Letters to the Editor

Skin reaction associated with chrysotherapy: An unusual case

Sirs,

We report the case of a 34 year–old Libyan woman with active rheumatoid arthritis (RA) and hyperpigmentated areas all over the body (Fig.1a). RA was diagnosed 2 years earlier according to ACR crietria. She was treated with intramuscular sodium aurothiomalate 50 mg weekly for 3 months and low dose steroids afterwards.

During hospitalisation in our Rheumatology Unit laboratory tests showed: ESR 74, CRP12, RALatex +++, FII Latex 1:2560, γ 25.5% (7.6 g/dl total proteins), antinuclear antibodies and anti-Ro/La antibodies were negative; DAS 28 was 5. X-rays showed erosive changes in the hands and feet.

Two punch skin biopsies of the hyperpigmentated lesions were obtained. Haematoxylin-eosin stained sections showed several macrophage-like cells containing dense pigment deposits, which maintained their brownish colour after prolonged bleaching with 30% hydrogen peroxide (Elftman's method) (Fig. 1b). With immunoperoxidase staining, most of the infiltrating lymphocytes appeared to be CD3+ (i.e., T cells), whereas the phagocyte pigmented cells were CD68+ (i.e., macrophages). Spectroscopic analysis of the other specimen was performed using an Inductive Coupled Plasma (ICP) instrument (VARIAN mod. ICP-OES) and confirmed the presence of gold.

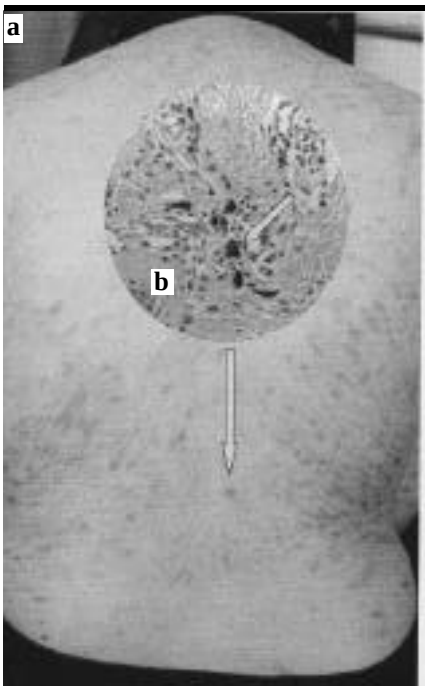

Fig. 1. (**a**) Trunk of the patient with discromic lesions persisting 2 years after discontinuation of gold salts therapy. The trunk has never been exposed to the sun. (**b**) Skin biopsy stained with haematoxylin-eosin and Elftman's method. In the dermis perivascular infiltrates can be observed. These contain densely pigmented macrophages. The top arrow points to gold salt deposits inside the cells (E.c. 250x).

Parenteral gold salts have been used in the treatment of RA since 1920s and they remain the first choice disease-modifying anti-rheumatic drug in some countries (i.e. Mediterranean Africa). Gold salts tend to accumulate and remain in the patient's tissues, concentrating particularly in the reticulo-endothelial system, but it is also found in the skin and other tissues such as the lungs, eyes, nails, liver and parotid glands (1). Adverse reactions due to gold salts include cutaneous eruptions, mouth ulcers, proteinuria, pneumonitis, thrombocytopenia, hepatitis and aplastic anaemia. Skin reactions are the most common side effects, accounting for 60% of all adverse manifestations; they usually appear early during the treatment and last for up to one year after discontinuation (2).

A permanent skin discoloration attributable to gold precipitation is an uncommon manifestation usually affecting sun-exposed areas. This pathologic pigmentation has been variously named – chryasis, auriasis, chrysoderma – and can assume different colours: grey, light grey, grey-purple, grey-blue, blue-violet, blue-green or brown-yellow (1). The cause of pigmentation and the exact pathogenetic mechanism of the skin toxicity are not known but either a tattoo effect of gold or a modification in reflectance and the amount of melanin have been suggested (3, 4). Among the possible risk factors previously linked to the appearance of mucocutaneous side effects, sun exposure seems to be the most relevant (1,3). Skin hyperpigmentation has been induced in unaffected areas with artificial ultraviolet light (5), and Trotter recently described the appearance of localized chrysiasis immediately after exposition to laser therapy in a patient with psoriatic arthritis under gold treatment (6). In our case, skin hyperpigmentation was still present 2 years after discontinuation of sodium aurothiomalate therapy and involved mainly the patient's trunk, which had never been exposed to the sun due to religion customs. Other known risk factors for adverse mucocutaneous effects associated with gold salts, such as the presence of anti-Ro antibodies, an atopic state and smoking, were also absent in our patient (7-9) who did not have any other symptom linked to a possible overlapping autoimmune disease. A strong correlation between the cumulative dose of gold salts and the severity of skin pigmentation has been advocated. In this patient a total of 600 mg had been administered over 3 months, which is less than the cumulative dose of 20 mg/kg considered to be the threshold for the appearance of chyriasis (1).

With this report we wish to underline the importance of investigating the past administration of gold salts in RA patients with hyperpigmentated skin lesions. This uncommon cutaneous side effect can be confirmed by histology and mass spectrometry.

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