

Nickel-elicited systemic contact dermatitis

A report of 20 cases and a review of the literature

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20 patients with systemic contact dermatitis due to nickel are described. Of these patients, 15 were female and 5 were male. Their mean age was 24.8 years (16–51 years). All had experienced contact dermatitis in the umbilical area due to continual contact with metal belt-buckles or buttons. Then, with long- or short-term aggravation of such periumbilical dermatitis, commonly in summer, lesions spread to other sites such as the side of the neck, the flexures of the extremities, etc. All patients showed a positive patch test to nickel sulphate (2.5% in petrolatum) and the dimethylglyoxime test demonstrated the presence of free nickel on metal buttons or belt-buckles. Punch biopsies performed in 7 patients showed subacute dermatitis. After avoidance of continual exposure to objects containing nickel and foods rich in nickel, as well as treatment with oral antihistamines and topical corticosteroids, all patients improved or cleared. It has been reported that nickel can cause systemic contact dermatitis by some internal systemic route, such as oral intake, transfusion, inhalation, implantation of metal medical devices, etc. In our patients, we found that continual local skin contact could also elicit systemic contact dermatitis.

Key words: nickel; allergic contact dermatitis; systemic contact dermatitis; eczema. © Blackwell Munksgaard, 2003.

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In 1943, Park (1) described 12 patients, who had been previously sensitized by topical sulfonamide, and who developed eruptions when they were given courses of oral sulfonamide the severity of the eruption varying with the sensitivity of the subject and the dose of sulfonamide given. At that time – the Second World War – sulphonamide in powder or petroleum jelly was the most frequently used topical application and the major cause of sensitivity reactions. Later, more and more drugs were reported to cause not only dermatitis on direct contact sites but also widespread dermatitis when given systemically, including streptomycin, neomycin, bacitracin, and penicillin. Fisher (2) named this ‘systemic contact-type dermatitis medicamentosa’ or ‘systemic contact dermatitis’. This is an inflammatory reaction in the skin resulting from a systemically administered allergen, which occurs in a person who has been sensitized to the allergen previously by skin contact. Apart from drugs, certain metals, and especially nickel, can cause systemic contact dermatitis. Here we describe 20 patients with systemic contact dermatitis due to nickel.

Patients, Methods and Results

Clinical data

From 1 May 2001 through 30 June 2002, 20 patients came to our clinic with widespread eczema. Of these 20 patients, 15 were female and 5 were male. Their age ranged from 16 to 51 years, with a mean age of 24.8 years. 75% of patients (15/20) were in the 15–25 years age group. 50% of patients (10/20) presented in summer (April to August). Disease duration ranged from 1 week to 6 years, the mean duration being 24.9 months. On examination, all patients showed widespread lesions, mainly involving the side of the neck, the flexures of the extremities and the trunk, with pruritus. However, the lesions around the umbilicus were especially severe, most such patients wearing a belt with a metal buckle or jeans with metal buttons when examined. Lesions were symmetrical, polymorphous and comprised erythema, papules, and vesicles, with small areas of erosion, exudation and crusting from scratching. All patients experienced almost the same evolution:

lesions first occurred in the umbilical area, relapsing in hot weather and remitting in cold weather; then, after long- or short-term aggravation, commonly in summer, lesions spread to other sites such as the neck, the flexures of the extremities, etc. Their past histories revealed that 9 patients had been sensitive to metal jewellery or metal watch bands. No patients had been exposed to metal occupationally.

Laboratory data

In all patients, patch tests were performed and all showed a positive reaction to nickel sulfate (2.5% in petrolatum). 12 patients also showed positive reactions to other allergens, such as ammoniated mercury (8 patients), fragrance mix (7 patients), imidazolidinyl urea (1 patient), potassium dichromate (1 patient) and rubber mix I (1 patient) (Table 1). In 2 patients, patch testing produced a flare consisting of more widespread eczema or a dyshidrotic eruption. The dimethylglyoxime test was positive on the metal buttons or belt-buckles tested, indicating the presence of free nickel. Punch biopsies of primary or secondary sites were performed in 7 patients and showed subacute dermatitis.

Treatment and clinical course

Treatment of the presenting eczema was the same as for allergic contact dermatitis and all patients were given oral antihistamines and topical corticosteroids. Only 1 patient was given corticosteroid systemically, because lesions were widespread and symptoms severe. Most importantly, all patients were asked to avoid continual exposure to objects containing nickel, such as metal jewellery, wristwatch bands, belt-buckles, eyeglass frames, coins, etc. Additionally, all patients were recommended to avoid certain foods rich in nickel, such as legumes, nuts, grains, potatoes, chocolate and fish.

Patients were followed up and all responded well after treatment for 2–4 weeks, combined

with avoidance of continual exposure. One patient's lesions improved dramatically after substituting their stainless steel cooking utensils.

Discussion

Nickel is one of the commonest causes of allergic contact dermatitis throughout the world. The prevalence of nickel allergy in populations can be 10–20% (3). A population survey in Stockholm showed that 15% of females and 3% of males were nickel allergic (4). In women, the commonest cause of nickel dermatitis is direct contact, primarily from jewellery, garments, wristwatches, or occupational contact in the metal industry, hairdressing, tailoring and hotel and restaurant work. In men, nickel dermatitis is predominantly occupational.

