

CLINICAL REPORTS

Gold-induced lung disease

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Summary

A 70-year-old female with seronegative rheumatoid arthritis developed interstitial pneumonitis while on chrysotherapy. The reversibility of lung disease and favourable response to steroid treatment support the diagnosis of gold-induced lung disease and distinguish this entity from other forms of interstitial lung disease associated with rheumatoid arthritis. The relevant literature related to gold-induced lung disease is briefly reviewed.

KEY WORDS: interstitial pneumonitis, pulmonary fibrosis, rheumatoid arthritis, gold salts.

Introduction

Interstitial pneumonitis in a patient suffering from rheumatoid arthritis presents a diagnostic problem unrecognized until several years ago.

Case report

A 70-year-old housewife was in good health until 2 weeks before her admission in February 1981. At that time she began complaining of severe joint pain involving first a few and then most of her limb joints. Examination revealed arthritis of hands, ankles and right knee with tenderness in all other limb joints with the exception of the distal interphalangeal joints. The full blood count was normal, with an erythrocyte sedimentation rate of 105 mm/hr. A search for rheumatoid factor, antinuclear factor and LE cells was negative. A diagnosis of seronegative rheumatoid arthritis was made. After a trial with full dose of 3 different anti-inflammatory drugs, given consecutively each for 7-10 days, had failed, she was started on chrysotherapy (aurothioglucose as Solganal®). At the same time, prednisone, 30 mg daily, was given for symptomatic relief. Subsequently pain

and morning stiffness improved markedly and the sedimentation rate was reduced to 25 mm/hr. Following discharge, prednisone was tapered to 10 mg/day given with 1.2 g ibuprofen. Two months following the start of chrysotherapy, after receiving a total dose of 435 mg aurothioglucose, given in weekly doses of 50 mg, she presented with a dry cough, fever, shortness of breath and general malaise of 2 days duration. On examination, she was found to be moderately dyspnoeic, with a regular pulse of 104/min, and temperature 38.2°C. Dry rales were heard over both lung bases. There was tenderness over limb joints with no swelling or redness. There was no leg oedema or cervical vein distention. Her previously normal chest X-ray showed bilateral infiltrates suggesting interstitial pneumonitis (Fig. 1). The white cell count and differential were normal, the erythrocyte sedimentation rate 65 mm/hr, and serology and urinalysis normal as before. Arterial blood gases showed marked hypoxaemia with P_{O_2} 43 mmHg, 82% O_2 saturation and a respiratory alkalosis with pH 7.5, P_{CO_2} 25 mmHg and bicarbonate 19 mmol/l.

Chrysotherapy was stopped and, after a trial of intravenous frusemide had failed, intravenous hydrocortisone, 200 mg/day, was started. Improvement was noticed within 2 days with marked alleviation of cough and dyspnoea. She was still mildly dyspnoeic 4 days after admission when pulmonary function tests were performed. These showed restrictive lung disease with marked reduction in static volumes and no evidence of obstruction. Treatment was continued with prednisone 40 mg/day. Repeat arterial blood gases a week after admission still showed respiratory alkalosis but the P_{O_2} was up to 62 mmHg with O_2 saturation of 93%. The inspiratory dry rales disappeared 2 weeks later. The patient was discharged after 18 days with no respiratory complaints. Repeat chest X-rays showed gradual improvement in the

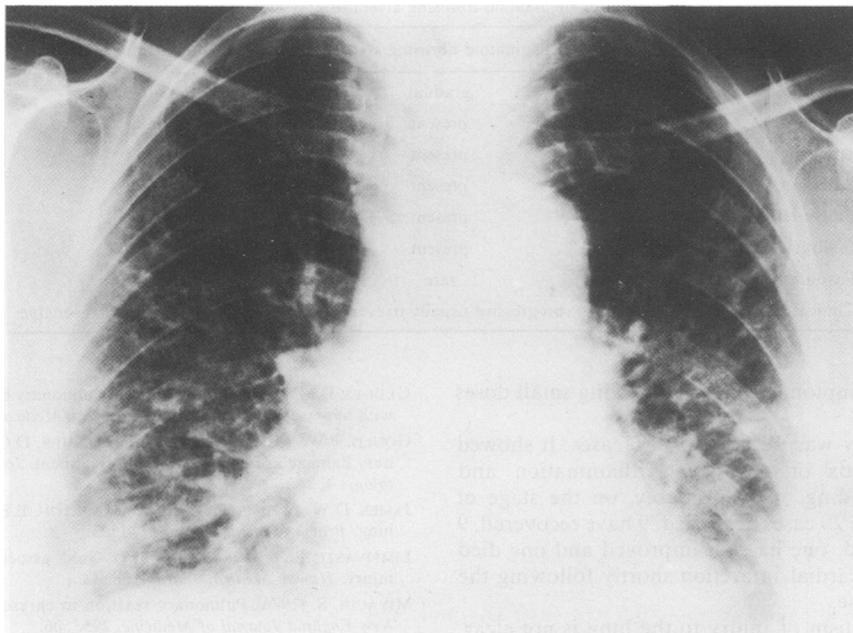


FIG. 1. Chest X-ray showing bilateral interstitial infiltrates.

pulmonary infiltrates, and 4 months later the lung fields were completely normal.

