Allergic and Irritant Contact Dermatitis

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Introduction

Contact dermatitis is an inflammatory skin disease induced by direct contact of a external agent to the skin. Contact dermatitis can be classified into two main types: Irritant contact dermatitis and Allergic contact dermatitis. Irritant contact dermatitis is the most common form of contact dermatitis and represents a non-specific cutaneous response to the toxic or physical effects of a wide variety of environmental agents. It is a dose and time dependent process that may occur in all individuals exposed [1]. On the other hand, ACD represents a type IV hypersensitivity reaction mediated by specific T cell-lymphocytes that recognize low molecular weight substances, called haptens. The development of ACD depends on an individual susceptibility and requires prior sensitization to the specific hapten [1].

The clinical presentation of ICD and ACD is highly variable and include macular erythema, edema, papules, vesicles, bullae, scaling and erosions in acute cases, and papules, plaques, lichenification, hyperkeratosis and fisures in the chronic. Although the clinical appearance of both types of CD may be similar and patch testing be the only current means of differentiation, several but not conclusive clinical clues may be helpful [2]. Irritant contact dermatitis may be produced after a single enviromental exposure with the onset of symptoms within minutes to several hours after the contact. There is usually a sharp circumspection of the dermatitis, with a lack of tendency for spread (Fig. 20.1). Allergic contact dermatitis, in contrast, requires a previous contact with the allergen and time to develop the sensitization. Dermatitis develops hours to days after the exposure and lesions are usually ill-defined (Fig. 20.2).

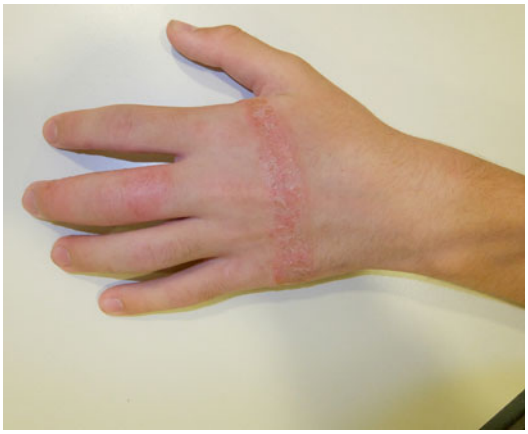

Fig. 20.1 Irritant contact dermatitis. Note the well demarcated and linear array erythematous plaque located on the back of the right hand and middle finger

In both types of CD the pruritus is a very common symptom, however, in ICD it is usually

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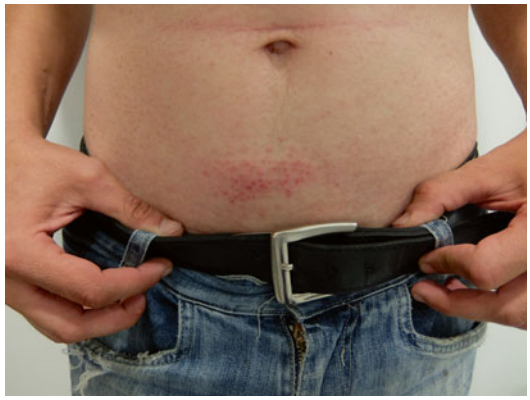

Fig. 20.2 Allergic contact dermatitis. Not well demarcated infraumbilical eczematous plaque due to allergic contact dermatitis to nickel present in belt buckle

mild and often replaced by a burning, pain and stinging sensation. Pruritus in ACD can be the most important symptom and is consider, as one of the main aspects strongly associated with the poor quality of life in patients [3]. Its presence probably reflects the allergic pathogenicity of ACD and also plays an important role in its severity and chronicity as it may lead to scratching and further skin damage with the secondary access for more allergens [4, 5]. Furthermore, occasionally pruritus may be the leading or only symptom that guides the clinician to suspect the diagnosis of CD. This is specially true when the process involves certain locations such as the anogenital regions or when the CD occurs in the elderly.

