Hemolytic uremic syndrome associated with streptococcus pneumoniae

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Abstract:

Hemolytic uremic syndrome (HUS) associated with infection by neuraminidase-producing Streptococcus pneumoniae usually presents with severe illness and has a high mortality rate. We report a 4-year-old boy presented with HUS associated with Streptococcus pneumoniae meningitis. The patient had also right lobar pneumonia with pleural effusion. The diagnosis of HUS was made by the classical triad: hemolytic anemia, renal failure and thrombocytopenia. The child was very sick and required ventilation for 7 days. He required peritoneal dialysis for 11 days, however, he recovered and his serum creatinine returned to normal. Conclusion: HUS must be considered in cases of renal failure and/or anemia associated with invasive pneumococcal infection. Equally, bacterial meningitis should be excluded in HUS patients with central nervous system involvement.

Introduction:

The HUS is characterised by the simultaneous occurrence of the triad of acute renal insufficiency, microangiopathic haemolytic anemia and thrombocytopenia. HUS is the most common cause of acute renal failure in infants and young children in the western countries. It could be classified into diarrhoea positive, D+ (typical) or diarrhoea negative, D - (atypical) HUS. In Europe and north America, the typical HUS is the most significant complication of infection by verocytotoxin (VT) -producing Escherichia coli (VTEC), usually of serotypes O57:H7. While in some developing countries like Bangladesh, South Africa and Zimbabwe, a more severe form of (D+) HUS was reported following shigella dysentery.
The atypical (D -) HUS has a worse outcome and could be recurrent. It might be inherited in autosomal dominant or recessive disorder like factor H deficiency and hypocomplementemia or

µmol/l) and to 8.2 mg/dl (721 µmol/l) on the fourth day (figure 1). He became anuric and his Hb dropped to 5.3 gm/dl. He received blood transfusion of unwashed packed red blood cells and unwashed platelets. He was commenced on automated peritoneal dialysis (APD) which continued for 11 days until his UOP improved as well as his serum creatinine (figure 1). LP was done on the fifth day of his illness and revealed high WBCs in the cerebrospinal fluid (CSF) (6550/ high powered field with 28% polymorphs), high protein (2.5 gram/ l) and the glucose was 3.1 mmol/l (blood glucose was 5 mmol/L). The CSF culture was negative; however the latex agglutination specific to SP was positive. On the sixth day of the illness the antibiotics was changed to meropenum as there was no improvement clinically. The patient improved gradually, extubated after 7 days of ventilation and his platelets returned to the normal level after 9 days (Figure 1). His renal function also improved and stayed so after discontinuation of APD. He was discharged from the hospital after 4 weeks. His results at discharge: serum creatinine 49 µl/L, Hb 9 g/dl, platelets 735 X 10^9/L. He was reviewed in the clinic 3 months later when a dramatic neurological recovery was observed and he maintained a normal kidney function with creatinine of 50 µ/L, urea 4.2 (3-6 mmol/l), platelets 470 X 10^9/L (150-500 X 10^9/L) and Hb 12.3 gm/dl.

Discussion:

We report a case of atypical HUS associated with invasive pneumococcal infection presented with pneumonia and meningitis. This serious condition with high mortality and morbidity had been described as a rare cause of HUS in the western medical literature (1, 4-5). However, to the best of our knowledge this is the first reported case from the Arab world. Brandt et al, described 12 children with HUS associated with SP infection, he described that pneumonia with empyema was the most common precipitating illness (67%), SP meningitis was present in 17% of children, pneumonia with bacteremia in 8%, and both pneumonia and meningitis in 8% (similar to our case). The pneumococcal organism produces an enzyme, which can expose an antigen (T-antigen) present on erythrocytes, platelets, and glomeruli. Antibodies to the T-antigen, normally found in human serum, bind the exposed T-antigen and the resultant antigen-antibody reaction (T-activation) can lead to HUS and anemia (4). All S. Pneumonia organisms produce neurominidase. However, not all pneumococcal infections results in T activation (4). Therefore, it is

associated with other infections like streptococcus pneumoniae (SP) (1) or as a complication of using chemotherapy
(D+) HUS was described in few studies from the Arab world (2). Similarly familial HUS was described in children from Saudi Arabia (3), Kuwait and Bedouin-Arab of Palestine. However, to the best of our knowledge, no case of SP- induced HUS was reported from the Arab world.
HUS associated with SP is a rare condition but well described in the literature as serious disease, which carries an increased risk of mortality and renal morbidity (1,4,5) compared with (D+) HUS.
We report the first case of SP-induced HUS from the Arab world. Paediatricians should be aware that this combination could have devastating complications in the pediatrics population.

