CLINICAL ASPECTS OF CONTACT HYPERSENSITIVITY

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Allergic contact dermatitis (ACD) represents the clinical manifestation of contact hypersensitivity. In a sensitized individual, ACD appears 24 to 96 hours after contact with the causative allergen (1). Its initial localization is at the site of contact. In contrast to irritant dermatitis, the severity of lesions does not usually depend to the amount of allergen. The edges of the lesions may be well demarcated, but unlike irritant contact dermatitis it may propagate in the immediate vicinity or to distant unrelated sites as ACD is result of an immunologic response.

Acute phase of ACD is characterized by erythema and edema, followed by the appearance of papules, closely set vesicles, oozing and crusting. In the chronic stages, the involved skin becomes lichenified, fissured and pigmented, but new episodes of oozing and crusting may supervene. ACD is usually accompanied by intense pruritis. Generalized induced eczema or hematogenous contact dermatitis is induced by oral or parenteral application of certain contact allergens in previously sensitized in dividuals (2-4). The best known example is the "flare-up" phenomenon at sites of previous eczematous skin changes following an experimental challenge by oral or parenteral application. Substances most often implicated in inducing hematogenous contact eczema are metal salts and drugs.

Histopathology of allergic contact dermatitis

Accprding to the severity of the inflammatory reaction, the histopathologic findings are different in acute and chronic contact dermatitis. The most common histologic feature is spongiosis, which results from intercellular edema. It is often limited to the lower epidermis but, if the reaction is severe, it may affect the upper layers. The clinical expression of intense fluid accumulation in the acute stage is the formation of vesicles that may rupture at the epidermal surface. The papillary vessels are dilated, with perivascular lymphohistiocytic infiltrate, and the upper dermis is edematous. The lymphohistiocytic infiltrate extends in the epidermis (exocytosis) and accumulates in the spongiotic vesicles. In subacute and chronic ACD the spongiotic pattern gradually fades out, the epidermis becomes hyperplastic, and parakeratosis develops.

Diagnosis

The site and clinical appearance of the lesions frequently suggest the etiologic factor when the patient is first seen. Thus sharply delineated geometric lesions are evocative of sensitivity to rosin in adhesive tape. Dermatitis at the site of contact with jewellery, blue jeans buttons, wrist watches, and other metallic objects are seen in nickel dermatitis. It is important to know the location of the initial skin changes and to try to establish a list of

possible contactants that may have caused them. If the dermatitis has taken a chronic course, the patient's observations about factors causing relapses may be helpful. A search for possible sources should concentrate on occupation, hobbies, clothing and personal objects, home environment, and past and previous treatment. A family history or a past history of atopy and psoriasis may be decisive particularly when a diagnosis of hand eczema is discussed.

Patch testing is the universally accepted method for the detection of the causative contact allergens. The positive patch test reproduces an experimental contact dermatitis on a limited area of the skin. A good patch test inicates contact sensitization of past or present relevance and produces no false-positive reaction. Patch tests are usually applied for 48 hours on the upper half of the back. Finn chambers and several other tape methods have been currently in use. Most allergens used in patch testing are well-defined chemical substances. To save place and time, mixes of chemically related chemicals may be used. The most frequently encountered contact allergens have been selected by various international contact dermatitis groups and included in standard patch test series. There are additional series aimed towards specific occupations and other spheres of activities. Most commercially available allergens supplied in syringes are incorporated in petrolatum. Considerable efforts have been made to standardize the concentration of the allergens to ensure comparable results worldwide. Great care must be taken in testing with non standardized chemicals not found in commercially available kits. Ointments, cosmetics, and other substances that are formulated for skin application may be tested undiluted.

Patches are read at least 20 minutes after their removal. It is recommended to perform a second reading 24 hours later. In doing an only reading, a large number of delayed reactions will be missed, while others due to early irritant effects will be considered allergic. The type of positive reaction that can safely be interpreted as indicating allergic contact sensitivity exhibits erythema, edema, and small vesicles extending slightly beyound the patch border. Pruritus and reactivation of previous eczematous skin lesions at the time of testing indicate allergy.

Common causes of allergic contact dermatitis

Contact dermatitis to proteins

A new concept in ACD is the finding that proteins even with a high molecular weight could penetrate the epidermis through the stratum corneum. Trans-epidermal penertation of proteins could be more important when there is and alteration of stratum corneum. The usual site for type of contact dermatitis is the hand. Hand contact with meat or fish proteins or with alpha amylase, an enzyme found in baking powder, is among the important causes of contact dermatitis in butchers, fishers or bakers, respectively. Patients with atopic dermatitis are highly susceptible to ACD to proteins.

Metals

Nickel is the most common cause of ACD in women in alomst all countries. The greater exposure of women to high-nickel content jewellery may be a predisposing factor. Ear piercing is considered to be a principal inducer of nickel contact dermatitis (5). Nickel is part of stainless steel and almost all alloys. Hand eczema in nickel sensitive patients is often of the dyshidrotic type and may be aggravated by nickel ingestion. The dimethylglyoxime spot test has been elaborated to detect nickel in alloys. Avoidance of nickel is extremely difficult because of the ubiquity of the metal.

