

S. Pneumoniae Infection Associated with a Hemolytic Uremic Syndrome in an Adult Patient: A Case Report

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Abstract

Hemolytic uremic syndrome (HUS) is a rare but severe entity characterized by the triad of acute kidney injury, microangiopathic hemolytic anemia, and thrombocytopenia. This disease is frequently observed in children after a diarrhea process secondary to *Escherichia coli* O157: H7. However, other disturbs may generate this disease, including pneumonia secondary to *S. pneumoniae*, which represents around 5% of all HUS cases. This type of HUS has demonstrated an increase in incidence in the population recently.

We report a case of an 83-years-old with hypothermia (33 °C) after being found at home on the floor. The blood revealed a severe anemia (hemoglobin 4.8 g/dL; hematocrit 15.3%; red blood cell count 1.54×10¹²/L), hemolysis (lactate dehydrogenase 615 U/L; potassium 5.8 mmol/L), acute renal failure (creatinine 4.22 mg/dL; urea 174 mg/dL), and thrombocytopenia (platelet count 57×10⁹/L). The peripheral smear was notable for toxic granulation in the neutrophils, large platelets, target cells, microspherocytes, and schistocytes. A chest X-ray showed right-sided lower lobe pneumonia, isolating *S. pneumoniae* infection in the urine culture. Due to the critical situation of the patient, intense fluid therapy, vasoactive drugs (dopamine), and temperature control by physical measurements was initiated as treatment. The evolution of the patient after the beginning of the treatment was torpid, resulting in a cardiorespiratory arrest and death.

The prognosis of patients with pneumococcal-HUS is strongly dependent on the effectiveness of antibiotic therapy as well as supportive intensive care (including steroids pulse therapy). Early recognition and prompt initiation of antibiotics with supportive intensive care may improve the outcome.

Keywords: DHemolytic uremic syndrome; Pneumonia; Adult patient; *Streptococcus pneumoniae*

List of abbreviations: HUS: Hemolytic uremic syndrome

Introduction

Hemolytic uremic syndrome (HUS) is a rare but severe entity characterized by the triad of acute kidney injury, microangiopathic hemolytic anemia, and thrombocytopenia [1]. This disease is most frequently observed in children and, in 90% of the cases, is preceded by a diarrhea prodrome, typically secondary to *Escherichia coli* O157: H7 [1]. This subtype of HUS is classified in the same group as typical HUS. In this group are also observed HUS secondary to solid organ transplantation, autoimmune diseases, drugs, pre-existing nephropathy, and others infections, including pneumonia secondary to *S. pneumoniae*. The last one represents around 5% of all HUS cases; however, the incidence is thought to be increased recently [2,3]. On the other hand, atypical HUS that

represents less than 5%, is defined as HUS without coexisting disease or condition, or specific infection [3].

We report a case of an 83-years-old patient affected by HUS secondary to *S.pneumoniae*. To our knowledge, this is an extremely rare entity, with very few cases reported in the literature.

Case report

An 83-years-old Caucasian male patient with a personal history of high blood pressure was accepted in the Emergency Department with hypothermia (33 °C). The patient was found at his home on the floor. It was unknown if there has been a loss of consciousness during the event.

During physical exploration, the patient did not refer any pain. At the arrival to the emergency department, the examination showed a blood pressure was 88/35 mmHg, temperature 33.5 °C, and oxygen saturation 90% while breathing ambient air. On physical examination, the patient was tachypneic, and hypoventilation on the right lung base was discovered. He was noted to be pale and mildly dehydrated. On neurological examination, the patient was observed in disturbance and disorientation.

During his admission, a blood test was performed revealing a severe anemia (hemoglobin 4.8 g/dL; hematocrit 15.3%; red blood cell count $1.54 \times 10^{12}/L$), hemolysis (lactate dehydrogenase 615 U/L; potassium 5.8 mmol/L), acute renal failure (creatinine 4.22 mg/dL; urea 174 mg/dL), thrombocytopenia (platelet count $57 \times 10^9/L$), total bilirubin 3.5 mg/dL, aspartate aminotransferase 243 U/L, alanine aminotransferase 110 U/L, Urinalysis showed proteinuria (50 mg/dL) and hematuria (hemoglobin 0.03 mg/dL). Urinary excretion of sodium was 14 mmol/L. The peripheral smear was notable for toxic granulation in the neutrophils, large platelets, target cells, microspherocytes, and schistocytes. A chest X-ray showed right-sided lower lobe pneumonia (Figure 1). Due to the renal failure, indication for an abdominal ultrasound was done without discovering any disturbance at renal level.



