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Review

Systemic contact dermatitis to nickel

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Abstract

Introduction

Nickel is one of the most common contact allergens in the modern world. Nickel allergy prevalence is constantly growing in many countries and represents a major health and socio-economical issue. In certain cases of nickel hypersensitive patients the allergic subjects could be challenged by the allergen not by direct skin contact but when the allergen is introduced to the organism by transmucosal, oral, intravenous, intramuscular, or inhalational route instead. Such process is known as systemic contact dermatitis. This review is devoted on this issue, its causes, clinical manifestations and treatment.

Conclusion

Although not being common in the general dermatological practice systemic contact dermatitis to nickel should be suspected and recognized by clinicians.

Introduction

Nickel is found almost ubiquitously as in the Earth's crust and water, and it is also an important microelement for the homeostasis of the human organism[1]. Since its discovery in the 18th century it is used in any industry as a part of alloys, silver substitutes, plating and stainless steel.

Contact eczema from nickel was first described in the late 1880s in the plating industry[1].

In 1925 Schittenhelm and Stockinger first performed patch testing for the confirmation of contact hypersensitivity to nickel. Nowadays the metal is among the most common and is a major cause for the development of contact dermatitis and its significance broadly exceeds the borders of the industrialized world[2].

The classical understanding for the pathophysiology of contact dermatitis /eczema accepts that the reaction develops in two phases: sensitization- when the subject is in primary contact with the allergen and is developing the specific hyperreactivity state of the immune system; and the elicitation phase- upon following repetitive contact with the allergen the activated immune system accomplishes skin inflammatory response. In the case of systemic contact dermatitis (SCD), the re-exposure is not direct through the skin surface but orally, transcutaneously, intravenously or by inhalation[3].

The aim of this paper is to review and to summarise the current knowledge on systemic nickel dermatitis. We present two clinical entities in the spectrum of SCD to nickel in cases from our practice.

Discussion

The authors have referenced some of their own studies in this review. These referenced studies have been conducted in accordance with the Declaration of Helsinki (1964) and the protocols of these studies have been approved by the relevant ethics committees related to the institution in which they were performed. All human subjects, in these referenced studies, gave informed consent to participate in these studies.

Historical perspective

Most probably the first clinical description of SCD was made by the British dermatologist Thomas Bateman who witnessed cases of disseminated dermatitis to mercury and named it eczema rubrum[4]. Schittenhelm and Stockinger in 1920s described spreading of nickel eczema after patch testing even to previously unaffected skin sites. In 1984 the term "baboon syndrome" was coined to describe diffuse erythema of the buttocks, upper inner surface of the thighs, and axillae after systemic exposure to allergens among which nickel[5]. More recently the acronym SNAS standing for Systemic Nickel Allergy Syndrome was introduced[6].

How common is SCD to nickel?

The majority of data on SCD to nickel is based on case reports and series. A novel study tried to find the exact prevalence of this condition. In a multicentre study in Italy of almost 2000 consecutive patients revealed that 5.78 % of all subjects had SCD to nickel. Nickel is the most common contact allergen. About 10% of the general population is affected[7,8,9]. It is almost four times more prevalent in women than in men[10,11]. The frequency of nickel hypersensitivity is constantly growing in general[12].

Certain factors such as piercing, occupational exposure, and history of atopic dermatitis contribute to the development of the disease[13].Younger age is associated with the development of nickel contact allergy[14,15]. Nickel hypersensitivity is more prevalent in previous and current smokers than in non-smokers[16]. Nickel allergy has been associated with joint prostheses and other implants failure[17,18]. No relation between coronary stent re-stenosis and nickel sensitivity has been revealed[19]. Leg ulcers patients are predisposed to the development of nickel allergy[20].

Sources of systemic nickel exposure

A prerequisite for SCD to nickel is the contact skin sensitization followed by systemic nickel administration. Food is a source of nickel with an average daily intake of 200 μg. Foods rich in nickel are green beans, broccoli, peas, canned vegetables and spaghetti, canned fruit,

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dried fruit, nuts, cocoa, and chocolate[21]. Tap water when first drawn contains large amounts of nickel[22]. Tobacco smoking increases the nickel intake with 4μg for each pack of cigarettes[23]. Metal surgical devices and implants are the major causes for iatrogenic SCD to nickel.

How does SCD look like?

SCD to nickel has many faces. The clinical spectrum of SCD manifestation on the skin is presented in figure 1. A variety of systemic symptoms have also been disclosed among which gastrointestinal (nausea and vomiting), headache, fever, joint pain and malaise[4,6,24,25]. Below we present two cases of SCD to nickel:

Clinical case 1

A 16 year old female Caucasian patient developed unilateral vesicles on her right palm 2 weeks after implantation of a metal stabilizing device for fracture of metacarpal bones (Figure 2a and Figure 2b). The eruption affected only the diseased palm and no lesion were noticed on the contralateral hand. Topical clobetasol propionate 0.05% cream was administered twice daily for 14 days with complete resolution of skin lesion. After 6 weeks patch testing with European baseline series was performed and yielded positive reaction to nickel on readings at days 2 and 3 (Figure 2c).