Pruritus and Anogenital Contact Dermatitis

Contact dermatitis of the anogenital region is a common phenomenom. The particular anatomic and physiologic characteristics of this region makes it very susceptible to develop allergic and irritant contact dermatitis. The skin is continually exposed to different secretions as well as the occlussion, friction and sweat characteristic of this region. In addition, several substances and topical medications, are often retained, increasing time exposure and resulting in more frequent and severe reactions. It is therefore not surprising that ICD and ACD are one of the most common causes of vulvar and perianal dermatitis [6–8]. Irritant contact dermatitis is usually produced by lack or excess of hygiene. Poor hygiene leads to prolonged exposure of physiological fluids or depositions that acts as strong irritants, as in the case of patients with urinary or fecal incontinence. On the other hand the excesive hygiene and exposure of detergents and soaps can also damage the skin and leads to ICD. In cases of ACD, the disease can be a primary disorder or a complication of a preexisting condition, including an ICD treated with multiple topical treatments [9]. Up to 57 % of patients with anogenital complaints report to applied different chemicals and medications to this particular area and positive patch test reactions have been found in up to 78 % of patients with anogenital symptoms [10]. The symptoms are usually nonspecific, being pruritus the most commonly reported. Fragances, topical antibiotics, over-the counter-remedies and topical anesthetics are the most common allergens implicated [11–14]. Other allergens such as spices, plants, rubbers and glues have also been reported. Some series report nickel as one of the most common allergen in vulvar pruritus, however, the relevance of nickel has to be assesed carefully as in many cases its relevance its questionable [6, 11, 12, 15, 16]. A single case of chronic anal pruritus was reported due to a systemic contact dermatitis to nickel [17]. Due the high prevalence of ACD in women with vulvar symptoms, patch test to rule out ACD is recommended for all patients with non-specific chronic vulvar symptoms, specially if they have pruritus.

Pruritus and Contact Dermatitis in the Elderly

Contact dermatitis manifested by acute or chronic pruritus is a common complaint among aged persons. The inflamatory reaction is more subtle in this population and dermatitis is therefore less visible, being pruritus the only symptom. The

likelihood of developing an ICD and ACD varies with the age and the type of irritant [17, 18]. The irritant response to the contact of a external agent is known to be higher in childhood and lower in the elderly. A decrease irritative response to various compounds such as sodium lauryl sulphate, dimethyl sulphoxide, histamine, ethynil nicotate, "croton oil", clorophorm-methanol and lactic acid has been shown in several studies. However, the elderly shows also an increase irritant response with other substances such as soaps and detergents which make them more prone to develop an ICD [17, 19–21].

In case of ACD, the prevalence in the elderly population has been reported to be up to 11 %, being more common in women than in men [22, 23].

Pruritus has been the most common complaint, with an overall prevalence of 29 % in subjects ranking in age from 50 to 91 years (mean age, 75 years [24]. In some cases a history of severe pruritus, without any visible sign of dermatitis has been associated with positive patch test results [24].

Patch test results in elderly are varied. Although elderly people present a decrease in their inmune system response with a decline of delayed contact reactions to some patch test allergenes, the abnormalities in permeability of the epidermal barrier and the long time and high level of exposure to new different allergens increase the potential of allergen sensitization [24–27]. A lower frequency of positive patch test reactions to thimerosal, nickel, epoxy resin and cobalt chloride has been reported [28–30]. Instead, other allergens such as primin, diaminiodiphenylmethane, neomycine sulphate, lanolin alcohols, paraben mix, Euxyl 400, quinoline mix and methylisothiazolinone showed higher sensitization rates [25, 31]. The use of topical treatments to treat leg ulcers or xerosis are often the most common cause of sensitization. Patients usually develop pruriginous eccematous reactions on their wounds and the surrounding skin. In addition, the frequent consumption of drugs chemically related to topics sensitizers leads them to develop eczematous rashes which are more extensive and symmetrical, and often associated with much itching. Therfore ICD and ACD should be consider in all elderly patient with acute or chronic pruritus, specially if they have eccema of unknown etiology.

