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Case Report

Haemolytic uraemic syndrome associated with H1N1 influenza

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Abstract

Haemolytic uraemic syndrome (HUS) is one of the two forms of thrombotic microangiopathies and is characterized by the triad of microangiopathic haemolytic anaemia, thrombocytopaenia, and acute renal failure. It has been associated with bacterial and viral infections as well as non-infective causes. We report a subject who presented with HUS associated with an influenza-like syndrome which was confirmed as an influenza A (H1N1) infection. There are reports of HUS associated with seasonal influenza, but there have been no reported cases of HUS after novel influenza A (H1N1) in the literature so far.

Keywords: H1N1 influenza; haemolytic uraemic syndrome; thrombotic microangiopathies

Introduction

Haemolytic uraemic syndrome (HUS) is a rare condition comprising the clinical triad of acute renal failure, microangiopathic haemolytic anaemia and thrombocytopaenia [1]. It was first described in 1955 by Gasser *et al.* [2] who reported HUS in children with preceding gastrointestinal infection with bloody diarrhoea. It is now known that HUS falls into the broader category of thrombotic microangiopathies (TMA).

There are two types of HUS [3]: (i) D+ HUS, the classic form, accounting for 95% of cases in children, and most commonly caused by an infection by a shiga toxin-producing *Escherichia coli*, specifically serotype O157:H7, and (ii) D− HUS or atypical HUS. This latter has been associated with various non-enteric infections (e.g. *Streptococcus pneumoniae*), viruses (e.g. Coxsackie, ECHO, varicella and Epstein–Barr), drugs (anticancer molecules, immunotherapeutics and antiplatelet agents), malignancies (prostatic, gastric and pancreatic cancers), transplantation, pregnancy, scleroderma or antiphospholipid syndrome [4].

The novel influenza A (H1N1) pandemic began in Mexico in March 2009. By January 2010, 47 million people were infected (~15% of the population) [5]. Fourteen thousand and one hundred forty-two have died [6], 97 in Portugal [7]. The complications of this infection are still far from known. We report the first case of HUS associated with H1N1.

Case report

A 37-year-old Caucasian male, previously in good health, complained of fever (38.3°C), cough and sore throat. Two days later, he developed increasing fatigue, and noted dark urine and jaundiced skin and sclerae. There was no history of recent travel or diarrhoea. His dietary history was unremarkable. He had not taken any vaccine or medication apart from 2 g of paracetamol. There was no significant family history of disease.

At admission (Day 5), physical examination showed that the patient had mildly icteric skin and sclerae. Temperature was 37.6°C, blood pressure was 156/90 mmHg and heart rate was 60 beats/min, but otherwise, the examination was unremarkable.

Laboratory findings were remarkable for anaemia, with haemoglobin 74 g/L (7.4 g/dL), thrombocytopaenia, platelet count 85 × 10^9/L (85 000/mm3), and elevated serum creatinine and urea [335.9 μmol/L (3.8 mg/dL) and 66.4 mmol/L (186 mg/dL), respectively]. Haemolytic anaemia was confirmed by low serum haptoglobin [0.88 μmol/L (8.8 mg/dL)], elevated serum lactate dehydrogenase (5376 U/L) and schistocytes on blood smear. The Coombs test was negative. Coagulation tests were normal. Total bilirubin and AST were slightly elevated [35.9 μmol/L (2.1 mg/dL) and 85 U/L, respectively], and ALT was normal. Serum complement levels were within the normal range. Urinalysis revealed protein 3+, bilirubin 2+ and blood 4+, and sediment showed rare blood cells and granular casts per high-power field, without quantification. Serologies for ANCA, ANA, anti-DNA antibody levels, HIV, hepatitis B and C, cytomegalovirus, and rheumatoid factor were unremarkable. Blood and urine cultures were negative. ADAMTS13 was below the normal range (0.33 μg/mL; normal range = 0.60–1.60 μg/mL), and rt-PCR for detection of H1N1 influenza was positive.

