We report a case of a 25-year-old female with juvenile onset systemic lupus erythematosus who developed systemic secondary amyloidosis with renal and gastrointestinal involvement. She has also had radiological signs of bilateral asymptomatic sacroiliitis without lower back pain or HLA-B27 antigen.

Key words  Systemic lupus erythematosus · Secondary amyloidosis · Sacroiliitis

Introduction

Systemic lupus erythematosus (SLE) is characterized by cutaneous manifestations, serositis, non-erosive arthritis, immune complex nephritis and typical immunological changes. Systemic secondary (reactive) amyloidosis (AA) is mainly encountered as a complication of chronic rheumatic diseases, particularly rheumatoid arthritis, juvenile chronic arthritis and ankylosing spondylitis, but has been rarely reported in SLE [1–10]. Sacroiliitis is the characteristic feature of patients with seronegative spondyloarthropathy. The association between sacroiliitis and SLE has rarely been described [10–13].

In this report, we present a SLE patient with the development of systemic amyloidosis involving the kidney and gastrointestinal tract and with asymptomatic bilateral sacroiliitis. The patient is on continuous treatment with immunosuppressive agents.

Case report

We present a 25-year-old female patient who has had systemic lupus erythematosus (SLE) since the age of 14 years. When this patient first presented to our department in 1987, she had a 1-year history of skin lesions, photosensitivity, fever, and pain in both hands, elbows and knees. On examination, we observed butterfly rash, alopecia, palmar and solar erythema and systemic fever. The initial laboratory tests showed the following: haemoglobin 7.8 g/dl; haematocrit 25%; leucocyte and platelet counts were normal; erythrocyte sedimentation rate was 130 mm/h; C-reactive protein was normal; urinary analysis showed proteinuria (<500 mg/day) and haematuria; positive anti-nuclear antibody (ANA; ++++, linear); anti ds-DNA antibodies were 96.14 IU/ml; hypocomplementaemia and polyclonal hypergammaglobulinaemia.

This patient fulfilled the 1982 revised American Rheumatism Association (ARA) criteria for the classification of SLE [14]. She was initially treated with anti-malarial and nonsteroidal anti-inflammatory drugs. A kidney biopsy showed only three glomeruli with a mild increase in the mesangial matrix. Clinical and laboratory features were stable with corticosteroid and azathioprine treatment between 1987–1992.

In December 1992, digital ulcers and ecchymoses developed on fingers and extremities, respectively. Furthermore, thrombotic events occurred in the venous system of the lower extremities. IgG anti-cardiolipin antibodies (ACA) were found to be high (22.5 GPL U/ml, normal value <15 GPL). These findings confirmed the presence of secondary antiphospholipid syndrome and low-dose aspirin was added to the treatment.

We observed that proteinuria increased (900 mg/day) and haematuria occurred despite treatment with corticosteroids and azathioprine. The anti-ds-DNA level was 130 IU/ml and serum C3 and C4 levels were low. The patient refused a second renal biopsy. In July 1995, proteinuria reached 2.6 g/day, serum albumin was 3.6 g/dl and total protein was 8.6 g/dl. Hypertension and oedema were not present. In August 1995, a second renal biopsy showed by hematoxylin and eosin staining, eosinophilic mesangial and basement membrane deposits with capillary narrowing and distortion of the glomeruli. Deposits showed birefringence under polarised light when stained with Congo red which stains metachromatically (Fig. 1). Granular depositions of IgG, IgM and C3 were observed along the basement membrane in most glomeruli by direct immunofluorescence.

Depositions resembling amyloid were also observed in rectal, gastric and duodenal biopsy specimens, but there was no indication of digestive involvement. Immunohistochemical staining revealed amyloid associated (AA) protein and P component in these locations (Fig. 2). Amyloid light chain (AL), transthyretin (TTR) and beta 2-microglobulin were negative.
Other systems were investigated to reveal the extent of systemic amyloidosis. The ventricular function and volumes of the heart were normal by echocardiography. There was no organomegaly. Radiologic examination showed sacroiliitis; tomography revealed blurred joint surfaces and subchondral sclerosis of the right iliosacral joint and width of the joint space, and subchondral sclerosis on the left joint (Fig. 3). The patient had not experienced back pain in the past or up to that time. Sacroiliac scintigraphy confirmed bilateral sacroiliitis.

HLA typing was A2, A11, B5, Bw4, DR2, DQ1. As noted, HLA-B27 was negative. Immunological tests were repeated and showed that ANA was positive (+++, linear), and anti-ds-DNA levels were 155 IU/ml. Hypocomplementaemia and polyclonal hypergamma-globulinaemia persisted.

Discussion

The secondary or reactive form of systemic amyloidosis is the AA type in which the fibril is derived from the acute phase protein serum amyloid A [15]. The disorders associated with AA deposition are chronic infectious diseases and noninfectious inflammatory conditions. In this patient there was no chronic infectious or inflammatory disease other than SLE. In the literature only a few cases on the development of AA type amyloidosis in SLE have been reported [1–10]. In most of the reported cases, the patient had suffered from long-standing SLE [1–3, 9]. In our patient, the interval between the onset of SLE and the diagnosis of amyloidosis was 10 years. The clinical course and the presence of AA-type amyloid fibrils detected by immunohistochemistry suggests the development of amyloidosis secondary to an underlying inflammatory disorder. Renal involvement is usually seen in systemic AA deposition. In all reported patients with SLE, the most frequently involved organ was the kidney [1–3, 6, 7, 10]. Renal with pulmonary [6], pulmonary alone [4, 5], gastrointestinal [7, 8] and hepatic involvement [9] have also been described. Postmortem examinations have revealed the deposition of amyloid in the heart, spleen [1], liver, skin and other connective tissues [7]. Renal involvement may vary from mild proteinuria to nephrotic syndrome. In our patient, proteinuria increased from 900 mg to 2.6 g/day in 1 year time and nephrotic oedema has not yet occurred.

Immunofluorescence findings demonstrate positive staining for IgG, IgM and C3 along the basement membrane in most glomeruli. Ter Borg et al. reported immune deposits in the mesangium and the glomerular basement membrane in a SLE patient with secondary amyloidosis [3]. Marenco et al. reported that open lung biopsy revealed lupus pneumonitis with positive staining for immunoglobulins and complement and pulmonary amyloidosis [4].

Early diagnosis is rare in the asymptomatic patients with gastrointestinal amyloidosis. In two SLE patients presenting with recurrent diarrhoea and gastrointestinal bleeding, the amyloid deposition was reported in the gastrointestinal tract [7, 8]. Our patient had no gastrointestinal symptoms. Amyloid deposits were also revealed in rectal, duodenal and gastric biopsy specimens after the diagnosis of renal amyloidosis.