzymes were assessed in view of upper abdominal pain and were within normal limits. Fever persisted, blood culture revealed growth of extensively-drug resistant Salmonella typhi (Sensitive to Imipenem, Meropenem). IV Meropenem was continued. Gradually, albumin improved to 3.2 g/dL, platelet counts normalized, and imaging showed reduced effusion and ascites. The patient became afebrile and oedema resolved. She remained stable and afebrile for 72 hours. After a 10-day hospital stay, she was discharged in a clinically stable condition, active and alert, with adequate oral intake, normal urine output, preserved mobility, and haemodynamically stable vital parameters (Vitals Table). A final diagnosis of extensively drug-resistant (XDR) typhoid fever complicated by capillary leak syndrome was made. On outpatient follow-up, she received typhoid vaccination, and was clinically stable.

Discussion

Capillary Leak Syndrome (CLS) results from increased vascular permeability, causing plasma leakage into tissues, leading to hypovolaemia, haemoconcentration, and hypotension that may progress to multi-organ dysfunction. It is commonly associated with viral infections, sepsis, autoimmune disorders, and malignancies[1], but rarely reported with typhoid fever. Typhoid usually presents with gastrointestinal and systemic symptoms[7]; CLS suggests a severe inflammatory response with cytokine-mediated endothelial injury.

Differentiating CLS from typhoid-associated sepsis is challenging as both conditions present with fever, hypotension, and systemic inflammation. Key features include elevated haematocrit, hypoalbuminaemia[8], and hypovolaemia despite tissue or pulmonary oedema. In CLS, excessive fluids can worsen oedema and organ compromise. Treatment is mainly supportive, cautious fluid replacement to maintain perfusion without worsening third-space fluid overload[9], targetted antibiotics for typhoid, and in severe cases, vasopressors or albumin. The benefit of corticosteroids in typhoid-related CLS is unclear.

Awareness of CLS as a potential complication of typhoid fever is essential for early recognition and appropriate management. Literature review found only one previously reported case from India.[10] More research is needed to determine its frequency, mechanisms, and optimal treatment strategies.

Socioeconomic Status: The parents are non-consanguineous, and there are two younger healthy siblings. Father works in Saudi Arabia and they belong to middle class socioeconomic status.

Mode of transmission: Faecal-oral route through contaminated water.

Conclusion

CLS although a very rare but fatal complication, should also be kept in mind in Extensively Drug-resistant cases of Typhoid fever so that they can be managed accordingly.

Consent: Parents provided their consent for reporting this case.

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Conflict of Interest: None.

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MA: Concept, critical review and final approval.
MB: Data collection, drafting and data analysis.
AA: Reference formatting.
SW: Literature search.
NK: Proofreading.