Streptococcus Pneumonia-Associated Hemolytic Uremic Syndrome: A Case Report


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Introduction
Hemolytic uremic syndrome (HUS) is one of the most common causes of acute kidney failure in young children [1]. It is characterized by the triad of microangiopathic hemolytic anemia, thrombocytopenia, and renal insufficiency [2]. S. pneumonia induced HUS is relatively rare in comparison with Ecoli induced HUS [3] The incidence of HUS following invasive pneumococcal infection has been reported to be between 0.4 to 0.6 % [4,5]. This article describes a 6-month-old boy with S. pneumonia meningitis which was complicated by HUS.

Case Report
A six-month-old boy was brought to the emergency department with a chief complaint of seizure. The child was febrile and irritable since two days ago. On initial physical examination, he was febrile and somnolent but no other abnormalities were noted. His first laboratory tests were as follows: Hematocrit 29.6 percent, platelet count 499000/mm3, BUN 12mg/dl and creatinine 0.6 mg/dl. CSF analysis was indicative of bacterial meningitis (WBC 1600/ml, PMN 70%, sugar <10 mg/dl, protein 192 mg/dl, and gram positive diplococci on gram stain). CSF and blood culture showed S. pneumonia. (Table 1)

Vancomycin and ceftriaxone were started immediately after LP, and the patient gradually became afebrile and conscious and his appetite improved until the fifth day of admission when the patient developed multiple seizures. On the same day, the child looked relatively pale in comparison with the previous days, which was attributed to
sampling, but the child became frankly pale the next morning and his CBC showed a hemoglobin level of 2.2 g/dl, PLT 45000/mm³, BUN 140 mg/dl, and creatinine 4.3 mg/dl. The peripheral blood smear showed signs of microangiopathic hemolysis (schistocytes, fragmented RBCs, Burr cells and helmet cells).

Table 1 Laboratory indices in patient with S. pneumonia HUS

<table>
<thead>
<tr>
<th>Lab index</th>
<th>Before hemolysis</th>
<th>After hemolysis</th>
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<tbody>
<tr>
<td>Hb (g/dl)</td>
<td>9.8</td>
<td>2.2</td>
</tr>
<tr>
<td>Platelet/(mm³)</td>
<td>499000</td>
<td>45000</td>
</tr>
<tr>
<td>BUN (mg/dl)</td>
<td>12</td>
<td>140</td>
</tr>
<tr>
<td>Cr (mg/dl)</td>
<td>0.6</td>
<td>4.3</td>
</tr>
</tbody>
</table>

PT and PTT were normal, retic count was 5%, direct and indirect coombs tests were both negative, and C3 and C4 were normal. According to the clinical picture, he was diagnosed with S. pneumonia associated hemolytic uremic syndrome. He received two packed cell transfusions. The first transfusion was not washed packed cell due to the emergency state of the patient but washed packed cell was used for the second time.

Our patient's kidney function returned to normal with supportive treatment without dialysis. After 16 months of follow-up, he had a normal kidney function but some neurologic sequelae were observed. To date, the patient has not experienced any other courses of HUS.

**Discussion**

Hemolytic uremic syndrome is a rare but severe complication of invasive pneumococcal infection [6]. Streptococcus pneumonia (SP) is the most common infectious cause of nondiarrheal HUS [7]. Pneumococcal HUS is most commonly associated with pneumonia and/or empyema and rarely with meningitis [8]. HUS has three main types which have different pathogeneses, clinical presentations and prognoses: 1- Typical (post diarrheal) hemolytic-uremic syndrome which is mediated by Shiga toxin. 2- Atypical (diarrhea-negative) HUS which is mediated by abnormalities of the complement system (factor H, factor I, thrombomodulin) or other heritable factors. 3- Pneumococcal associated HUS (SP-HUS) mediated by neuraminidase, which, in spite of occurring without diarrhea, has little relation with diarrhea-negative HUS associated with complement factor mutations [9]. As a toxin-mediated disease, pneumococcal-associated HUS is more similar to typical HUS mediated by Stx. Neuraminidase removes N-acetylneuraminic acid from cell-surface glycoproteins and exposes the hidden T antigen (Thomsen-Friedenreich) on erythrocytes, platelets, and glomeruli. The serum contains anti-T immunoglobulin M (IgM) and causes damage to RBCs and the kidney [10]. In the case series, there was no case of S pneumonia induced HUS [11]. SP-HUS is a clinical diagnosis without specific diagnostic tests; simultaneous presence of microangiopathic hemolytic anemia, thrombocytopenia, acute renal failure, and bacteriological evidence of pneumococcal infection is sufficient to make the diagnosis [12]. T antigen activation test, Coombs test, or peanut lectin assays have been suggested as specific tests [7]. A relatively common cause of acute anemia during the course of bacterial meningitis is GI bleeding due to the stress ulcer or side effects of dexamethasone therapy. In our country, where H. influenza is still the most common cause of childhood meningitis, hemolytic anemia during the course of acute bacterial meningitis is highly suggestive of H. influenza meningitis in which immune hemolytic anemia occurs due to the absorption of capsular polysaccharide antigens to red cells [13-14]. Acute anemia accompanied by thrombocytopenia (due to DIC) is common in meningococcal meningitis which can be accompanied by acute renal failure due to hypoperfusion. Although sickle cell anemia is a rare disorder in Khorasan province, sickle cell hemolytic crisis can occur during the course of pneumococcal and hemophilus influenza meningitis in endemic areas like the southwest of Iran [12]. Drug induced hemolytic anemia has been reported during treatment with ceftriaxone for bacterial meningitis [15].

Karimi reported a case series of 20 patients with HUS (1991-2004) from the southwest of Iran in which the mean age of the patients was 3.5 years, 69% were post dysenteric, 73% required hemodialysis, and the case fatality rate was 19.8% [12]. In the case series, there was no case of S pneumonia induced HUS [11]. In another study, Jafari reported that STEC was a relatively common cause of diarrhea in Tehran. In
this study of 808 cases of acute diarrhea (among children and adults), STEC (6.4% of the cases) was the second common organism after Shigella (18.2%) [16]. Banerjee, in cooperation with 11 pediatric infectious centers in North America, reported 37 cases of SP-HUS between 1997 and 2009, which is the largest multicentric study of SP-HUS in North American children. In this case series, the median age of the patients was 2 years, most of the patients (84%) presented with pneumonia, 11% of them had meningitis, 73% required dialysis during hospitalization, 13% had neurologic sequelae, and 3% died [4]. In the US, D+ hemolytic uremic syndrome is much more common than D- hemolytic uremic syndrome and swimming outbreaks, followed by person-to-person transmission, are the most common transmission routes [17]. In china, pneumococcal HUS is much more common than shiga toxin induced HUS and, in contrary to North American case series, at least the medium-term prognosis for renal recovery is excellent [7].

**Conclusions**

Streptococcus pneumonia invasive infections must be taken into consideration in any patient presenting with changes in consciousness and signs of acute renal failure and hemolysis.

**Conflict of Interest**

None declared

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**References**