LETTER TO THE EDITOR

Gold induced aplastic anaemia unresponsive to G-CSF

Sir: Haematological toxicity is the most serious adverse effect of gold treatment and may be manifested by thrombocytopenia, neutropenia or, more rarely, pure red cell aplasia or aplastic anaemia. A number of therapeutic interventions are described for stimulating marrow recovery after this complication, including anabolic steroids, plasma exchange, and thymoglobin. More recently, myeloid growth factors, as used for the treatment of haematological malignancy, have suggested the possibility of new approaches to the management of this problem. Indeed, the successful use of granulocyte macrophage-colony stimulating factor after gold induced marrow suppression has been reported. We report the case of a 55 year old woman with psoriatic arthritis, who developed aplastic anaemia after gold treatment, in whom granulocyte-colony stimulating factor (G-CSF) failed to stimulate marrow recovery.

On presentation she had active synovitis. The erythrocyte sedimentation rate was 112 mm/h and C reactive protein was 70 mg/l. Rheumatoid factor and antinuclear factor were negative and radiography showed erosive disease, mainly at the feet and distal interphalangeal joints. HLA-DR status was not known. Treatment with sulphasalazine was started but discontinued after two months because of mouth ulcers. Blood monitoring had been satisfactory. Six weeks later, treatment with weekly intramuscular gold was started. At this stage her white cell count was 9.2 × 10^9/l and platelet count 471 × 10^9/l. After a total dose of 360 mg gold had been reached the platelet count fell abruptly to 121 × 10^9/l. Gold was discontinued, but one week later she was admitted to the haematology unit with a platelet count of 6 × 10^9/l. Her other drugs—co-proxamol and diclofenac—were also discontinued.

Her white cell count, initially 5.4 × 10^9/l, fell after admission and failed to respond to high dose corticosteroids and attempts to chelate gold with N-acetylcysteine. The haemoglobin and platelet count were maintained by regular transfusion. Treatment with G-CSF was started in a dose of 1.5 µg/kg, the first three doses given on alternate days, but after a further 10 days of daily dosing this was abandoned owing to lack of effect (figure). Marrow aspirate and trephine, which initially showed a severe disturbance compatible with gold induced aplasia, was repeated after G-CSF treatment and showed even less cellularity. Supportive measures, including parenteral feeding and intensive antibiotic treatment, were continued, but she developed an invasive pulmonary mucormycosis, an infection seen exclusively in patients with a complete lack of circulating neutrophils. She died some two months after the onset of her aplasia.

In a previous review of 10 cases of gold induced marrow suppression, predating the availability of myeloid growth factors, corticosteroids were used in nine cases as in this case. Other frequently used treatments include anabolic steroids, and the use of antithymocyte globulin was highlighted. In this patient infective complications made the use of antithymocyte globulin difficult, and her age was considered a contraindication to bone marrow transplantation, though the issue was discussed. The absence of response to G-CSF probably indicates a complete lack of marrow progenitor cells at the start of treatment.

In view of both the financial and clinical implications, the place and timing of myeloid growth factor treatment and available alternative treatments deserves further discussion. Gold treatment may not now carry the mortality reported by Girdwood in 1974, but this case serves as a reminder that fatal outcomes still occur. Attempts to limit risk of serious toxicity to HLA status have not proved of practical usefulness and perhaps more discussion and experience of growth factor treatment will be valuable in further reducing the mortality in severe aplasia.

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