

Hypogammaglobulinaemia associated with gold therapy

A. K. L. SO, S. A. PESKETT, AND A. D. B. WEBSTER

From the Divisions of Rheumatology and Clinical Immunology, Northwick Park Hospital, and Department of Rheumatology, Chelmsford and Essex Hospitals.

SUMMARY Two patients with seronegative arthropathy were noted to be hypogammaglobulinaemic after receiving gold. The clinical course and features suggest that gold is a cause of immunodeficiency.

Arthritis is an unusual complication of late-onset hypogammaglobulinaemia. Septic arthritis forms a well recognised subgroup. Aseptic, non-erosive chronic polyarthritis, distinct from rheumatoid arthritis (RA), has also been described.^{1,2} Earlier reports of an arthritis indistinguishable from classical RA³ have not been found in the more recent literature. These cases probably represented unrecognised septic arthritis with mycoplasmal organisms.

Drug treatment is a known cause of hypogammaglobulinaemia, the best known examples being phenytoin and drugs used in cancer chemotherapy. Gold and penicillamine therapy in adult RA have been reported to lead to lowering of immunoglobulin levels and IgA deficiency.^{4,5} We have seen two patients who we believed became hypogammaglobulinaemic after gold therapy for seronegative arthritis.

Case reports

CASE 1

A 59-year-old female developed an asymmetric erosive polyarthritis affecting the wrists and proximal interphalangeal joints at the age of 58. Initial investigations showed negative tests for rheumatoid and antinuclear factors, normal full blood count, and an erythrocyte sedimentation rate (ESR) of 10 mm/h. X-rays of hands and wrists showed erosive changes. A diagnosis of seronegative arthritis was made. Two months later sodium aurothiomalate (Myocrisin) was started. Chrysotherapy was stopped

after 300 mg because she developed a sudden respiratory illness with persistent cough and widespread fine crepitations. Investigations showed hypogammaglobulinaemia (Table 1), and peripheral eosinophilia of $1.56 \times 10^9/l$. Hypogammaglobulinaemia persisted despite improvement of her respiratory illness. Treatment with intramuscular gamma-globulin was started, but after 14 months of therapy, there was no improvement in her joint disease.

CASE 2

A 72-year-old female presented with a painful swollen right wrist when aged 57. A synovectomy was performed, and histological examination showed chronic inflammatory changes consistent with RA. Over the next two years the disease progressed to affect her shoulders, wrists, and knee joints. Tests for rheumatoid factor were persistently negative and the ESR was initially raised at 50mm/h. Gold was started at 10 mg/week and continued at 20 mg/week. Chrysotherapy was stopped after she had received 3000 mg, when she was admitted to

Table 1 *Total globulins and serum immunoglobulins of cases 1 and 2 before and at diagnosis of hypogammaglobulinaemia*

	Case 1	Case 2	Normal range (g/l)
Immunoglobulins on diagnosis of hypogammaglobulinaemia			
IgG	0.7	1.3	4.8-10.7
IgA	0.1	0.1	0.5-3.7
IgM	0.1	0.1	0.4-2.5
Total serum globulins before gold	24	28	20-35
on diagnosis	16	16	

Accepted for publication 10 January 1984.
Correspondence to Dr A. K. L. So, Tissue Antigen Laboratory, Imperial Cancer Research Fund Laboratories, Lincoln's Inn Fields, London WC2A 3PX.

hospital with a respiratory illness characterised by dyspnoea and chest pain. Investigations at that time showed hypogammaglobulinaemia (Table 1). Two years later the immunoglobulin levels were unchanged, and she suffered recurrent upper respiratory tract infections. Immunoglobulin replacement therapy was started, but no improvement in her polyarthritis was seen after five years of treatment.

Discussion

These two patients differ significantly from previously described cases of arthritis associated with late-onset hypogammaglobulinaemia. There was no history of infections preceding the diagnosis, and their joint disease failed to respond to replacement immunoglobulin therapy. Features of septic arthritis were absent, and aspirate of a finger joint from case 1 failed to grow mycoplasmal organisms.

Both patients received parenteral gold, with benefit in case 2, until they were admitted to hospital with acute respiratory illnesses. In the light of these unusual clinical features we feel that gold therapy is the most likely cause of hypogammaglobulinaemia, and their respiratory illness may be a concurrent manifestation of toxicity to gold. Serum immunoglobulins were not measured at the onset to allow precise identification of development of immunodeficiency in relation to treatment, but indirect evidence from total serum globulins indicated that the fall occurred after the introduction of gold therapy.

Gold therapy is known to depress serum immunoglobulin levels in patients with classical RA and juvenile chronic arthritis.⁶ In adult RA the maximal suppression is in IgM, which is apparent six months after starting therapy. The duration of suppression may be for up to four years.⁴ Selective IgA deficiency has been attributed to gold and is

frequently accompanied by evidence of drug toxicity. There are no data to show if suppression of immunoglobulin levels is reversible on stopping treatment.

The mode of action of gold in the treatment of arthritis is unknown, though experimental evidence indicates that it can have an immunosuppressive effect on lymphocytes from normal subjects and patients with RA. The effect on immunoglobulin synthesis may be mediated by gold's action on monocyte/macrophage function.^{7,8}

It is important to document serum immunoglobulins in patients receiving gold, especially those with seronegative arthritis. Further studies will be needed to determine the incidence of its effects on immunoglobulins in this group of patients and the mechanisms underlying it.

References

- 1 Asherson G L, Webster A D B. *Diagnosis and treatment of immunodeficiency diseases*. Oxford: Blackwell, 1980: 37-60.
- 2 Webster A D B, Loewi G, Dourmashkin R D, Golding D N, Ward D J, Asherson G L. Polyarthritis in adults with hypogammaglobulinaemia and its rapid response to immunoglobulin treatment. *Br Med J* 1976; **i**: 1314-6.
- 3 Good R A, Rotstein J, Mazzitello W F. Simultaneous occurrence of rheumatoid arthritis and agammaglobulinaemia. *J Lab Clin Med* 1957; **49**: 343.
- 4 Lorber A, Simon P, Leeb J, Peter A, Wilcox S. Chrysotherapy: suppression of immunoglobulin synthesis. *Arthritis Rheum* 1978; **21**: 785-91.
- 5 Stanworth D R, Johns P, Williamson N, Shadforth M, Davies D F, Thompson R. Drug induced IgA deficiency in rheumatoid arthritis. *Lancet* 1977; **i**: 1001.
- 6 Barkley D O, Hohermuth H J, Howard A, Webster A D B, Ansell B M. IgA deficiency in juvenile chronic polyarthritis. *J Rheumatol* 1979; **6**: 219-24.
- 7 Lipsky P E, Ziff M. Inhibition of antigen and mitogen induced human lymphocyte proliferation by gold compounds. *J Clin Invest* 1977; **59**: 455-466.
- 8 Scheinberg M A, Santos L M B, Finklestein A E. The effect of auranofin and sodium aurothiomalate on peripheral blood monocytes. *J Rheumatol* 1982; **9**: 366-9.