Lethal Pancytopenia Associated with Chilblain Lupus Erythematosus

Sir,

Chilblain lupus erythematosus is a rare form of chronic lupus presenting with relapsing chilblains of the fingers, toes and, more rarely, ears and nose. It is predominantly seen in women and is often associated with, or preceded by, facial discoid lesions (1). Treatment of acral lesions is disappointing. Transformation to systemic lupus erythematosus (SLE) is rare and has been estimated by Millard & Rowell (1) to occur at a rate of 17.6%. In this series, neurologic and renal complications seemed to be predominant. We describe here a case of chilblain lupus erythematosus associated with severe pancytopenia with a fatal outcome.

CASE REPORT

A 70-year-old woman presented with a 6-month history of relapsing chilblains of the fingers, toes, nose and ears, occurring in the winter. She had a 30-year history of Raynaud's phenomenon. Her general state of health was good. Physical examination showed livid, purplish-blue discoloration of the backs of the arms and fingers and the toes, nose and ears. There were no sign of viral infection and she was not receiving any myelotoxic treatment.

Biological tests showed mild pancytopenia (leukocytes 2.56×10^9/l, neutrophils 1.69×10^9/l, hemoglobin 119 g/l, platelets 82×10^9/l) and the erythrocyte sedimentation rate was 30 mm/h. Tests for anti-cardiolipid antibodies, cryoglobulin and antiplatelet antibodies and Coombs test were all negative. Tests for antinuclear antibodies were positive (1/20) and the C_3 component was slightly reduced (49 mg/l; normal 55–93 mg/l). Levels of serum folates and vitamin B_{12} and red blood cell folates were normal.

Histological examination of a skin biopsy showed epidermal acanthosis with orthokeratosic differentiation and some focal keratinocyte necrosis within the suprabasal layers. Perivascular mononuclear cells were present within the dermis. A direct immunofluorescence study was positive along the dermoepidermal junction with anti-C3 antibody. Cytological examination of bone marrow aspirate revealed mild hypoplasia, without either cytologic abnormalities or myelodysplasia. Sideroblastic score was normal and bone marrow biopsy did not reveal any signs of medullar invasion, necrosis, myelofibrosis or hemophagocytosis. Growth of a normal bone marrow culture in the presence of the patient's serum was inhibited. This may indicate that the serum contained factors which inhibited medullar growth.

The chilblains worsened the following winter, despite treatment with diltiazem and hydroxychloroquin. Pancytopenia worsened (hemoglobin 104 g/l, leukocytes 2×10^9/l, neutrophils 1.24×10^9/l, platelets 85×10^9/l), with an increase in antinuclear antibodies to 1/400. Corticosteroids were administered at 1 mg/kg/day, with an initial improvement in cutaneous and hematologic signs; however, pancytopenia always recurred as treatment was tapered, so that corticotherapy could not be stopped.

Three years after the onset of chilblains the patient was hospitalized for severe pancytopenia (hemoglobin 86 g/l, leukocytes 1.18×10^9/l, neutrophils 0.74×10^9/l, platelets 37×10^9/l), despite corticotherapy. She died from severe infection and cerebral hemorrhage.

DISCUSSION

Chilblain lupus erythematosus was established by the presence of the following criteria: perniotic skin lesions; direct immunofluorescence findings from the skin biopsy; and elevated antinuclear antibodies. This is the second case of chilblain lupus with pancytopenia. Kelly & Dowling (2) described a patient with perniotic lesions, pancytopenia, monocytosis and myeloid hyperplasia on a myelogram, consistent with the diagnosis of chronic myelomonocytic leukemia. This hematologic disease was associated with chilblains in other cases (3). In our case, bone marrow examination revealed medullar hypoplasia without neoplastic invasion or clonal proliferation. Coombs test and tests for anticardiolipid antibody were negative. Inhibition of the proliferation of normal bone marrow by the patient's serum could be due to the presence of a humoral factor able to inhibit differentiation or proliferation of stem cells. This factor could be an antibody or a cytokine.

Bailey et al. (4) described a case of SLE with central pancytopenia and found an IgG antibody that inhibited culture of both blast-forming units-erythroid and granulocyte-macrophage progenitor cells (CFU-GM). This antibody disappeared after treatment with corticosteroids and plasmapheresis, with remission of lupus pancytopenia. However, peripheral T-lymphocytes may inhibit colony-forming megakaryocytes (5) and CFU-GM (6) in some cases of SLE.

Pancytopenia was the sole non-cutaneous manifestation in our case, but it was fatal. It could be due to myelodysplasia, which occurs frequently at this age. However, pancytopenia and chilblain lupus erythematosus were diagnosed simultaneously and both diseases worsened in parallel, so that they could be causally related. This emphasizes the possible gravity of chilblain lupus erythematosus and the difficulty of treating this rare form of chronic lupus erythematosus.

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