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STREPTOCOCCUS PNEUMONIAE HAEMOLYTIC URAEMIC SYNDROME: A CASE REPORT.

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ABSTRACT

Streptococcus pneumoniae-associated Haemolytic Uraemic Syndrome is a combination of acute haemolytic anaemia, thrombocytopaenia and acute kidney injury in a patient with *S. pneumoniae* infection. It constitutes 5-15% of all HUS cases while the incidence of HUS following invasive *S. pneumoniae* infection is estimated at 0.4-0.6%. We describe two paediatric patients aged 16 months and 18 months respectively, who were admitted for *Streptococcus pneumoniae* pneumonia. They subsequently developed Haemolytic Uraemic Syndrome a few days after admission. Both of the cases required renal replacement therapy. One of them recovered fully with normal renal function while the other progressed to chronic kidney disease. These two cases summarise an uncommon but serious complication and outcome of patients with *Streptococcus pneumoniae*-associated Haemolytic Uraemic Syndrome.

Keywords: Haemolytic-Uraemic Syndrome, Pneumococcal Pneumonia, Pneumococcal Vaccine, Renal Failure, *Streptococcus pneumoniae*.

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Keywords: Haemolytic-Uraemic Syndrome, Pneumococcal Pneumonia, Pneumococcal Vaccine, Renal Failure, *Streptococcus pneumoniae*.

INTRODUCTION

*Streptococcus pneumonia*e (*S. pneumoniae*) is the most common cause of bacterial pneumonia, sepsis and meningitis in children. The mortality caused by *S. pneumoniae* range from 700000 to 1 million per year worldwide.[1-3] *S. pneumoniae* associated Haemolytic Uraemic Syndrome (Sp-HUS) is a combination of acute haemolytic anaemia, thrombocytopaenia and acute kidney injury in a patient with *S. pneumoniae* infection. Sp-HUS usually develops 3–13 days after a pneumococcal infection.[4] Although it is not a common presentation, it is associated with significant short and long-term morbidities. Sp-HUS constitute for 5-15% of all HUS cases while the incidence of HUS following invasive S. pneumoniae infection is estimated at 0.4-0.6%.[4] Pneumonia occurs in 65-92% of patients with Sp-HUS and is more commonly associated with pleural effusion or empyema.[4,5]

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The aim of this case report is to summarise an uncommon but serious complications and long-term outcomes associated with *Streptococcus pneumoniae*-associated Haemolytic Uraemic Syndrome following an initial pneumococcal pneumonia. We would also like to highlights the possible role of pneumococcal vaccine in reducing the burden of disease in pneumococcal infections.

CASE REPORTS

Case 1

MJ is a 16-month boy who was previously well, presented with fever, cough and rhinorrhoea for 6 days. There was no history of di-

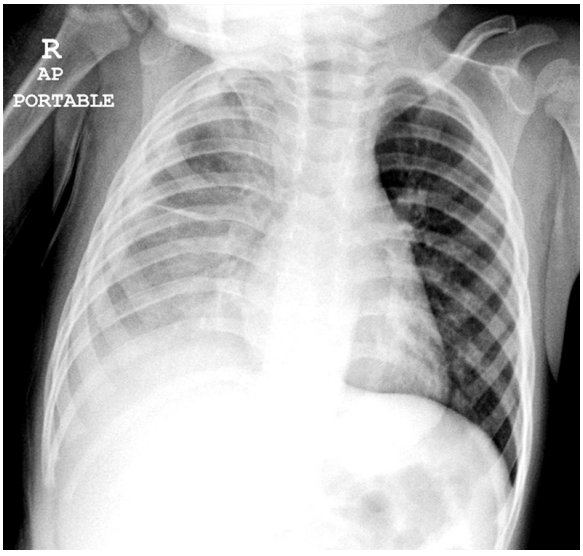

Figure 1: Chest X-ray on admission showing a right pleural effusion.