Discussion

This patient with seronegative rheumatoid arthritis presented with interstitial lung disease of acute onset. Congestive heart failure and bacterial infection were ruled out. The acute onset, rapid response to steroids and reversibility of this lung disease make cryptogenic fibrosing alveolitis, a variant of rheumatoid lung disease, or any of the other connective tissue diseases which may have pulmonary manifestations, highly unlikely. In all of these, the onset is gradual, the disease progressive, generally not responding to steroids and largely irreversible.

By exclusion, the most possible diagnosis for this patient is gold-induced interstitial pneumonitis. This entity, first described in 1948 (Savilahti, 1948) was brought to wider medical attention in 1976 (Winterbauer, Wilske and Wheelis, 1976). Since then, about 20 cases have been described in the English literature (Geddes and Brostoff, 1976; Alarcon and Gotuzzo, 1976; Scharf *et al.*, 1977; Gould, McCormack and Palmer, 1977; Weaver and Law, 1978; Sepuya *et al.*, 1978; James, Whimster and Hamilton, 1978; Tala *et al.*, 1979; Limpisvasti and Jones, 1979; Podell *et al.*, 1980; Smith and Ball, 1980; Scott *et al.*, 1981). The typical picture is that of an acute or sub-acute onset of dyspnoea and cough in a patient on chrysotherapy.

Interestingly, gold sodium thiomalate was used in all previously reported cases. The average duration from start of gold treatment to symptoms was 11 weeks (average total dose 484 mg) while the average duration of the rheumatoid disease was 6.5 years, suggesting a cause-effect relationship between chrysotherapy and lung disease. The most common physical finding was that of dry rales over the lung bases while rash, though a common manifestation of gold toxicity, was present in less than a third of the cases and fever in even fewer (3/19). Clubbing was absent in all cases, contrary to its usual presence in rheumatoid fibrosing alveolitis. Infiltrates were seen on all chest X-rays. Other laboratory tests were not very specific with mild leucocytosis in some cases and eosinophilia in 50% of them. Hypoxaemia is probably common although few articles report on blood gases. Only 60% of these patients had a positive test for rheumatoid factor, suggesting that rheumatoid disease in patients with gold-induced pneumonitis is not particularly severe. The main features distinguishing gold-induced lung disease from rheumatoid fibrosing alveolitis are summarized in Table 1.

Most of the patients were treated with corticosteroids following withdrawal of gold therapy and the great majority of them showed a rapid and favourable response. The 5 patients who were not treated with steroids had a somewhat more prolonged course. In 2 patients, where rechallenge with gold was

TABLE 1. Comparison of rheumatoid fibrosing alveolitis and gold-induced pneumonitis

	Rheumatoid fibrosing alveolitis	Gold-induced pneumonitis
Onset	gradual	acute/sub-acute
Dyspnoea	present	present
Dry cough	present	present
Rales	present	present
Finger clubbing	present	absent
Infiltrates on chest X-ray	present	present
Favourable response to steroids	rare	common
Clinical course	progressive usually irreversible	completely or partially reversible

performed, symptoms recurred following small doses of the drug.

Lung biopsy was performed in 6 cases. It showed either alveolitis or interstitial inflammation and fibrosis depending, most probably, on the stage of disease. Of the 20 cases described, 9 have recovered, 9 have improved, one has not improved and one died of acute myocardial infarction shortly following the onset of disease.

The mechanism of injury to the lung is not clear. Gold concentrations were not higher in 'gold lungs' than in lungs of patients who did not develop this reaction to chrysotherapy (Miyachi, 1976). It is therefore surmised that the mechanism of injury might be immunological rather than direct toxicity resulting from accumulation of the drug, but positive evidence for an immunological mechanism is lacking. Eosinophilia, as previously mentioned, was present in half the cases. *In vitro* blastic transformation of lymphocytes by gold was positive in one case (Geddes and Brostoff, 1976) but negative in all others tested (Sepuya *et al.*, 1978; Smith and Ball, 1980).

Gold is one of a rapidly growing list of drugs capable of causing interstitial lung disease. Gold-induced lung disease presents a challenge in differential diagnosis in patients with rheumatoid arthritis who may develop lung disease in the course of their rheumatoid process.

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