A rare case of multiple myeloma associated with severe Coombs-positive hemolytic anemia is described. A 60-year-old woman was hospitalized for acute hemolysis due to an IgG warm autoantibody with panagglutinin specificity. Serum and urine electrophoresis revealed the presence of a monoclonal IgGk protein and a BJk protein, respectively. Bone marrow aspirates showed diffuse infiltration with plasma cells, and skeletal survey revealed lytic lesions in the skull and diffuse osteoporosis. Treatment with prednisone, and subsequently with melphalan, cyclophosphamide and vincristine resulted in hematological improvement within two weeks. A reduction of paraprotein below 50% of the initial levels was found after six months of therapy.

Key words: multiple myeloma, autoimmune hemolytic anemia

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classical multiple myeloma with Coombs-positive hemolysis have been reported. A possible autoimmune Coombs-negative hemolytic anemia was recently reported by Patel and Salamassi in a patient with IgG multiple myeloma. This patient had a marked anemia with low serum haptoglobin levels, renal failure, and elevated total serum proteins. The autoimmune nature of the hemolysis was deduced from its response to treatment with prednisone. Ludwig and Pavelka reported on a case of multiple myeloma with phagocytic plasma cells and a weakly positive Coombs’ antiglobulin test.

In our patient the diagnosis of multiple myeloma was clear. The eluted autoantibody from the surface of the erythrocytes was an IgG warm antibody with panagglutinin specificity. There was no evidence that the serum IgG paraprotein was the same molecule as that of the autoantibody since the indirect Coombs’ antiglobulin test was negative.

The pathogenesis of autoimmune hemolytic anemia in myeloma patients is unclear; multiple myeloma is a B-cell malignancy. Autoimmune Coombs-positive hemolytic anemia is observed in approximately 8-15% of patients with B-cell chronic lymphocytic leukemia. It has been suggested that marked immune disturbances in this disorder may allow normally suppressed clones to develop and produce autoantibodies against red cell surface antigenic molecules. However, the incidence of autoimmune hemolytic anemia in myelomatosis is extremely low despite the presence of pronounced immune abnormalities. These observations indicate that unknown factors other than immunosuppression are probably implicated in the pathogenesis of autoimmune hemolytic anemia in multiple myeloma.

Discussion

Coombs-positive autoimmune hemolytic anemia in myelomatosis is a very rare phenomenon. To our knowledge, only seven cases of

References


Atins 2.3 g/L, α2-globulins 7.1 g/L, β-globulins 8.6 g/L, and γ-globulins 37.8 g/L. A narrow spike was observed in the γ-region on electrophoresis, which was identified immunoelectrophoretically as an IgGk paraprotein. Serum immunoglobulin levels were IgG 37.40 g/L, IgA 0.5 g/L, and IgM 0.60 g/L. Blood urea was 12.9 mmol/L, serum uric acid 387 μmol/L, creatinine 87 μmol/L, calcium 2.6 mmol/L, bilirubin 30.8 μmol/L (conjugated 7.7 μmol/L), and lactate dehydrogenase 380 U/L. No clotting abnormalities were observed. Urinalysis showed a mild proteinuria (1.25 g/L). Protein electrophoresis of 10-fold concentrated urine demonstrated a paraprotein spike with β2-mobility. This paraprotein fraction was composed of Bence Jones k light chains, as was shown by an immunofixation technique using a panel of rabbit anti-human polyclonal antibodies (Dako, Denmark). Chest x-rays and ECG were normal. Skeletal survey showed several lytic lesions in the skull and diffuse osteoporosis.

Bone marrow aspiration revealed a striking erythroid hyperplasia with some megaloblastoid features, and diffuse plasma cell infiltration. Plasma cells represented 15.4% of the 4000 nucleated cells counted.

The patient was given five units of packed red blood cells and since she was diagnosed as having autoimmune hemolytic anemia, she was immediately started on prednisone 100 mg daily. Two weeks later, the patient’s hematocrit had risen to 35.8% and the reticulocyte count had dropped to 4.5%, while the direct Coombs’ test remained slightly positive. Prednisone therapy was tapered, and the patient was treated with a vincristine-melphalan-cyclophosphamide-prednisone regimen for the underlying multiple myeloma. Complete hematological recovery and a significant decrease of the serum paraprotein below 50% of its initial value were noted after completion of six monthly courses of treatment.