Pathogencity

While the mechanisms underlying the pathogenicity of the inflammatory cutaneous response in irritant and allergic contact dermatitis has been widely studied, little is known about the mechanisms leading to pruritus. Inflammation in ICD is known to be produced by multiple mechanisms including skin barrier disruption and epidermal changes, which leads to inflammatory infiltrates and cytokine release. Exposure to an irritant would disrupt the epidermal barrier inducing the release of proinflammatory cytokines such as interleukin (IL-1), IL-1beta, IL-6 and tumour necrosis factor (TNF) alpha from keratinocytes injured. Several other inflammatory cells, cytokines and intracellular adhesion molecules help to maintain the inflammatory process [32].

In ACD the inflamation results from a T cell-mediated, delayed type hypersensitivity (DTH) reaction. The process can be divided into two phases: The sensitization or aferent phase and the elicitation or eferent phase. The sensitizaton phase involves profesional antigen presenting cells which initiate an adaptative immune response. As a result a clonal expansion of hapten-specific memory/effector T cells is created. This cells can be found in lymph nodes, blood, and the skin of sensitized individuals and are activated upon reexposure with the same antigen in the elicitation phase. The elicitation phase is the responsible for the cutaneous manifestations of the ACD. The offending hapten activates $CD8^+$ T cells which then initiate the inflamatory response.

Pruritus in contact dermatitis is known to be produce by excitation of small sensory nerves by the inflamed skin, however the exact pruritic pathway of activation is not well understood. The fact that antihistaminics usually do not subside pruritus does raise the possibility that pruritus associated with contact dermatitis may be mediated by hista-

mine-independent inflammatory pathways [33, 34]. Several nonhistaminergic mediators such as substance P, Endothelin 1, 5-Hydroxytryptamine (5-HT), chloroquine, BAM8-22 peptide, leukotriene B4 and prostaglandin E2 induced pruritus when injectec to skin [4].

Animal models have shown that some of this mediators may act through downstream activation of transient receptor potential (TRP) cation channel, subfamily A, member 1 (TRPA1) ion channels. Inhibition of TRPA1 or its genetic deletion (TRPA1 −/−) in mice showed diminished chronic dermatitis and reduced scratching behavior. In addition, the Neurokinin-1 receptor (NK1R) may also be involved since its inhibition effectively suppressed dermatitis and pruritus in ACD. Furthermore, the inflammatory process also seems to play an important role in the development and persistence of pruritus. Bradykinin, an algesic chemical, which normally induce pain in healthy skin of humans and mice, evokes pruritus in a skin contact dermatitis [35]. Mediators that are chronically elevated in ACD such as 4-hydroxynonenal (4-HNE) may increase the activity of TRPA1 channels in sensory nerves resulting in pruritus. There is thus a direct relationship between pruritus and inflammation and probably neuronal TRPA1 channels and other receptors serve as major integrator of the neuronal and inflammatory process.

Treatment

The primary therapeutic intervention to treat and prevent irritant and allergic contact dermatitis is withdrawal and avoidance of the causative agent. Treatment of pruritus is also one of the main therapeutic goals as it leads to scratching and secondary access to more irritants, allergens or pathogens. The first line treatment for localized CD are topical corticosteroids [36]. The potency of the corticosteroid is subject to the location and severity of the dermatitis. Topical corticosteroids have shown efficacy in eczema-related itch and relief of pruritus is usually achieved in the first 3 days of treatment [37–42]. Addition of other antipruritic agents such as pramoxine may also increased the anti-itch efficacy [42]. In cases of bacterial superinfection topical or oral antibiotics may be added to the treatment. Systemic treatment with oral corticosteroids is used in cases with great extension (involvement of more than 20 %) or cases of acute dermatitis involving face or genitalia [43, 44].

In chronic localized dermatitis without response, or with partial response to topical corticosteroids, topical calcineurin inhibitors such as tacrolimus or pimecrolimus can be effectively used [45–47].

Systemic treatment with phototherapy or immunosuppressive drugs such as azathioprine, mycophenolate mofetil and cyclosporine may be used in exceptional cases without response to corticosteroid treatment [48, 49].

Regular use of barrier creams and emmolients may also help to mantain the skin barrier function and prevent the development of dermatitis [36, 50].

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