Gamma/delta T cells and human skin reactivity to heavy metals

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Abstract Gamma/delta T cells may act as a first line of defence and respond to stress signals from the surrounding tissue. In the present investigation the occurrence of gamma/delta T cells was studied in the human skin after application of heavy metal salts by a routine epicutaneous patch-testing procedure. Gamma/delta cells were not found in normal skin. They were observed in all 14 allergic or irritant patch-test reactions to gold chloride and in 6/8 such reactions to mercuric chloride, where they comprised $16 \pm 6\%$ and $15 \pm 6\%$, respectively, of the CD3$^+$ cells in the dermis. They were also epidermotropic. Very few of these cells were found in reactions to salts of nickel and silver, except that they were increased in hair follicle epithelium in a reaction to silver nitrate. The gamma/delta cells expressed the V delta 2 and the V gamma 2 gene segments and were CD4$^-$8$^-$, indicating that they had the same phenotype as gamma/delta lymphocytes in the peripheral blood. Moreover, they were 'memory' T cells. These results indicate that gamma/delta lymphocytes play a role in the skin defence against highly reactive heavy metals.

Key words Gamma/delta T cells · Heavy metals · Human skin

Introduction

Gamma/delta T cells have receptors consisting of gamma and delta chains, instead of alpha and beta chains, linked with the invariant CD3 complex of proteins [1]. They have been reported to occur in normal human intestine, lung and skin, though only in small amounts compared with mice (for references see reference 2). Gamma/delta cells may act as a first line of defence by responding to stress signals from the surrounding tissue rather than recognizing diverse foreign antigens directly. Besides eliminating infectious agents, gamma/delta cells may have a function in immunological disorders such as rheumatoid arthritis, sarcoidosis and coeliac disease [2]. Gamma/delta cells are rare in the majority of inflammatory and neoplastic dermatoses [3], except in chronic cutaneous lupus erythematosus [4, 5].

Heavy metals may exert their effect in the human skin through stress signals and may be involved in the development of eczematous, lichenoid, granulomatous and vasculitic reactions. In the present investigation, different heavy metal salts, applied by a routine epicutaneous patch-testing procedure, were tested for their ability to attract gamma/delta cells to the human skin.

Materials and methods

Tested metal agents

Chloroauric acid was obtained from Johnsson Matthey (Sheffield, UK). Mercuric chloride, nickel sulphate and silver nitrate were obtained from Merck (Darmstadt, Germany). The salts were dissolved in 0.9% saline before being used in the patch-testing procedure.

Subjects and biopsy specimens

Patients being investigated for hypersensitivity to dental restorative materials were patch-tested for 48 h by the epicutaneous route with 1% gold chloride ($n = 14$), 0.1% mercuric chloride ($n = 8$), 5% nickel sulphate ($n = 7$) and 2% silver nitrate ($n = 9$) using polypropylene-coated Finn Chambers (Epitest, Helsinki, Finland) mounted on Scanpor (Norgesplaster, Oslo, Norway). Lesional skin in patients with positive reactions was biopsied. As controls, biopsy specimens were taken from non-lesional skin of the same patients.

The reactions were mainly papular and infiltrated to gold chloride, vesicular and infiltrated to nickel sulphate, papular and erythematosus to mercuric chloride and erythematosus to silver nitrate. All the reactions to nickel sulphate, 8/14 reactions to gold chloride and 4/8 reactions to mercuric chloride were regarded as truly allergic. The remaining reactions and also the reactions to silver nitrate
were regarded as irritant. The evaluation of the reactions as allergic or irritant was mainly based on the patient’s history. A positive history of reaction to gold was indicated by an inflammatory skin reaction to red gold jewellery and/or oral vesicular lesions adjacent to gold fillings, and to mercury by an oral lichenoid reaction adjacent to amalgam fillings, which, like the former lesions, disappeared after removal of the fillings.

Two of the reactions to mercury and seven of the reactions to gold chloride persisted for more than 4 weeks.

Processing of specimens

The skin biopsy specimens were immediately frozen in liquid nitrogen and then stored at −70°C. They were subsequently sectioned at 6 μm in a cryostat, after embedding in Tissuetek (Histolab, Gothenburg, Sweden). After air drying for 10 min the sections were fixed in acetone for 10 min and then kept in a freezer at −20°C until processed for staining.