Case Report:

A previously well four-year-old boy admitted with fever and impaired level of consciousness. He was treated initially with 3-day course of oral azithromycin as a case of upper respiratory tract infection, before his presentation to us. However, he continued to be febrile and lethargic. On admission, he was drowsy, blood pressure 113/41 mmHg, temperature 38^0 C, respiratory rate 30/ minute and pulse 138 beats/minute. He looked very sick with labored breathing. There was no rash and the rest of systemic examination was un-remarkable. He was ventilated and commenced on intravenous ceftriaxone for suspected meningitis. Lumber puncture (LP) was not done initially as the patient was unstable. His initial investigation showed normal haemoglobin (Hb) 11.8 g/dl and high WBC 29.6 X 10^9/L, with 41% neutrophil (12.14 X 10^9/L). He had low platelets 26 X 10^9/L, normal PT 14.6(11-15) , slightly prolonged PTT 50.6 (23-36), very high D dimmer 5595 and high FDP 320 (<5). He had high C reactive protein (CRP) 226 and disturbed liver function tests: AST 441 (15-37U/L); ALT 118 (30-65U/L) and LDH 2574(150-50 U/L). His chest radiograph showed partial collapse of the right lung with pleural effusion. His initial serum creatinine 3.4mg/dl = 299 µl/L (35-80 µ/L) was and his serum urea was 44 (3-6 mmol/L).

On the second day of admission, he passed dark urine and the analysis of urine revealed hematuria with numerous red blood cells. His urine out put (UOP) decreased and became oliguric with progressive increase in his serum creatinine to 5 mg/dl (440

important to diagnose red cell activation once it is suspected. Early detection of T antigen is beneficial, as it will result in avoidance of transfusion of unwashed blood. Unfortunately, detection of T antigen is not available to our services.

Our patient had severe illness and required ventilation and dialysis. This is similar to previous reports of SP-induced HUS, which is known to be a cause of severe acute hematological disease including DIC or renal disease, leading to death in 29-50% of cases (5). Long term prognosis is also guarded, Nathanson et al reported that out of 11 patients, 4 died during the acute phase, among the 7 survived patients, 5 developed end-stage renal failure (ESRF) 4-17 years later (5). In contrast, Krysan et al documented in their comprehensive literature review, that out of 38 well-documented cases of SP-associated HUS, only 3 of which progressed to ESRF, including, their reported case which was transplanted successfully (1). They observed that children who progressed to ESRF had a greater duration of oligo-anuria compared with cases who did not progress to ESRF (1). They also stressed on the significant adverse effect of unwashed blood products, and a possible influence of female gender on outcome (1). As the use of blood products containing IgM may aggravate this disorder, early recognition of HUS with SP neuraminidase production may lead to improved patient outcome through the judicious use of blood products. Our patient has received unwashed blood before identifying the SP by agglutination test. However, luckily, no deterioration in clinical condition or aggravation of hemolysis were observed. This may support the view of Nathanson in his report were 7 of 11 patients transfused unwashed red blood cells and none exhibited a life-threatening disease or worsening of hemolytic anemia. He concluded that despite the theoretical risk, an adverse effect of unwashed blood transfusions containing limited amounts of plasma remains to be demonstrated in SP-induced HUS (5). Furthermore, some investigators recently have questioned the risk of transfusing plasma in patients demonstrating T-activation and others have suggested that these events are the result of infection with a verocytoxin-producing strain of S. peunmoniae, and not the result of neuaminidase activity (4). Our patient was olig-anuric and needed only 11 days of dialysis, while the reported mean duration of dialysis on such patients is 32 days (5). This may also have influenced the favorable outcome of our patient.