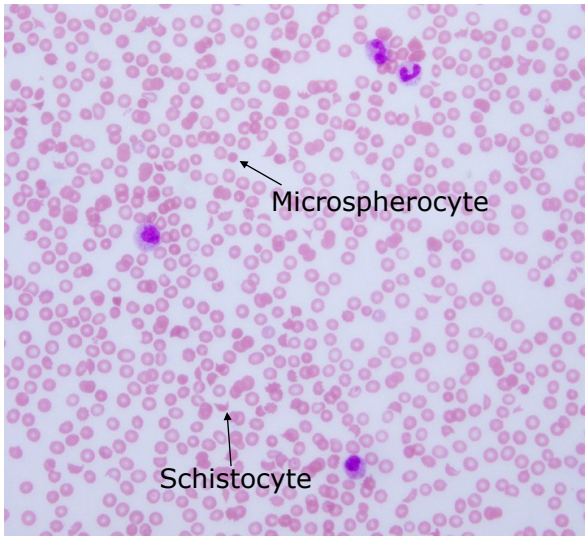

Figure 2: Full blood picture showing microspherocytes and helmet cells (schistocytes) suggestive of MAHA with thrombocytopaenia.

arrhoea or urinary tract infection. On examination, he was in respiratory distress and lung examination revealed reduced breath sounds in the right lower zone with dullness on percussion. Chest radiograph showed right pleural effusion (Figure 1). He was subsequently intubated on the day of admission for worsening respiratory distress.

After 12 hours of admission, he developed acute kidney injury with oliguria and fluid overload. Blood urea increased from 3.9 to 10 mmol/L and creatinine increased from 39 to 97 micromol/L. His haemoglobin dropped from 11g/dl to 9.5g/dl and there was associated thrombocytopaenia with platelet count dropping down to 8 x 10^9/L on the same day of admission. Full blood picture (FBP) showed evidence of a microangiopathic haemolytic anaemia (MAHA) (Figure 2). His blood culture was positive for *S.pneumoniae*. Patient underwent renal replacement therapy (CVVHD) from day 1 of admission for a total of 5 days. His serial renal profile is documented in the Figure 3. His renal function normalized after 4 weeks.

He was intubated for 18 days and required non-invasive respiratory support for a further 6 days. Ultrasound thorax showed right lung pneumonia with multiloculated right parapneumonic effusion. Video-assisted thoracoscopy (VATS) and decortication was subsequently performed. He received penicillin for a total of 6 weeks. He developed hypertension after 2 weeks of illness and was started on oral Nifedipine 5mg TDS and Labetalol 25mg BD. He was discharged after 6 weeks of admission with antihypertensive therapy. Hypertension resolved after 3 months. Currently, at the age of 3 years old, he has normal renal function.

Case 2

MA, an 18-month old boy, who was previously well, presented with fever and cough for 4 days. On examination, he was in respiratory distress and lung examination revealed reduced breath sounds in the left lower zone with dullness on percussion. He was intubated on day 2 of admission for worsening respiratory distress. His blood culture was positive for *S. Pneumoniae*. He developed acute kidney injury on day 2 of admission with initial urea of 3.6 and creatinine 150 with haemolytic anaemia. His haemoglobin drop to 4g/dL and platelet count of 6 x 10^9/L. Full blood picture showed microangiopathic haemolytic anaemia.

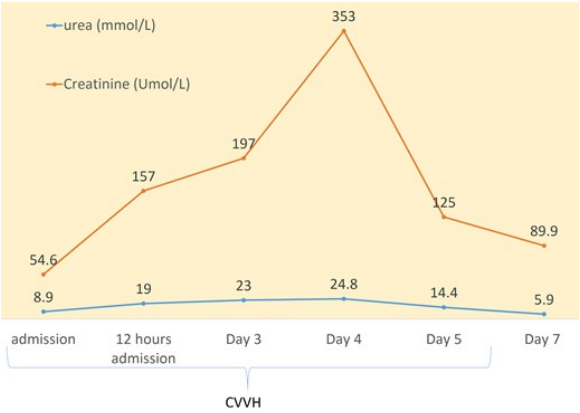

Figure 3: Serial urea and creatinine level according to days of admission in Case 1.