Nickel can elicit dermatitis by direct skin contact. It may also elicit widespread dermatitis by an internal systemic route, for example, oral intake, transfusion, inhalation, implantation of metal medical devices, etc. This may be regarded as a type of systemic contact dermatitis elicited by nickel.

Nickel dermatitis has been classified into 2 types (3):

- *primary*: areas in direct contact with metal, such as eruptions usually being eczematous, but occasionally just papular;
- *secondary*: selective symmetrical areas that are involved when the dermatitis spreads. The secondary eruption behaves like autosensitive haematogenous spread similar to an 'id' phenomenon. It is usually symmetrical and is related to the activity of the primary site. Secondary eruptions may localize in the elbow flexure, on the eyelids, sides of the neck, and face, and may sometimes become widespread.

Our patients presented with widespread lesions involving the neck, extremities and trunk. However, the periumbilical lesions were more severe where the skin came into direct contact with metal buckles or buttons. A careful history revealed that in all patients the lesions first occurred in the periumbilical area, usually relapsing in hot weather, and then spreading to other sites, such as lesions being eczematous. Patch testing results showed that nickel sulphate was positive in all patients and the dimethylglyoxime test proved the presence of free nickel on the surface of belt-buckles and jeans buttons. Biopsies from both periumbilical and other sites showed subacute dermatitis. Similar cases have been reported by another investigation (5): 38 children presented with prominent subumbilical and periumbilical

Table 1. Patch test results

Allergens	Total positive cases	Positive reaction classification		
		+	++	+++
Nickel sulfate	20	5	14	1
Ammoniated mercury	8	5	3	
Fragrance mix	7	6	1	
Imidazolidinyl urea	1	1		
Potassium dichromate	1	1		
Rubber mix I	1	1		

papules and a widespread lichenoid papular dermatitis. Patch tests were performed in 9 patients and all were positive to nickel. The authors thought this phenomenon an id reaction. But we conclude that this may be a type of systemic contact dermatitis caused by nickel.

But how does only skin contact with nickel elicit allergic contact dermatitis at distant sites? Some (3) believed that wandering, perspiring fingers might convey nickel from metallic objects to distant sites and elicit allergic contact dermatitis. One study (6) showed that, after skin application, nickel salts are retained in the skin for an extended period of time and this could lead to prolonged antigen processing and consequent immune responses in dermal tissue. Recent studies (7–9) showed that, in contact with the skin, nickel is oxidized to form soluble, stratum corneum-diffusible compounds which may penetrate the intact stratum corneum by the shunt pathway, intracellular/intercellular and transappendageal routes, which have the potential to elicit allergic reactions. So we may draw the conclusion that in our patients, with continual direct contact with metal-buckles and jeans buttons in hot weather, nickel released and formed nickel salts, which could penetrate into the skin by diffusion or into the circulatory system by the shunt pathway or lymphatic vessels and then elicit allergic reactions over the whole body. In 2 of our patients the lesions were aggravated after patch testing. In 1 patient, vesicles and even bullae occurred on the palms and soles, like pompholyx. This phenomenon may be evidence that, in a hypersensitive state, skin contact can elicit allergic reactions all over the body, as in the other ways mentioned above.

Certain other studies (10–12) have partly demonstrated the immune mechanism of systemic contact dermatitis. Now it has to be concluded that this reaction may be mediated by both a Type III and a Type IV mechanism.

Although it has been reported (13) that oral administration of nickel can induce a high frequency of anergic T cells with persistent suppressor activity, thus achieving sustained tolerance to nickel in mice, at present avoidance of exposure remains the most important treatment. Patients should be recommended to avoid direct skin contact with metal objects containing nickel. Chelating agents such as diethylenetriamine penta-acetic acid and L-histidine in protective barrier creams have proved to be helpful (14, 15). In some cases the small amounts of nickel in foods may be responsible for the dermatitis continuing, so it is necessary to avoid foods rich in nickel, such as legumes, nuts, grains, potatoes, chocolate and

fish. In our practice, we observed that 1 patient improved dramatically after substituting their stainless steel cooking utensils, and another patient, with both local and widespread eczema after implantation of stainless steel screws in her elbow joint for a fracture, cleared after removal of the screws. It has also been reported (16) that pentoxifylline, an inhibitor of TNF-alpha, can inhibit the contact sensitivity response elicited by nickel, though only during drug administration.

In conclusion, we have described 20 patients with systemic contact dermatitis due to nickel. The 20 patients experienced almost the same course: repeated periumbilical dermatitis due to continual local skin contact with nickel, then spread to distant sites, and the results of patch testing, the dimethylglyoxime test and biopsies confirmed nickel allergy. So, in hypersensitive patients, repeated skin contact can elicit widespread lesions and avoidance of such skin contact is the key to getting better. Dermatologists should therefore remind such nickel-allergic patients to pay more attention to avoiding all kinds of nickel exposure in their daily life and work.

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