Giacomo D. Simonetti · Kristina Dumont-Dos Santos
Jana M. Pachlopnik · Gianpaolo Ramelli
Mario G. Bianchetti

Hemolytic uremic syndrome linked to infectious mononucleosis

Received: 4 February 2003 / Revised: 24 June 2003 / Accepted: 24 June 2003 / Published online: 12 September 2003
© IPNA 2003

Abstract A 12-month-old boy developed a mild hemolytic uremic syndrome with no acute diarrheal prodrome. The typical clinical, hematological, and serological features of infectious mononucleosis were also noted. The clinical course of both hemolytic uremic syndrome and infectious mononucleosis was uneventful. A review of the literature disclosed that hemolytic uremic syndrome has been noted in two adolescents with infectious mononucleosis.

Keywords Epstein-Barr virus · Hemolytic uremic syndrome · Infectious mononucleosis

Introduction

In childhood, hemolytic uremic syndrome mostly follows an acute diarrheal prodrome caused by shigatoxin-producing strains of *Escherichia coli* or *Shigella dysenteriae* type 1 [1, 2]. Invasive infections with neuraminidase-producing *Streptococcus pneumoniae* are a further rather rare but well-recognized cause of hemolytic uremic syndrome [3, 4]. In the remaining 10%–30% of cases, the etiology of hemolytic uremic syndrome remains a matter of discussion, but has sometimes been attributed to viral infections [1]. We report an infant with hemolytic uremic syndrome and infectious mononucleosis.

Case report

A 12-month-old boy of Caucasian origin was in good health until January 2002. At that time he developed fever and an erythematous facial flushing that rapidly spread to the trunk and the extremities. Fever and rash resolved spontaneously over 5 days. Two weeks later the child was admitted with a 4-day history of irritability, restlessness, and pallor but without any diarrhea. The unrelated parents and two siblings were healthy. Physical examination disclosed a body temperature of 37.8°C, moderate arterial hypertension (116/74 mmHg), pallor, yellow scleral pigmentation, mild rhinopharyngitis, and an enlarged spleen up to 5 cm below the left costal margin. The remaining physical findings were normal. Urinalysis revealed hematuria, red cell casts, and severe proteinuria (albumin/creatinine ratio 943 mg/mmol, normal ≤ 20 mg/mmol). Hematology revealed anemia (hemoglobin 60 g/l, normal 100–150 g/l), thrombocytopenia (37×10^9 /l, normal $150\text{--}450 \times 10^9$ /l), and leukocytosis (18.9×10^9 , normal $3.0\text{--}12.5 \times 10^9$). The blood film revealed severe red blood cell fragmentation, many polychromatophilic erythrocytes, mild lymphocytosis (10.0×10^9 , normal $1.0\text{--}9.0 \times 10^9$), and some atypical lymphocytes (0.3×10^9). The polyspecific direct anti-globulin test was negative. Alanine aminotransferase (96 U/l, normal ≤ 34), aspartate aminotransferase (131 U/l, normal ≤ 47), lactate dehydrogenase (5,120 U/l, normal ≤ 850), total bilirubin (52 μ mol/l, normal ≤ 22 less), creatinine (97 μ mol/l, normal ≤ 67), and urea (16.5 mmol/l, normal ≤ 8.0) were pathologically increased. Plasma sodium (131 mmol/l, normal 132–145) and albumin (27 g/l, normal 36–43) were slightly decreased and plasma potassium was normal (3.6 mmol/l, normal 3.6–5.4). The diagnosis of hemolytic uremic syndrome without diarrheal prodrome was made.

No pathogens harboring genes for shigatoxin were detected in fecal specimens [5]. IgM antibodies against the Epstein-Barr viral capsid antigen and IgG antibodies against the early Epstein-Barr viral antigen, two good markers of acute infectious mononucleosis, were present [6, 7].

