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.

P.V. VOULGARI[1], *MD, Lecturer*
A. KARALI[2], *MD, Fellow*
V. ALYMARA[2], *MD, Fellow*
A. CHAIDOS[2], *MD, Fellow*
K.L. BOURANTAS[2], *MD, Professor*
A.A. DROSOS[1], *MD, FACR, Professor*

[1]Rheumatology Clinic and [2]Haematology Clinic, Department of Internal Medicine, Medical School, University of Ioannina, Ioannina, Greece.

Address correspondence to: Prof. Alexandros A. Drosos, MD, FACR, Rheumatology Clinic, Department of Internal Medicine, Medical School, University of Ioannina, 45110 Ioannina, Greece. E-mail: adrosos@cc.uoi.gr

References

1. SAXENA VR, MINA R, MOALLEM HJ, RAO SP, MILLER ST: Systemic lupus erythematosus in children with sickle cell disease *J Pediatr Hematol Oncol* 2003; 25: 668-71.
2. KALOTERAKIS A, FILIOTOU A, HAZIYANNIS A, VAIOPOULOS G, LUTRADI–ANAGOSTOU A: Sickle cell/beta-thalassemia and systemic lupus erythematosus (letter). *Lupus* 1999; 8: 778-81.
3. FLANAGAN G, PACKHAM DK, KINCAIND-SMITH P: Sickle cell disease and the kidney. *Am J Kidney Dis* 1993; 21: 325-73.
4. HOCHBERG M: American College of Rheumatology revised criteria for the classification of systemic lupus erythematosus. *Arthritis Rheum* 1997; 39: 403-4.
5. CASTELLINO G, TROTTA F, GOVONI M: β-thalassemia trait and systemic lupus erythematosus (letter). *Clin Exp Rheumatol* 2004; 22: 382-3.
6. UPPAL SS, MAROUF RA, AL MUTAIRY M, AL HERZ, KORTOM MA, AL WAZAN H: First report of osteonecrosis of the calcaneum in a young Kuwaity female with hemoglobin E/beta thalassemia (letter). *Clin Exp Rheumatol* 2003; 21: 522.
7. VOULGARI PV, CHAIDOS A, TZOUVARA E *et al.*: Antierythropoietin antibodies in thalassemia patients. *Ann Hematol* 2004; 83: 22-7.
8. SMOLEN JS, MORIMOTO C, STEINBERG AD *et al.*: Systemic lupus erythematosus: delineation of subpopulations by clinical, serologic, and T cell subset analysis. *Am J Med Sci* 1985; 289: 139-47.
9. SAHASRABUDHE DM, DUSEL J, JEDLIKA S: Suppression of delayed type hypersensitivity by desferoxamine. *J Immunother* 1991; 10: 112-9.
10. YU TW, ANDERSON D: Reactive oxygen species-induced DNA damage and its modification: a chemical investigation. *Mutal Res* 1997; 379: 201-10.

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