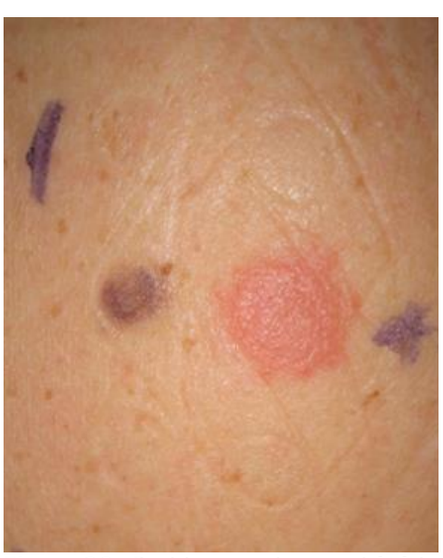

Figure 2C: Positive reaction to nickel in the same patient.

figure 1

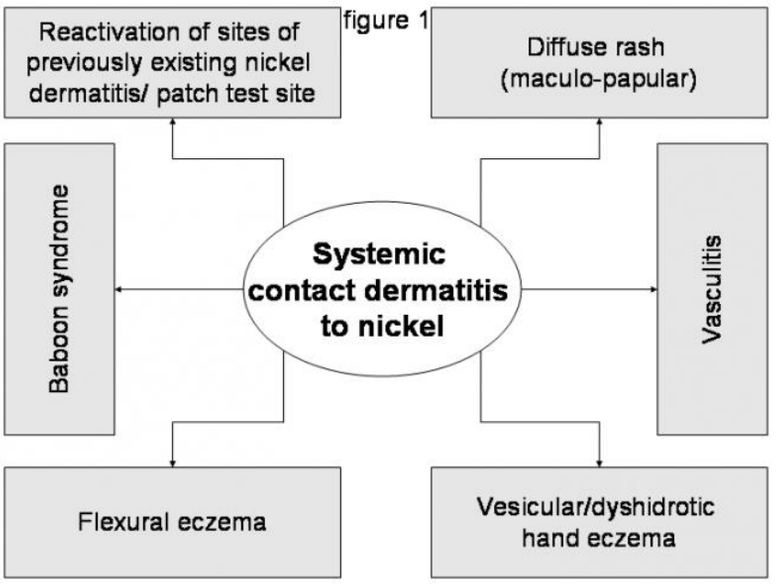

Figure 1: Clinical spectrum of the skin manifestations of systemic contact dermatitis to nickel.

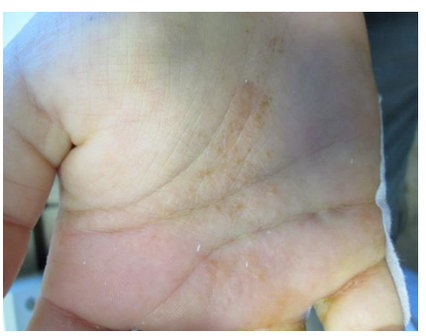

Figure 2A: Vesiculation on the palm of the patient after implantation of a metal orthopedic device.

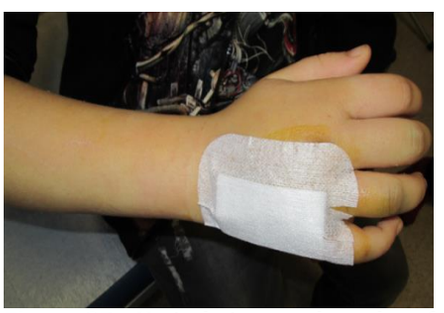

Figure 2B: Vesiculation on the palm of the patient after implantation of a metal orthopedic device.

Clinical case 2

A 47 year old female Caucasian presented with itching and painful bullas with surrounding erythema on the skin of the back of her right foot (Figure 3a and Figure 3b). The lesions developed 10 days after implantation of fixating the metal device for foot bone fracture. Topical application of clobetasol propionate 0.05% cream twice daily improved significantly the condition within the first week and the lesions healed completely after removal of the metal implant.

The consecutive patch test revealed weak positive reactions to nickel and potassium dichromate (Figure 3c).

How to diagnose SCD to nickel?

The golden standard for diagnosing nickel allergy remains epicutaneous (patch) test with 5% bivalent nickel sulphate in petrolatum. A drawback of this method is the possible flare of preexisting dermatitis or the development of such at previously unaffected skin sites. Interpretation should be made by a trained observer as the number of false positive and irritant reactions should not be underestimated.

In vitro tests such as the lymphocyte stimulation test and the investigation of metal induced cytokine profiles from primary peripheral blood mononuclear cells could be useful although not standardized and being mainly used for scientific purposes[6]. The major advantage of using such in vitro test is the risk avoidance for eczema flare-up.

