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Acute Mercury Intoxication with Lichenoid Drug Eruption Followed by Mercury Contact Allergy and Development of Antinuclear Antibodies

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A 31-year-old black man was examined for evaluation of a suspected occupational disease. Three years earlier he had been suffering from acute mercury intoxication during work in a mercury recycling factory. Skin symptoms then had been a lichenoid drug eruption, patchy alopecia and stomatitis, which had all disappeared rapidly after systemic glucocorticosteroid treatment. The examination revealed positive patch test reactions to metallic mercury and inorganic mercury compounds, an elevated titre of serum antinuclear antibodies and normal IgE levels. The induction of antinuclear antibodies by mercury has been shown in animal experiments. It can be hypothesized that this patient, who may have had an increased individual susceptibility, became allergic to mercury by the mercury intoxication.

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The increasing exposure to harmful environmental chemicals has been discussed as a possible cause of immunologic disturbances in the human organism (1).

In animal experiments mercuric chloride can induce immune-complex glomerulonephritis, increase in immunoglobulin production (especially IgE), increase in B cells and T helper cells and the production of antinuclear antibodies (2, 3, 4).

In man, so far, mercury allergy is the only known immunologic disturbance. Mercury allergy can be of the anaphylactic type (e.g. anaphylactic reaction to thiomersalate, an organic mercury compound (5) or of the delayed type hypersensitivity (contact dermatitis, lichenoid reactions in red tattoo areas or adjacent to amalgam fillings, or baboon-syndrome (6–14)).

In lichenoid reactions caused by mercury positive patch test reactions are only rarely found. It is supposed that lichenoid eruptions, like other symptoms of mercury intoxication, are highly dependent on an individual susceptibility (15, 16).

The patient reported is a man who had developed a lichenoid eruption during acute mercury intoxication and in whom later antinuclear antibodies and positive patch test reactions to mercury were found.

CASE REPORT

A 31-year-old black man was examined in our clinic for assessment of a possible occupational disease. Three years earlier he had worked in a mercury recycling factory, where security measures against mercury contamination had been extremely deficient.

After only three weeks' work he had developed symptoms of acute mercury intoxication like stomatitis, patchy alopecia, generalized pruritus and subsequently a lichenoid rash. In his urine mercury was found in a concentration of 380 µg/l (the tolerable limit of urinary mercury concentration is 200 µg/l). The hospital treatment had consisted of systemic glucocorticosteroids and dimercaprol to accelerate the excretion of mercury. Healing of skin symptoms occurred rapidly as well as normalization of total mercury excretion. The definite diagnosis, confirmed histologically, was "lichen planus, presumably caused by mercury intoxication".

Other eliciting factors of lichen planus or lichenoid drug eruption like psychological stress, certain drugs, contact with aminoglycoside containing creams or certain film developers were excluded (8, 9, 20). There was no history of a previous allergic reaction.

Shortly after the mercury intoxication the patient complained about a generalized itch sensation after sun exposure, which he had not experienced earlier.

Dermatologic examination

Healthy looking slim black man with reticulate macular hyperpigmentations on the upper chest and the upper back. No signs of alopecia. Oral cavity without pathologic findings: one amalgam filling with normal surrounding gingiva.

Serologic examination

Direct immunofluorescence repeatedly showed antinuclear antibodies with a homogeneous pattern on Hep2 cells and a titre of 1:640. No evidence of ENA-, Ro-, La- and anti-ds-DNA-antibodies. The following parameters were normal: ESR, red and white blood chemistry, serum IgE level (8 kU/l; normal <100 kU/l). Hepatitis serology showed immunity for hepatitis A, no immunity for hepatitis B: Syphilis serology was negative. Human leukocyte antigens were HLA-A28, -A29, -B49 and Bw4. HLA-DR testing was negative for HLA-DR2 and HLA-DR3 (Prof. Dr. E. Albert, Kinderpoliklinik, Ludwig-Maximilians-University Munich).

Patch test (Table I)

The patch test ws performed and evaluated according to the rules of the International Contact Dermatitis Research Group using standard test reagents (Hermal, Reinbek and Dr. Brinkmann, Mönchengladbach) which had been proven to be non-irritative in 20 healthy volunteers. There were positive reactions to mercuric chloride (= sublimate), ammoniated mercury and mercuric amidochloride.

No test reactions were found towards the organic mercury compounds thiomersal sodium timerfonate, phenylmercuric borate and phenylmercuric nitrate.