He underwent dialysis on day 3 of admission for 12 days for oligouria with fluid overload and was intubated for 30 days. Bedside ultrasound showed loculated pleural effusion requiring chest tube drainage at second week of admission. He received penicillin for a total of 6 weeks. He was discharged after 5 weeks of intensive care with creatinine level of 120 micromol/L. He continued to have a slow decline in renal function over the years and currently, at age 13 years, has chronic kidney disease stage IV. His serial renal profile were shown in Figure 4.

DISCUSSION

The actual pathogenesis of Sp-HUS remains unclear. The most accepted theory involves the Thomsen-Friedenreich antigen which is a hidden antigen found on the surface of red blood cell, platelets and glomeruli.[4] *S. pneumoniae* produces neuraminidase which cleaves N-acetylneuraminic acid from glycoproteins on the surface of cell membranes, thus exposing the Thomsen-Friedenreich antigen. Once exposed, the Thomsen-Friedenreich antigen will interact with preformed immunoglobulin M (IgM) antibodies resulting in hemolysis, polyagglutination and endothelial injury and haemolytic uraemic syndrome phenotype.[4]

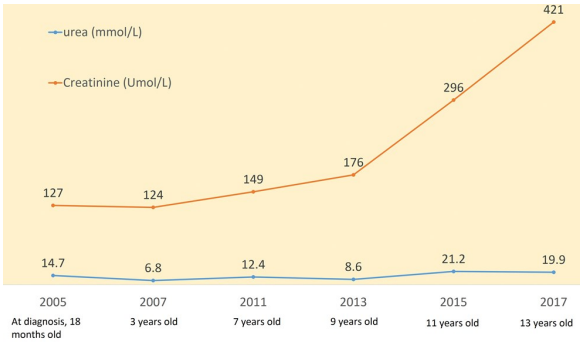

Figure 4: Serial urea and creatinine levels according to years/age in Case 2.

Treatment of Sp-HUS is mainly supportive together with treatment of underlying infection. Management includes managing fluid and electrolyte imbalance, adequate nutrition and use of washed blood products and platelets if indicated. Dialysis is often indicated in 43–84% of patients with SpHUS.[4]

Sp-HUS has higher mortality and long-term morbidity rates than Shiga toxin producing Escherichia coli HUS[4, 6]. In a study by Spinale et al, 12% died, 10% progressed to end-stage kidney disease, and 16% survived with chronic kidney disease or hypertension.[4] In a series from Banerjee et al, mortality was 11% and on follow up, 40% had complete recovery of renal function, 37% had elevated serum creatinine concentration and 8% required renal transplantation for end stage kidney disease.[7]

Vaccination is important to prevent Sp-HUS. There are total 91 *S.pneumoniae* serotype that have been identified. The most predominant serotype associated with Sp-HUS prior to pneumococcal conjugate vaccine era were 14, 6B, 9 V, 19, 3, 8 and 23F.[4] Pneumococcal 13-valent conjugate vaccine (Prevnar 13) protects against most of these serotypes.[4] A case- control study by Moore et al in 2016 found that Prevnar 13 is highly effective against invasive pneumococcal disease among children in USA.[8] This study involved 722 children with invasive pneumococcal disease and 2991 controls. They found that vaccine effectiveness against PCV13 serotypes was

86·0%.[8] Unfortunately, both of the cases did not received pneumococcal vaccine.

CONCLUSION

S.pneumoniae continues to be a common pathogen amongst children and can lead to potentially severe disease as illustrated in these two cases with Sp-HUS. The complications associated with these severe manifestations can lead to further long-term morbidity and strains on healthcare systems. Prevnar 13 has been shown to be effective against PCV13 invasive pneumococcal serotypes and hopefully a pneumococcal vaccination programme may play an important role in reducing disease burden of invasive pneumococcal infection and associated morbidity and mortality in developing countries.

DECLARATION

The authors declare not conflict of interest or any financial interest and confirmed that consent has been given for publications of the images.

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