Letters to the Editor

Systemic lupus erythematosus in a patient with beta-thalassemia major

Sirs,

Systemic lupus erythematosus (SLE) is an autoimmune disease while beta-thalassemias are common hereditary disorders which result in reduced or absent beta-globin chain synthesis. Although the coexistence of sickle cell disease and SLE has been described (1) the occurrence of beta-thalassemia with SLE is rare (2, 3). We describe the case of a man with beta-thalassemia major and SLE affecting mainly the joints and kidneys.

A 37-year-old Greek man presented at the outpatient Rheumatology Clinic of the University Hospital of Ioannina on October 2002 with fatigue, arthritis, fever (38°C), anemia and acute renal failure. In 1974 beta-thalassemia major had been diagnosed based on hemoglobin (Hb) electrophoresis and genotype characterization and the patient was being followed up in the Hematology Clinic. Blood transfusions have been required since 1989 and desferoxamine was administered regularly.

Physical examination revealed moderate hepatomegaly, arthritis of the knees and wrists, and icteric conjunctiva. Laboratory results showed Hb: 7.4 g/dl, erythrocyte sedimentation rate: 131 mm/h, creatinine 2.2 mg/dl, urea 99 mg/dl, total billirubin 3.1 mg/dl (direct 0.74 mg/dl), and direct Coombs positive. Twenty-four hour urine protein was 648 mg. The immunological evaluation showed positive antinuclear antibodies (ANA) (title: 1/1280, homogenous pattern), positive anti-dsDNA antibodies: 79 IU/ml (negative < 10 IU/ml), C_3: 75 mg/dl (range 79-181 mg/dl), and C_4: 5 mg/dl (range 16-64 mg/dl). Transfusions of red packed cells and hydration were administered. Renal biopsy showed mesangial glomerulonephritis type II. Thus, SLE was diagnosed according the American College of Rheumatology revised criteria (4).

The patient was treated with methylprednisone (60 mg/day) followed by tapering and remission 6 months later. In addition, lymphocyte characterization revealed a low CD_4^+:CD_8^+ ratio of 0.71 and the HLA typing was A2, A30, B14, B18, CW2, CW8, DR1, DR16, DQ5 and DQ51. In November 2004, the patient had normal renal function and no arthritis. The Coombs test was negative, C_3 and C_4 had returned to normal while anti-dsDNA and ANA remained positive. His current treatment includes small doses of steroids, folic acid, calcium and vitamin D supplementation.

The coexistence of SLE and beta-thalassemias is extremely rare. To date, only two cases of sickle cell/beta-thalassemia with SLE have been described (2, 3). In addition, SLE patients with beta-thalassemia trait have been reported (5), while osteonecrosis in a patient with hemoglobin E/b thalassemia has been recently published (6). At the best of our knowledge this is the first report of the coexistence of SLE and beta-thalassemia major.

The relationship between the two diseases remains unclear. Genetic factors may contribute to their pathogenesis. Our patient had gene mutation resulting in abnormal beta-globin chain synthesis and HLA typing: B18, DR16 that have been associated with lupus. Furthermore, multiple transfusions may alter the immunological response of thalassemia patients. Experimental transfusion of plasma containing alloantibodies has been shown to lead to autoantibody formation. Therefore, the immune status of the patient as well as the effect of multiple allogeneic blood transfusion can induce antibody formation. The perpetuation of antibody formation may result from the continuous stimulation of the immune system.

Autoantibody production has been described in thalassemia patients (7) with variable clinical significance. They may exhibit the characteristics of natural autoantibodies or, under unclear circumstances, they may become the pathogenic autoantibodies that are found in SLE. It is known that T cell subsets play a pivotal role in the pathogenesis of SLE. On the other hand, T lymphocytes from thalassemic patients are activated *in vivo* and they present several abnormalities. Thus, the lymphocyte background in thalassemic patients may under the influence of a triggering factor contribute to the development of SLE. Our patient had a low CD_4^+:CD_8^+ ratio, which has been described in lupus nephritis patients (8). In addition desferoxamine, which modifies T-cell-mediated immune responses, may also play a role in SLE expression (9, 10).

In conclusion, we described a patient with beta–thalassemia major and SLE. Further studies will clarify whether the association of these two diseases is real or if it constitutes an occasional coexistence.

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Seronegative spondyloarthropathy associated with Takayasu's arteritis in a child

Sirs,

Takayasu's arteritis (TA), a relatively uncommon disease in childhood, is a chronic idiopathic vasculitis that involves the aorta and its main branches (1). Ankylosing spondylitis is characterized by progressive inflammatory arthritis of the spinal and sacroiliac joints (2). Both of the diseases are infrequent and their association is even more rare.