Figure 1: Chest X-ray showing right side lower lobe pneumonia

Due to the critical situation of the patient, treatment was started with intense fluid therapy, vasoactive drugs (dopamine), and temperature control by physical methods. The evolution of the patient after the beginning of the treatment was torpid, resulting in a cardiorespiratory arrest and progressed to death.

Post-mortem results revealed an *S. pneumoniae* infection isolated in the urine culture.

Discussion

The pathophysiology of all forms of HUS is the presence of endothelial cell lesions in the microvasculature of the kidney and, less frequently, of other organs [4]. This entity typically presents in children after a diarrhea process, generally secondary to *Escherichia coli* O157: H7 [1]. However, Pneumococcal associated HUS is a rare, but potentially fatal disease that may complicate pneumonia or, less frequently, meningitis caused by *S. pneumoniae* [5]. It occurs mainly in children under the age of two, while in adults, it is scarce [6]. Nevertheless, some authors suggested that this entity may be underdiagnosed [7].

Pathogenesis of HUS secondary to pneumonia is caused by the amount of neuraminidase that is generated by *S. pneumoniae* to cleave N-acetylneuraminic acid from the glycoprotein on the cell membrane of erythrocytes, platelets, and glomerular cells [8]. This feature exposes the Thomsen-Friedenreich antigen (T-antigen), which can then react with anti-T IgM antibodies of human plasma. As a result of this antigen-antibody reaction, a poly-agglutination of red blood cells occurs, generating a positive Coombs'

test (HUS usually show a negative Coombs' test) [9]. Also, in the acute phase, patients had decreased levels of C3 and C4 and reduce the residual activity of the classical as well as alternative pathways of complement activation, indicating severe complement consumption [6].

In our patient, the diagnosis of HUS secondary to *S. pneumoniae* infection was based on the classical triad of nonimmune microangiopathic hemolytic anemia, thrombocytopenia, and acute renal failure, in the absence of a diarrheal prodrome. Also, the diagnosis was confirmed post-mortem due to the isolation of *S. pneumoniae* in the urine culture.

The prognosis of patients with pneumococcal-HUS is strongly dependent on the effectiveness of antibiotic therapy [10]. Because of that, early recognition and prompt initiation of antibiotics with supportive intensive care improve the outcomes. The main antibiotics used are amoxicillin or third-generation cephalosporin in case of meningitis [10]. While plasma either infused or exchanged is useful in HUS, in pneumococcal-HUS is contraindicated due that plasma contains anti-Thomsen–Friedenreich antibodies, which might enhance agglutination of Thomsen–Friedenreich-anti-Thomsen–Friedenreich and worsen the HUS course. Because of that, these patients should be treated only with antibiotics and washed red cells [11]. Also, some authors suggested that methylprednisolone pulse therapy would be useful in early stages due to the systemic release of proinflammatory cytokines that occurs in pneumococcal-HUS [12].

For our knowledge, few adult cases of pneumococcal-HUS have been reported [13-17]. In the literature, patients with splenectomy have an increased incidence of pneumococcal-HUS. Also, the early treatment with antibiotics as well as the steroids pulse therapy improves the outcome [1,4,5]. In our case, the belated recognition of the disease, as well as the long-term evolution, led to the death of this patient.

Conclusion

HUS is a rare, but severe most frequently observed in children. In 90% of the cases, is preceded by a diarrhea prodrome, typically secondary to *Escherichia coli* O157: H7. However, HUS may also be produced secondary to other diseases including pneumonia secondary to *S. pneumoniae*, which represents around 5% of all HUS cases. The early recognition and prompt initiation of antibiotics with supportive intensive care (including steroids pulse therapy) in pneumococcal-HUS improve the prognosis.

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