Oral provocation tests with nickel have been used in diagnosing SCD to nickel. The greatest challenge of those is the reactivation of the dermatitis in the tested patients.

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Treatment of SCD to nickel

Avoidance of the contact with the allergen is the mainstay in the treatment of SCD. Patients with previous nickel hypersensitivity should undergo medical procedures suggesting implantation of nickel-containing devices. The use of such should be avoided and alternatives should be preferred whenever possible.

The administration of nickel-free diet is controversial. Controlled studies are needed to show the effect of the dietary allergen avoidance. Several studies have shown beneficial effect witnessed by improvement of the dermatitis seen 4 to 6 weeks after nickel diet[26,27]. Not all of the study subjects responded to that treatment.

Chelation of nickel ions could be potential strategy for dealing with nickel sensitivity[28,29]. Disulfiram has been applied in studies though showing hepatic toxicity[30] as well as recall of nickel dermatitis[31] due to the initial mobilization of nickel. Agents decreasing nickel absorption such as disodium cromoglycate could be a potential option[32]. Desensitization with oral nickel administration can be helpful in nickel sensitized patients[33].

Conclusion

Mucosal contact to low doses of nickel can be the basis for tolerance induction. The future belongs to challenging all these methods in a prospective and controlled manner.

Topical anti-inflammatory treatment with either topical steroids or calcinurin inhibitors can alleviate skin symptoms and is widely used in the everyday clinical setting.

Consent

Written informed consent was obtained from the patient for publication of this review and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

figure 3 a

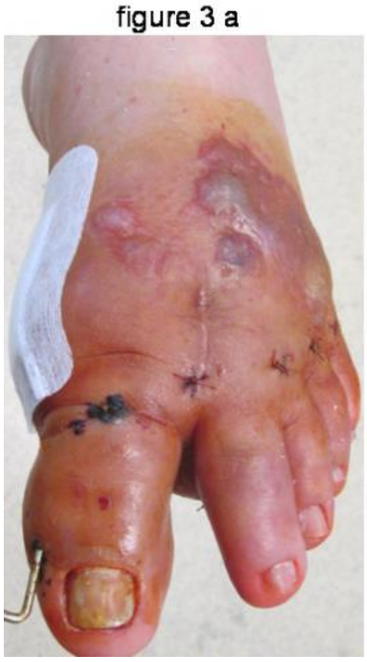

figure 3 b

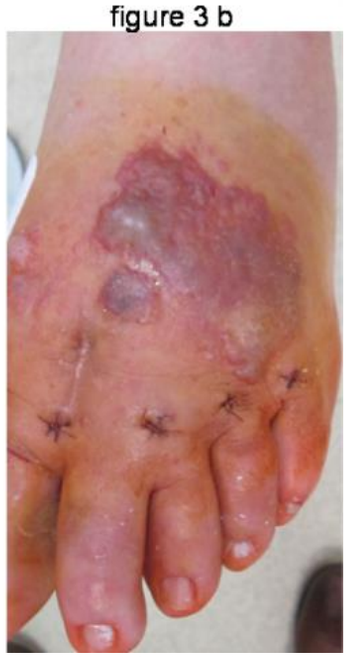

Figure 3 A & B: Erythema and bullas on the back of the right foot of the patient after.

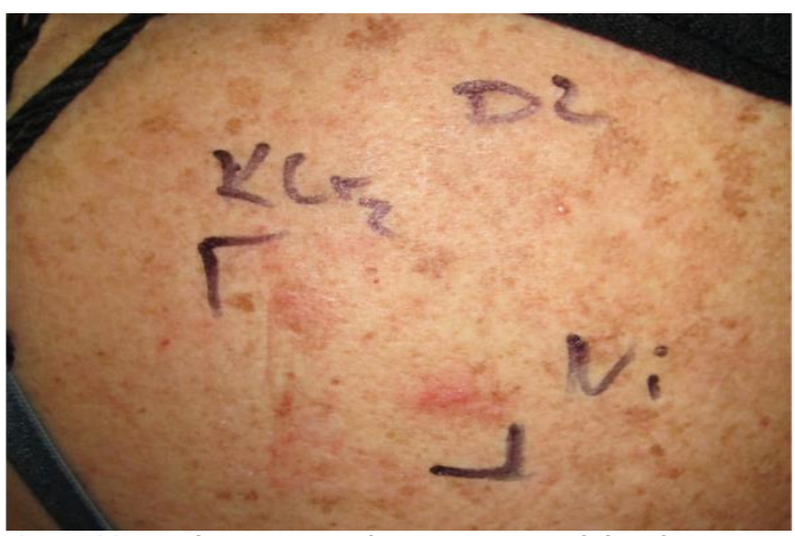

Figure 3C: Weak positive patch reactions to nickel and potassium dichromate in the same patient on day 2.

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