A 14-year-old girl with a history of leg and low back pain for 4 years, who had previously been followed at various centers with the diagnosis of acute rheumatic fever and juvenile rheumatoid arthritis was admitted to our hospital. She had been operated on for a right ureteropelvic stricture one year ago. Two months after the operation the patient was admitted to her local hospital with signs of severe hypertension unresponsive to medical treatment. Radiological examinations that included DMSA angiography

revealed that her left kidney had become nonfunctional. Left nephrectomy was carried out, after which her hypertension was controlled. However, after 6 months her hypertension returned and radiological examination showed multiple stenoses throughout a long segment from the origin of the right renal artery. Based on these findings the diagnosis of "unclassified vasculitis" was made and therapy with prednisolone and cyclophosphamide was started.

When the patient was admitted to our clinic, she had a history of low back pain that was worse in the early morning hours and after prolonged rest. The pain diminished with physical activity. On physical examination, she showed growth retardation (height and body weight under the 3rd percentile), blood pressure 150/90 mmHg, and decreased amplitude of her pulses; differences of more than 20 mmHg in the blood pressure between the two arms was noted. A murmur was heard over the carotid regions bilaterally. Articular examination revealed severe spine limitation, loss of lumbar lordosis and an abnormal Schober test. A complete blood count, urinalysis and kidney function tests were all normal. The erythrocyte sedimentation rate (ESR) was 66 mm/hr, and C-reactive protein (CRP) was 52 mg/L. Renal artery Doppler US revealed stenosis throughout a long segment of right renal artery. Angiography depicted a high degree of stenosis in the right carotid artery (Fig. 1), irregularity in the proximal part of the left carotid artery, stenosis in the superficial femoral artery, and segmental occlusion of the superior mesenteric artery in its proximal portion, confirming the diagnosis of Takayasu arteritis. Sacroiliac MRI, planned for the etiology of low-back pain, revealed sacroileitis. She was negative for HLA B27 and RF. Treatment with doses 40 mg/day of corticosteroid and 2 mg/kg/day of azathioprine was started. One month after the beginning of treatment ESR and CRP values returned to normal and control imaging studies are scheduled for 6 months later.

The case presented here shows that TA remains a challenge for clinicians. It has been reported to occur in association with certain diseases including rheumatoid arthritis, Still's disease, polymyositis, polymyalgia rheumatica and ankylosing spondylitis (3). Sacroiliac MRI to study the etiology of our patient's inflammatory low back pain revealed bilateral sacroileitis. The absence of a family history, uveitis and HLA B27 are consistent with the diagnosis of seronegative juvenile onset spodyloarthropathy. Review of the published work revealed only a few patients with seronegative spondyloarthropathy and a small number of these were in the pediatric age (4-10). The cause of the occurrence of two such rare diseases together is unknown, but a common immunological mechanism or undefined genetic susceptibilities have been proposed in the pathogenesis of TA and ankylosing spondylitis (1, 4). Our patient's history and clinical course led us to believe that the two diseases had a simultaneous onset. However, the predominance of symptoms such as leg and low back pain that are not specific for TA resulted in the delay of the diagnosis and the progression of arterial involvement.

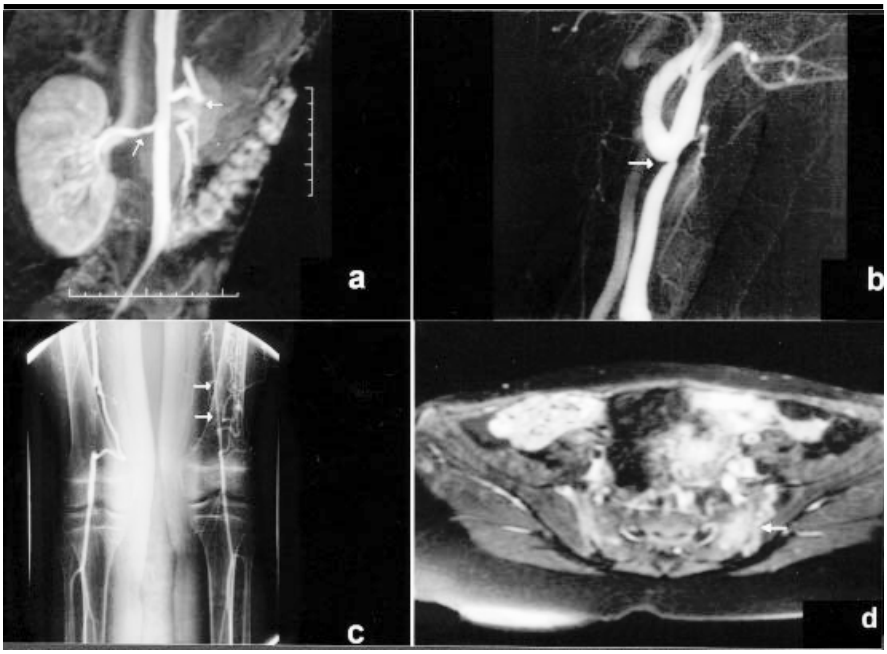

Fig. 1. Angiography showing stenosis of right renal artery and the segmental occlusion of superior mesenteric artery (**a**), high grade stenosis of the right common carotid artery (**b**), and stenosis in the superficial femoral artery (**c**). Contrast-enhanced axial T1-weighted MR image reveals bilateral sacroileitis (**d**).

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