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Nickel contact dermatitis in children

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Abstract Nickel is the most commonly detected cutaneous allergen on patch testing in the United States for children. The ubiquitous nature of nickel as a hardening agent in metal products makes avoidance difficult. Allergy in childhood can be hard to recognize, especially when a strong idiopathic response is noted. Although the standard belt buckle and jewelry trigger still occur, newer sources include technology equipment, such as cases for mobile phones, computers, and tablet devices This contribution reviews the various clinical appearances of nickel contact allergy in childhood, as well as strategies for treatment and avoidance.

Introduction

Nickel is the most commonly detected cutaneous allergen on patch testing in the United States for children, with sensitization to nickel being reported to be as high as 26.8%.[1,2] It is ubiquitous in the environment, being found in a large host of diverse products and materials, lending to almost constant levels of exposure.[3] The incidence of nickel allergic contact dermatitis (Ni ACD), which appears to be increasing, is estimated to be 14% to 20% of women and 2% to 4% of men in the United States,[4] and often is associated with skin piercing and adornment practices.[4] That said, nickel sensitization is being recognized in nonpierced children and, despite the high prevalence of this disorder, recognizing the varied forms of allergic manifestations can be challenging for the practitioner.

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Presentation

Ni ACD can be classified as local, ectopic, idiopathic, or systemic. Localized contact dermatitis appears in those areas that come into direct contact with metallic sources (eg, belt buckles) and usually presents acutely with a monomorphic grouping of erythematous to flesh colored papules at sites of metal contact, which can include pruritus, erythema, edema, and vesiculation. Less intense, or subacute, reactions can present with only mild edema, erythema, and minimal vesiculation. Chronic allergic contact dermatitis can present with xerosis, fissuring, lichenification, erythema, and excoriations, as is commonly seen on the earlobes or fingertips.[5] Chronic rubbing of sites of Ni ACD may cause lichen simplex chronicus and/or lichenoid papules and plaques.

Idiopathic ("id" reaction) Ni ACD is typically a symmetric hypersensitivity reaction, also termed auto-eczematitization, which characteristically involves the flexural extremities, eyelids, and sides of the neck and face, but can

become generalized as well with time or with systemic nickel exposures. Skin-colored, erythematous, or lichenoid papules over the extensor skin surfaces or potentially across the full body surface area may be seen. Less common presentations of Ni ACD include erythema multiforme, urticaria, or prurigo.[6]

Of note, children with atopic dermatitis (AD) may experience an exacerbation of their atopic pruritus secondary to comorbid Ni ACD. The incidence of Ni ACD in atopic dermatitis, explored in a European cohort of adolescents and adults, was 28; 2% being the leading allergen in a patch test series.[7] A series of Danish eighth graders with Ni ACD followed for 15 years revealed that Ni ACD was present in 11.8%, with an 80.8% clinical relevance.[8] Patients with atopic dermatitis were more likely to have long-standing issues with Ni ACD and very few lost patch test positivity to nickel over time.[9] The coexistence of AD often obfuscates the initial diagnosis of Ni ACD, especially in idiopathic- and systemic-type response with flexural involvement. Unlike AD, Ni ACD may at times be slower to clear with topical corticosteroids than atopic dermatitis; therefore, a therapeutic trial with a midpotency topical corticosteroid in children may obviate the presence of Ni ACD (personal observation, N.S.). The disease is usually more widespread in atopic patients; however, Ni ACD in one series was not associated with AD, while fragrance was associated.[10,7]

Ectopic reactions have been observed in association with patient transfer of nickel residue via sweaty fingers that touch the primary area and then transfer the nickel to other parts of the body (eg, fingertips to eyelid after repeated handling a nickel lanyard, S.E.J. observation); this could then be the source of disease eccentric to the primary sites of exposure.[11] In addition, secondary contact points have also been reported (eg, flip phones where the metallic buttons touch the screen and then the nonmetallic screen transfers the nickel to the patient's face).

Systemic immune hypersensitivity (as part of the systemic nickel allergy syndrome) to nickel has been reported in association with ingested nickel and can result in the appearance of a type IV mediated hypersensitivity presenting as generalized dermatitis. This presentation is likely more common than previously realized.[12] Additionally, one group of authors has postulated that the systemic nickel allergy syndrome leaves patients more susceptible to recurrent infections, which may further aggravate disease appearance.[13]

Pathology

The histopathology of active lesions of nickel dermatitis reveals inflammation with intraepidermal intercellular edema, that is, spongiosis, as well as monocyte and histiocyte infiltration in the dermis, suggestive of a cell mediated immune response, typical of allergic contact dermatitis.[14]

Pathogenesis

The pathogenesis of nickel allergic dermatitis begins with the nickel antigen being taken up by the skin's dendritic cells, which in turn process and present the antigen to T cells (Th1 and Th17 cells).[15] These sensitized T cells become clonal and traffic through the circulation to different skin areas. Such sensitized T cells mediate the release of cytokines from other cells all over the body.[16] The release of these specific T-cell mediated cytokines, induces apoptosis of nickel-loaded keratinocytes through a perforin-dependent mechanism.[17] In non–nickel-allergic individuals, the expansion of specialized T cells with regulatory function prevents an inflammatory response from occurring as well as reactive T cells from forming.[18] In allergic individuals, there is a limited amount or absence of these T cells and, therefore, an inability to suppress an allergic immune response from occurring.[5] There can be a genetic basis to Ni ACD caused by a T-cell receptor mutation in the CDR loops, which leaves patients prone to allergy to nickel.[19] It is, therefore, not uncommon for patients to have a positive family history of nickel allergy. Nickel exposure appears to induce an effect on the innate immune system, engaging a toll-like receptor 4 (TLR-4) induced inflammatory response (inflammasome) in addition to the standard type IV mediated immunity, which is a specific human host cell response that is not present in mice.[20] In this setting, Ni triggers the inflammasome complex by hetereodimerization of hTLR4/ hMD2, resulting in MYD-88-dependent activation of the IKK2/ NFKB and MKK3/6/p38 pathways mediated by mutation in hTLR4(19). CD 4+ T cells in patients with Ni ACD appear to produce IL-17, IL-22, and IFN-γ as effectors of cutaneous inflammation.[21]

Sources of exposure

Piercings and costume jewelry (watches), belt buckles and clothing fasteners (buttons, studs, and grommets) remain top sources for epicutaneous sensitization with dermatitis in the earlobes and infraumbilical areas predominating. One study found that 13% of 960 girls aged 8 to 15 with pierced ears were nickel allergic, whereas only 1% of those without pierced ears were.[22] Interestingly, a Danish series found ear-piercing was associated with Ni ACD before EU legislation but not after.[9]

Sweat and friction of buttons and buckles against the skin can induce subclinical maceration, increasing the release of nickel and enhancing reactivity to metal, which comes in contact with the skin at the waistline. Other sources of nickel exposure can be the ball and chain metal dog tag necklaces, which are stylish for young children.[23] In warmer climates, metal tabs on seating in school chairs can be a source of nickel contact.[24] Exposure to nickel through release from technologic devices, such as metallic cell phone cases/