Uncommon presentation of granulomatosis with polyangiitis in association with subclinical coeliac disease

Sirs,

Granulomatosis with polyangiitis (GPA) is a systemic necrotising vasculitis affecting mainly the respiratory tract and the kidneys. Liver and spleen involvement in GPA is rare, though potentially fatal. On the other hand coeliac disease (CD) is a disorder caused by an immunologic response to gluten. Approximately 40% of patients with positive serologic tests consistent with CD have no symptoms. We report on a patient who presented with hepatosplenomegaly and diagnosed with biopsy proven GPA and subclinical CD.

A 35-year-old man was admitted to the hospital with arthralgias, myalgias, fevers, weight loss and hepatosplenomegaly. A few hours later he presented abdominal pain without nausea. Past medical history was unremarkable. Laboratory evaluation showed elevated aspartate aminotransferase: 123 U/L (10–35), alanine aminotransferase:77 U/L (10-35), gamma-glutamyl transpeptidase: 144 U/L (10–52) and alkaline phosphatase: 254 U/L (35–125) as well as aldolase: 11,8 (0–7.7) U/L. Erythrocyte sedimentation rate was 42mm/1st hour and C-reactive protein was 79 mg/l (normal values<6). The haematocrit, haemoglobin level, glucose, electrolytes, creatinine, total protein and thyrotropin were normal. Urine test was positive for protein +2 and for haemoglobin +2. Blood and urine cultures were sterile. Tuberculosis skin test and interferon gamma release assay were negative. Tests for B and C hepatitis as well as human immunodeficiency virus were negative. Syphilis, brucellosis, leishmaniasis were excluded while immunoglobulin G (IgG) antibodies for Epstein Barr and cytomegalovirus were positive. Chest x-ray showed no pulmonary opacities. Chest computed tomography (CT) showed multiple nodules (up to 1cm) and ground glass areas. CT of the abdomen confirmed hepatomegaly and splenomegaly (Fig. 1.a). Heart sonography and electromyography were unremarkable. Endoscopic examination of upper gastrointestinal tract showed superficial gastritis. Biopsy of small intestine showed findings compatible with CD. IgA anti-gliandin and anti-transglutaminase antibodies as well as endomysial antibodies were positive. Subclinical CD was diagnosed.

Liver biopsy revealed nonspecific inflammation without fibrosis. Total protein of 24-hour urine collection was 5gr/day. The patient underwent bronchoscopy which complicated with haemoptysis, dyspnea and radiographic alveolar infiltrates compatible with haemorrhage. Immunologic evaluation showed anti-neutrophil cytoplasmic antibodies (C-ANCA): 1/80, proteinase-3 positive and renal biopsy revealed pauci-immune necrotic glomerulonephritis with crescent formation (Fig. 1.b). A diagnosis of GPA was made and the patient was treated with pulses of methyl-prednisolone: 1g/day for 3 days followed by prednisolone 1mg/kg/day and pulses of cyclophosphamide 0.5gr/m^2/15 days. Three months later he showed clinical and laboratory improvement. He continues treatment with steroid tapering.

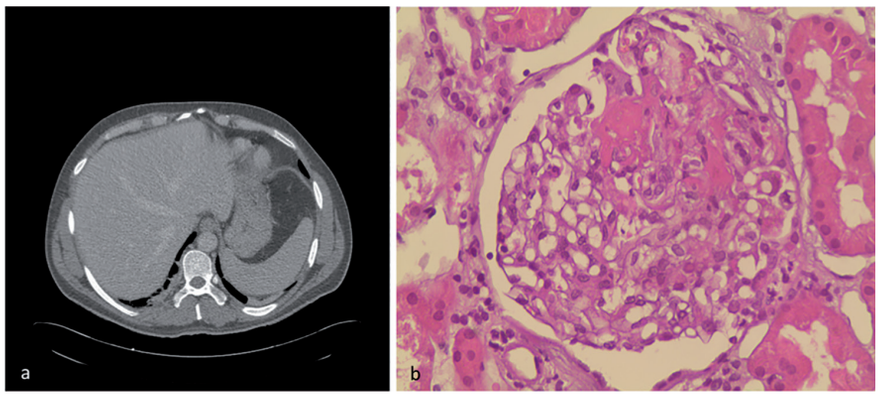

Fig. 1. a: Abdomen computed tomography: hepatomegaly and splenomegaly; **b**: Segmental glomerular fibrinoid necrosis in an early stage without prominent crescent formation (H&E X 400).

GPA is a C-ANCA positive multisystem vasculitis (1, 2). Fever is present in 23% of patients while arthralgias and myalgias are common (33%) at disease onset. True inflammatory myopathy is unusual (3). Liver involvement in GPA is rare and is associated with severe disease. Granulomatous necrotising hepatic involvement and mild nonspecific lobular hepatitis have been described (4-7). Both a cholestatic and a hepatocellular pattern have been reported in 2–25% (6). Wegener in 1936 described splenic lesions in 2 of the 3 patients with GPA. Spleen involvement in GPA includes splenomegaly, capsular adhesion, dysfunction and infarction (8, 9). Autopsy studies have shown a high percentage (78–100%) of spleen lesions such as vasculitis, granuloma formation, necrosis and capsulitis (9). Asymptomatic spleen involvement seems quite common, usually detected as an incidental finding on imaging studies. Abdominal pain and vomiting have been described in splenic infarction (9) which may be complicated with abscess, bleeding, rupture and functional hyposplenism.

On the other hand, mild increase in transaminases may be present in patients with CD. GPA in association with CD may share common genetic background. Thus, polymorphisms of genes such as Cytotoxic T lymphocyte antigen-4 and protein tyrosine phosphatase non-receptor type 22 offer susceptibility for CD and ANCA associated vasculitis (10).

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