Prick test

No type-I-reaction to aero-allergens nor to thiomersal, no type-III-reaction to thiomersal.*

Photosensitivity testing

Minimal erythema dosis for UV-B was normal, i.e. no erythema even at 220 J/cm^2 (polychromatic light, testing on gluteal region).

* In the pricktest performed with standard aero and food allergens as well as with thiomersalate (1% and 10%) there were no immediate wheat and flare reactions nor any positive reactions after 48 and 72 hours.

Table I. *Results of patch test with inorganic and organic mercury compounds*

	48 h	72 h
Inorganic mercury compounds:		
Metallic mercury 0.5% pet.	–	+
Amalgam (as is)	–	–
Ammoniated mercury 1% pet.	+	+
Mercury bichloride (sublimate) 0.1% pet.	+	+
Mercuric amidochloride 1.0% pet.	+	+
Organic mercury compounds:		
Thiomersal 0.2% pet.	–	–
Sodium timerfonate 0.1% pet.	–	–
Phenylmercuric nitrate 0.005% pet.	–	–
Phenylmercuric borate 0.005% pet.	–	–
Other compounds of standard patch test series	–	–

The histologic examination of a positive patch test reaction showed pronounced signs of a type-IV-reaction such as parakeratosis, spongiosis and exocytosis of lymphocytes, dense perivascular lymphocytic infiltrate in the upper dermis intermingled with eosinophils and reaching partly down to the mid dermis.

Direct immunofluorescence of this sample: There were no deposits of immunoglobulins (IgG, IgM, IgA), complement, nor fibrinogen.

DISCUSSION

The case presented here demonstrates the occurrence of mercury contact allergy and antinuclear antibodies after acute mercury intoxication. It is assumed – although not proven – that these changes were not present before the occupational exposure.

The patient seemed to have a certain susceptibility to react with symptoms of mercury intoxication, while other workers in the factory did not show any symptoms despite of even higher exposure as measured by increased urinary mercury concentrations.

An individual susceptibility is regarded as important factor in developing lichen planus, the differential diagnosis versus lichenoid drug eruption. yet, lichen planus is usually a chronic disease, which may be associated with autoimmune diseases or may occur during graft-versus-host reaction and which often shows an association with the histocompatibility antigen HLA-A3 (7, 17, 18, 22, 23, 24, 25).

The diagnosis "lichenoid drug eruption" caused by mercury compounds is supported by the following criteria: rapid healing after mercury excretion, absence of HLA-A3 together with the positive patch test reactions to mercury and inorganic mercury compounds.

Lichenoid contact dermatitis has been described in patients with sensitization to aminoglycoside antibiotics and colour film developers (19, 20). Moreover, it is known that contact allergy to mercuric sulphide (cinnabar), the red tattoo colour, may induce lichenoid lesions or, rarely, lesions resembling discoid lupus erythematosus (7, 22, 26, 27, 28).

In animal experiments mercuric chloride has been shown to transiently induce immune-complex glomerulonephritis, development of nuclear antibodies, a marked increase in serum IgE as well as activation of B cells and T helper cells in some species. This induction is rather independent from a total body mercury dose but related to a genetic, strain-specific susceptibility (3, 4, 23).

In our patient, antinuclear antibodies showing a homogenous staining pattern in indirect immunofluorescence on Hep2-cells were present in a titre of 1:640. In animals treated with mercuric chloride antinuclear antibodies also showed the homogenous pattern and, differing from one patient, a nucleolar pattern (3). The nuclear antigen reacting with antinuclear antibodies of the homogenous type has not yet been identified; the antinucleolar antibodies found in mice treated with mercuric chloride treated are probably directed against the nucleolar antigen fibrillain (29). No explanation for the presence of antinuclear antibodies other than mercury intoxication was found in our patient, who was otherwise healthy. In particular, there were no clinical signs compatible with the diagnosis of a collagen-vascular disease, i.e. lupus erythematosus, systemic scleroderma or dermatomyositis. The family history was also negative (30, 31). Only the fact that the patient was suffering from generalized pruritus after sun exposure since the time of the mercury intoxication might – very speculatively – be seen in the context of an increased light sensitivity of an incipient otherwise silent lupus erythematosus. Therefore, a possible clinical relevance of the increased antinuclear antibodies in the future cannot be excluded. Follow-up studies will show whether the patient's symptoms are transient, as they were in animal experiments, and whether the antibody titres will decline. This would be a further indication that, also in man, mercury compounds could act as precipitating factors initiating an abnormal autoimmune response.

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