The subsequent acute course was characterized by a transient slight increase in plasma creatinine (to 132 μ mol/l) and urea (to 18.1 mmol/l) and a decrease in hemoglobin (to 56 g/l). No dialysis was instituted and no blood or fresh plasma was given. The child was discharged 7 days after admission. At the time of follow-up, 3 and 12 months later, the child was well with a normal blood pressure. The total cell count and creatinine and urea were normal. Urinalysis did not disclose hematuria or pathological proteinuria (albumin/creatinine < 2.0 mg/mmol).

G. D. Simonetti · K. Dumont-Dos Santos
J. M. Pachlopnik · M. G. Bianchetti
Department of Pediatrics, University of Berne,
Inselspital, Berne, Switzerland

G. Ramelli · M. G. Bianchetti (✉)
Department of Pediatrics, San Giovanni Hospital,
Bellinzona, Switzerland
e-mail: mario.bianchetti@pediatrician.ch
Tel.: +41-91-8118668, Fax: +41-91-8118787

Discussion

It is impossible to prove that infectious mononucleosis was the cause of hemolytic uremic syndrome in this patient. Nonetheless there is little question that he did have both infectious mononucleosis [6, 7] and hemolytic uremic syndrome [1, 2].

Thrombocytopenia is common in infectious mononucleosis. However, in this disease hemolytic anemia occurs rarely and is usually linked to a positive direct antiglobulin test [6, 7]. In our patient the antiglobulin test was negative, suggesting that anemia and thrombocytopenia developed in the context of microangiopathic anemia.

Hemolytic uremic syndrome has been noted in two adolescents with the typical clinical, hematological, and serological features of infectious mononucleosis. Both patients also had a history of severe, sometimes bloody, diarrhea [8, 9]. Nonetheless, no stool testing for germs harboring genes for shigatoxin was performed [5]. It is therefore tempting to assume that these patients had concurrent infectious mononucleosis caused by Epstein-Barr virus and classic hemolytic uremic syndrome caused by micro-organisms that produce shigatoxin [1, 2]. In our patient the history and the laboratory values strongly argue against a causal link between pathogens that produce shigatoxin and hemolytic uremic syndrome.

Infectious mononucleosis is a benign, self-limited clinical illness [6, 7]. It is therefore tempting to assume that some inherited abnormality of the immune system

might account for the link between infectious mononucleosis and hemolytic uremic syndrome in our patient. However, his history and the very benign clinical course argue against this hypothesis.

In conclusion, the present patient and cases from the literature indicate that hemolytic uremic syndrome may occur linked to infectious mononucleosis.

References

1. Stewart CL, Tina LU (1993) Hemolytic uremic syndrome. *Pediatr Rev* 14:218–224
2. Ray PE, Liu XH (2001) Pathogenesis of Shiga toxin-induced hemolytic uremic syndrome. *Pediatr Nephrol* 16:823–839
3. Erickson LC, Smith WS, Biswas AK, Camarca MA, Waecker NJ Jr (1994) *Streptococcus pneumoniae*-induced hemolytic uremic syndrome: a case for early diagnosis. *Pediatr Nephrol* 8:211–213
4. Vigier RO von, Seibel K, Bianchetti MG (1999) Positive Coombs test in pneumococcus-associated hemolytic uremic syndrome. A review of the literature. *Nephron* 82:183–184
5. Essers B, Burnens AP, Lanfranchini FM, Somaruga SG, Vigier RO von, Schaad UB, Aebi C, Bianchetti MG (1999) Acute community-acquired diarrhea requiring hospital admission in Swiss children. *Clin Infect Dis* 31:192–196
6. Okano M (1998) Epstein-Barr virus infection and its role in the expanding spectrum of human diseases. *Acta Paediatr* 87:11–18
7. Peter J, Ray CG (1998) Infectious mononucleosis. *Pediatr Rev* 19:276–279
8. Shashaty GG, Atamer MA (1974) Hemolytic uremic syndrome associated with infectious mononucleosis. *Am J Dis Child* 127:720–722
9. Lee MH, Cho KS, Kahng KW, Kang CM (1998) A case of hemolytic uremic syndrome associated with Epstein-Barr virus infection. *Korean J Intern Med* 13:131–135