Progressive Systemic Sclerosis Complicated with Immune Thrombocytopenia during D-penicillamine Therapy

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Immune thrombocytopenia is a rare complication of progressive systemic sclerosis (PSS). A 47-year-old female with PSS treated with D-penicillamine developed immune thrombocytopenia, which promptly responded to prednisolone and withdrawal of D-penicillamine. Platelet-associated IgG was elevated and the bone marrow megakaryocyte count was normal. There was an inverse relationship between the level of platelet-associated IgG and the platelet count. A lymphocyte stimulation test sensitized by D-penicillamine was positive. The present case suggests that immune thrombocytopenia may be regarded as one of the D-penicillamine-related immune abnormalities. To our knowledge, its association with PSS has never been reported.

Key words: platelet-associated IgG, drug-induced thrombocytopenia

Introduction

Thrombocytopenia is a rare but recognized complication of progressive systemic sclerosis (PSS) (1-4). Although immune mechanisms have been suggested to be partly responsible for thrombocytopenia in PSS, platelet-associated IgG (PAIgG) has not been assayed previously (1-4). This appears to be the first case report of D-penicillamine-induced immune thrombocytopenia developing in a patient with PSS.

Case Report

A 47-year-old Japanese woman was first seen at the University of Tsukuba Hospital in 1981 because of Raynaud's phenomenon of an 8 year duration. A diagnosis of PSS was made on the basis of proximal scleroderma. In February 1987 D-penicillamine (100 mg/day) treatment was started. Her platelet count just before D-penicillamine therapy was 217,000/µl. In October 1987, a bleeding tendency was noted. In February 1988, the patient was admitted because of nasal and gingival bleeding.

Physical examination revealed skin and palatal petechiae, nasal and gingival bleeding, tight facial skin, sclerodactyly and crepitant rales at the base of both lung fields. Sensory loss corresponding to bilateral ophtalmic and maxillary nerves was noted. There was no hepatosplenomegaly.

Examination of the blood showed a hemoglobin level of 10.7 g/dl, a white cell count of 5,700/µl with a normal differential count, and a platelet count of 13,000/µl. Bone marrow aspiration smears revealed roughly normal numbers of nucleated cells and megakaryocytes, but clot section could not be made due to insufficient amounts of aspirates. Erythrocyte sedimentation rate was 52 mm/h. Blood chemistry and urinalysis were normal. Roentgenogram of the chest disclosed a diffuse reticulonodular shadow in the lower lung fields bilaterally.

Serological and immunological tests were as follows: CRP was negative, C3, C4 and CH50 were within the normal limits. Serologic test for syphilis was negative. Immunoglobulin analysis revealed IgG 3,164 mg/dl, IgA 500 mg/dl and IgM 73 mg/dl. Antinuclear antibody was strongly positive with a speckled pattern. Anti-RNP antibody was strongly positive, however, anti-Scl-70 antibody and anti-DNA antibody was negative. Direct and indirect Coombs tests were negative. PAIgG level was elevated at 820 ng/10^7 cells (N 9 to 25).

D-penicillamine was withdrawn and prednisolone,
Discussion

Thrombocytopenia is a rare complication of PSS (1–4). Three etiological elements have been suggested: 1) complication of Coombs positive hemolytic anemia and/or SLE (1, 2), 2) microangiopathic hemolytic anemia secondary to scleroderma kidney (2), 3) incidental combination of idiopathic thrombocytopenic purpura (1–4). Although D-penicillamine-induced bone marrow suppression is widely known (5, 6), immune thrombocytopenia due to D-penicillamine has not been reported to our knowledge.

In the present case, the levels of PAIgG were measured by a micro ELISA technique (7). The level of PAIgG when the platelet count was 8,000/μl, was 820 ng/10^7 cells. Although this value of PAIgG seems very high, a close inverse correlation (r = 0.96 p < 0.05) between the platelet counts and the levels of PAIgG observed in this patient makes this elevated value creditable.

In this patient, thrombocytopenia appeared after 6 months of D-penicillamine therapy. A lymphocyte stimulation test using D-penicillamine-sensitized mononuclear cells collected before steroid therapy revealed an abnormal stimulation index indicating sensitization to D-penicillamine (Table 2). It is difficult to explain why thrombocytopenia recurred 10 months after the withdrawal of D-penicillamine. Haberhauer found that D-penicillamine-induced anticentromere antibody persists 8–16 months after D-penicillamine withdrawal (8). D-penicillamine has been shown to be excreted slowly from the soft tissues and skeletal system in animals (9). It seems possible that D-penicillamine-induced immune abnormalities may persist for some months after the drug withdrawal.

References