Case Report

Haemolytic–uraemic syndrome in patients with Crohn’s disease

M.-N. Peraldi, K. Akposso, J.-P. Haymann, A. Lahlou and J.-D. Sraer

Service de Néphrologie A, Hôpital Tenon, Paris, France

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Introduction

Typical haemolytic–uraemic syndrome (HUS), defined by the association of microangiopathic haemolytic anaemia, peripheral thrombocytopenia, and acute renal failure, occurs after a gastrointestinal tract infection by enterobacteria which produce Shiga-like toxins [1]. Gastrointestinal infarctions have been described in severe forms of HUS and the clinical picture can mimic Crohn’s disease or ulcerative colitis [2,3]. We describe here the clinical course of two patients with HUS occurring several years after the initial diagnosis of Crohn’s disease was established. One patient had Shiga-like toxins detected in the stools. Both patients had complete renal remission. We suggest that Crohn’s disease can be listed as a predisposing factor for the development of HUS.

Case report 1

A 53-year-old man was admitted for acute renal failure. Seven years before admission, he presented with persistent bloody diarrhoea and abdominal pain. The diagnosis of Crohn’s disease was made on clinical and pathological data (ileal biopsy), and salazopyrin was prescribed. Between the initial diagnosis of Crohn’s disease and admission for acute renal failure, he suffered three different episodes of severe abdominal pain. At admission, he presented with anorexia, diarrhoea, abdominal pain, and confusion. Blood pressure was 140/80 mmHg. Temperature was 37°C. Serum creatinine was 1430 µmol/l with severe oliguria. Haemoglobin was 101 g/l with 127.10⁹/l nucleated red blood cells. Numerous schistocytes were present on the blood smear. The platelet count was 90.10⁹/l. Haptoglobin level was 0.06 g/l. A percutaneous renal biopsy was performed and showed thrombotic microangiopathy with pure glomerular lesions. Arteries appeared normal and there was some moderate degree of tubular necrosis. Stool culture was negative, as well as the search for Shiga-like toxins in the stools.

Colonoscopic examination demonstrated oedematous areas with diffuse congestion. Histological examination showed necrotic lesions and important areas of mononuclear cell infiltration, compatible with Crohn’s disease. As a specific treatment for HUS, the patient received fresh frozen plasma for 17 days and corticosteroids (1 mmg/kg/day) for 1 month. Haemodialysis was performed three times during the first week. On the second week, renal function began to improve and gastrointestinal symptoms disappeared. He left the hospital 1 month after admission with normalization of the platelet count, disappearance of the microangiopathic anaemia and a normal renal function (serum creatinine 115 µmol/l).

Case report 2

The patient was a 24-year-old young man. Two years before admission, he had bloody diarrhoea, abdominal pain and 10-kg weight loss. He was admitted to another hospital where the diagnosis of Crohn’s disease was made after clinical, radiological, and pathological tests. Ileal biopsy was considered typical of the disease. The symptoms resumed after treatment with corticosteroids and mesalazine. Two months before admission, he had a new bout of diarrhoea. Colonoscopic examination showed diffuse inflammatory activity and mesalazine and amoxycillin were given. Gastrointestinal symptoms persisted and he was admitted for bloody diarrhoea and severe oliguria. At entry, blood pressure was 135/65 mmHg, temperature was 37°C. He complained of diffuse abdominal pain. Urinary output was less than 100 ml/day. Serum creatinine was 975 µmol/l. Haemoglobin level was 89 g/l and there was 12.3% schistocytes on the blood smear. Platelet count was 124.10⁹/l. Lactate dehydrogenase serum level was 2790 IU/l and haptoglobin was 0.06 g/l. A renal biopsy was performed 3 days after admission and showed thrombotic microangiopathy with pure glomerular lesions. Haemodialysis was needed during the first week. He received six plasma exchanges and...
1 mg/kg/day corticosteroids. Colonoscopic examination confirmed the activity of Crohn’s disease (ileal and colonic biopsies showed cryptic abscesses and infiltration by mononuclear cells). There was no sign of pseudomembranous colitis. Mesoalazine was continued and parenteral nutrition was necessary for 2 weeks. Diarrhoea persisted during this period. Repeated tests did not show any micro-organisms in the stools but Clostridium difficile toxin and Shiga-like toxin 2 were detected. Oral vancomycin was begun and digestive symptoms completely disappeared within 2 weeks. Renal outcome was excellent since the patient left the hospital with a serum creatinine concentration of 60 μmol/l.

Discussion

We describe here for the first time the association of Crohn’s disease and HUS. In both cases, the diagnosis of Crohn’s disease was made several years before the occurrence of acute renal failure, by clinical, radiological, and histological findings. Shiga-like toxin was present in the stools of the second patient, who also had Clostridium difficile toxin. The latter has never been incriminated as a cause of HUS, although there are occasional reports of pseudomembranous colitis associated with HUS [4].

There is now some evidence that thrombosis at the microvascular level plays a major role in the pathogenesis of inflammatory bowel disease. Microthrombi formation and thromboembolic complications occurring in patients with Crohn’s disease are increasingly reported and are associated with a high mortality [5,6]. The thrombogenic process is documented in the mucosal capillaries of the gastrointestinal tract with multifocal gastrointestinal infarctions [5], but also in the large-sized arteries, such as cerebral arteries [7] and in the veins [8]. In a recent study it has been estimated that multiple thrombotic episodes occurred in 13% of patients with Crohn’s disease [9].

In HUS, the formation and the persistence of microthrombi is linked to increased plasma level of type 1 plasminogen activator inhibitor (PAI-1) [10]. Similarly, in Crohn’s disease, impaired fibrinolytic response to the venous occlusion test, with decreased tissue-type plasminogen activator release and residual PAI-1 activity has been described [11]. Increased coagulability has also been proposed as an important mechanism involved in the formation of microthrombi [12], and heparin treatment has been associated with clinical improvement in small, uncontrolled studies [13]. A recent study examined the clinical setting of thromboembolic events in 52 patients with Crohn’s disease or ulcerative colitis. Specific coagulation defects were absent in most cases. In these patients, the development of thrombosis was related to active bowel inflammation and increased mortality was associated with thrombosis [9]. To our knowledge, if mucosal capillary microthrombi are frequently seen on bowel biopsies in patients with Crohn’s disease, extradigestive capillary thrombi are rare [14]. A recent paper reports the case of a woman in whom Crohn’s disease was diagnosed concomitantly with thrombotic thrombocytopenic purpura [14]. This case and our two patients suggest that thrombotic microangiopathy can be considered as one of the thrombotic complications of Crohn’s disease. They strengthen the hypothesis that microthrombotic process is an important feature in the pathogenesis of Crohn’s disease.

References


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