A chest radiograph was unremarkable. An abdominal ultrasound showed a mild hepatomegaly (135.8 mm). A renal ultrasound was unremarkable, the right kidney was

111.8 mm and left kidney 125.4 mm. The abdominal CT scan showed no abnormalities.

Starting on admission day (Day 5), he was treated with daily plasma exchange for 5 days. On Day 7, oseltamivir was initiated and maintained for 7 days.

Following admission and over the next 15 days, his thrombocytopaenia resolved [Day 20, 570×10^9/L (570 000/mm^3)], his haemoglobin increased progressively [Day 20, 102 g/L (10.2 g/dL)] and serum creatinine slowly decreased to baseline [Day 20, 106.1 μmol/L (1.2 mg/dL)].

Discussion

D− HUS or atypical HUS has been associated with various viral infections. We suspected influenza H1N1 due to the influenza-like illness. This is a disease that spreads via the airway and can be severe. World Health Organization data indicate that ~40% of severe cases occur in previously healthy children and adults, usually under the age of 50 years old [8]. Thus, we performed rt-PCR for H1N1 (real-time polymerase chain reaction), which was positive. No other causal or associated factors were identified in our patient.

Platelets bind to endothelium via von Willebrand factor (vWF). ADAMTS13 is a zinc-containing metalloprotease that cleaves large vWF multimers, thereby decreasing their prothrombogenic properties [9]. Deficiency of ADAMTS13 leads to the appearance of large prothrombogenic multimers of VWF in the circulation that is associated with thrombocytopaenia and intravascular haemolysis [10]. A previous report has shown that, although a deficiency of ADAMTS13 diagnoses TTP, some patients with D− HUS also share this finding [9]. Our patient had low ADAMTS13 during the acute episode. A plasma sample for determination of ADAMTS13 was not collected after remission.

The patient was treated with oseltamivir, following WHO guidelines that recommend treating serious cases immediately [8]. Oseltamivir acts by inhibiting neuraminidase, which is a glycoprotein on the surface of influenza virus that decreases the release of viruses from infected cells and thus prevents viral spread. Plasma exchange or infusion is considered the therapy of choice in patients with HUS. The patient underwent plasma exchange for 5 days, obtaining clinical and renal function improvement.

To our knowledge, this is the first reported case of HUS associated with H1N1 influenza. Further accumulation of clinical data is necessary to confirm whether HUS has a real association with H1N1 influenza.

Conflict of interest statement. None declared.

References

1. Sens YA, Miorin LA, Silva HG *et al*. Acute renal failure due to hemolytic uremic syndrome in adult patients. *Ren Fail* 1997; 19: 279–282
2. Gasser C, Gautier E, Steck A *et al*. Hämolytisch-urämische syndrome: bilaterale nierenrindennekrosen bei akuten erwobenen hämolytischen anämien. *Schweiz Med Wochenschr* 1955; 85: 905–909
3. Proesmans W. Typical and atypical haemolytic uremic syndrome. *Kidney Blood Press Res* 1996; 19: 205–208
4. Siegler R. The hemolytic uremic syndrome. *Pediatr Clin North Am* 1995; 42: 1505–1529
5. http://www.who.int/csr/disease/swineflu/en/
6. Pandemic (H1N1) 2009—CIDRAP >> CDC sharply raises H1N1 case estimates; kids hit hard. http://www.cidrap.umn.edu/cidrap/content/influenza/swineflu/news/dec1009estimates
7. www.dgs.pt
8. World Health Organization website: http://www.who.int/csr/disease/swineflu/notes/h1n1_use_ antivirals_20090820/en/
9. Furlan M, Robles R, Galbusera M *et al*. von Willebrand factor-cleaving protease in thrombotic thrombocytopenic purpura and the hemolytic-uremic syndrome. *N Engl J Med* 1998; 339: 1578–1584
10. Moake JL, Turner NA, Moake JL *et al*. Involvement of large plasma von Willebrand factor (vWF) multimers and unusually large vWF forms derived from endothelial cells in shear stress-induced platelet aggregation. *J Clin Invest* 1986; 78: 1456–1461

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