Recent reports described an increased association of S. pneumoniae and HUS (4) and therefore there is a need for more awareness among paediatricians about this serious condition.

References

1) Krysan DJ, Flynn JT. Renal transplantation after Streptococcus pneumoniae-associated hemolytic uremic syndrome. Am J Kidney Dis 2001; 37(2):E15.

(2) Al Eisa A, Al Hajeri M. Hemolytic uremic syndrome in Kuwaiti Arab children. Pediatr Nephrol 2001; 16(12):1093-1098.

(3) Mattoo TK, Mahmood MA, al Harbi MS, Mikail I. Familial, recurrent hemolytic-uremic syndrome. J Pediatr 1989; 114(5):814-816.

(4) Cochran JB, Panzarino VM, Maes LY, Tecklenburg FW. Pneumococcus-induced T-antigen activation in hemolytic uremic syndrome and anemia. Pediatr Nephrol 2004; 19(3):317-321.

(5) Nathanson S, Deschenes G. Prognosis of Streptococcus pneumoniae-induced hemolytic uremic syndrome. Pediatr Nephrol 2001; 16(4):362-365.

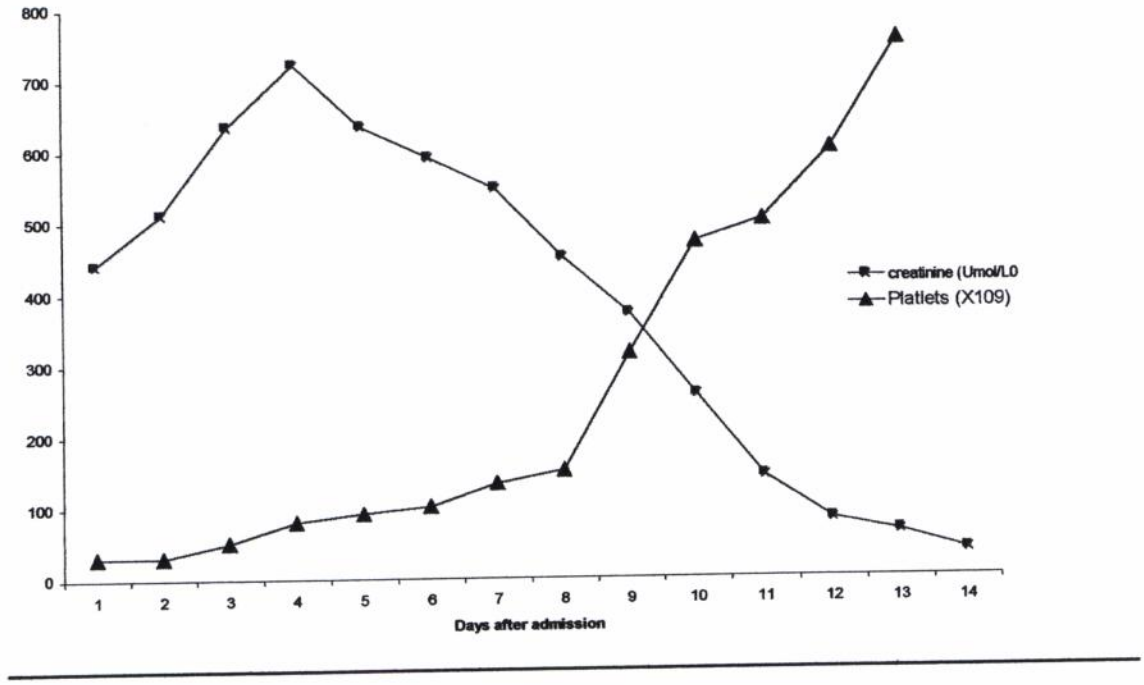

Figure 1: The change in serum creatinine (μmol/L) and platelets ($X10^9$/L)during the disease course. Dialysis started on the 4^{th} day of admission for 11 days.