Chromate is the most common contact allergen in men and sensitization to it is usually occupational. Chromium is also ubiquitous. Occupational exposure is most frequent in construction workers who handle cement. Other common sources are chrome-tanned leather, bleaching agents, paints, printing solutions.

Cosmetics and Skin Care Products

About 5% of patients with contact dermatitis have positive patch tests related to cosmetics (6). The most common causes of contact dermatitis to cosmetics are:

FRAGRANCES: Cinnamic alcohol, cinnamic aldehyde, alpha amyl cinnamic alcohol,

hydroxicitronellal, eugenol, isoeugenol, oak moss absolute, geraniol are the allergens most frequently incriminated in contact sensitization to perfumes. They are included in the European standard patch test series as the "fragrance mix".

HAIR DYES: Contact dermatitis to paraphenylene diamine and related crossreacting dyes involves the scalp, face and neck of persons who have recently had their hair dyed. Paraphenylene diamine is the main cause of allergic hand eczema in hairdressers and sensitizationa to it usually necessitates a job change.

PRESERVATIVES. ANTIOXIDANTS AND ANTISEPTICS are numerous and some of them are found in cutting oils and other industrial products as well. Formaldehyde, which is included in the European standard patch test series is released by a number of biocides.

VEHICLES: of all the vehicle components of cosmetics, lanolin and propylene glycol are the most prominent causes of contact dermatitis(6).

Nail cosmetics. Toluenesulphonamide formaldehyde resin in nail varnish is a frequent sensitizer (7). Nail varnish dermatitis is a diagnostic problem, as periungual lesions are often absent and lesions are scattered on the eyelids, cheeks and neck. Acrylates in artificial nails have also been identified as sensitizers.

Dermatitis from clothes and Shoes

Clothes dermatitis is usually located in the axillae, which is due to the release of allergens from textile under the action of sweat and friction. Clothing dermatitis from formaldehyde is rare nowadays. Formaldehyde may be present in greater quantities in new clothes. The incidence of textile dye dermatitis varies from 1% to 15,9% (8). Leather articles contain several substances that may cause ACD: chrome, adhesives (paratertiary butyl phenol formaldehyde resin), and dyes (paraphenylene diamine). A number of accelerators and antioxidants used in the production of synthetic rubber may also cause contact dermatitis.

Allergy to latex is going to be among the most important causes of contact dermatitis among the health professionals with a prevalence of about 3 to 10%. This high rate is largely due to the use of gloves in latex. Prick test is widely accepted as the most useful test for diagnosis of allergy to latex. At least 9 different allergens have been identified as the cause of latex allergy among which three important ones are: 1) protein acid C serique (Hev b5 - M.W. 16 KDa),2) prohevin (Hev B 6 - M.W. 20 kDa) and 3) hevein (Hev b6.1 - M.W. 4.7 kDa).

Drug Dermatitis

Drug dermatitis may be elicited by the active ingredient of a topical drug, by the vehicle or by a preservative. Contact sensitization to antibiotics, antiseptics, and anaesthetics is relatively frequent, especially in leg ulcer patients.

ACD from topical corticosteroids has been reported with increasing frequency (9). Some molecules found in topical corticosteroids as budesonide, toxicortol, hydrocortisone, 17-butyrate hydrocortisone or amcinonide are particularly allergen. 17-valérate betaméthasone is by contrast a weak allergen The anti-inflammatory effect of corticoids is among the important factor that made difficult the interpretation of corticoids allergic tests.

It is important to note that systemic application of a drug to which an individual has been sensitized by a previous cutaneous exposure may also cause systemic contact dermatitis (10,11).

Plant Dermatitis

Plant dermatitis can manifest itself in a variety of ways, depending upon the plant and the means of exposure. Airborne contact dermatitis mimicking photodermatitis may be caused by sesquiterpene lactones found in the *Compositae* family, while contact dermatitis to plants from th *Liliaceae* and *Alstroemeriaceaese* families may present as a dry painful dermatitis of the fingers in bulb growers, called "tulip fingers" (12). Urushiol, present in poison ivy and poison oak is the most common cause of ACD in the United States, with 50% of the adult population clinically sensitive to it (13).

Treatment

The only available etiologic treatment of ACD is elimination of the contact allergen. The patients should be informed about the identity of the offending agent and the possible sources of the sensitizer. Cross-reacting substances should be listed.

Topical steroids are used in the acute stage and are gradually replaced by indifferent ointments and cold cream as the skin lesions withdraw. Antihistamines are administered for their antipruritic effect, and if ACD is widespread and severe, systemic corticosteroids may be indicated for a short period of time.

Reducing the total body load of nickel has been attempted in nickel eczema by means of nickel-restricted diet and by treatment with disulfiram. Trials have yielded conflicting results as to the clinical effect of the treatment and the application of the metal-chelator disulfiram was limited by serious side effects (14,15).

Oral hyposensitization to urushiol and nickel has been attempted but is not as yet performed in practice. It has been found that it is possible to hyposensitize a sensitive to urushiol individual by oral feeding of gradually increasing amounts of active allergenic extracts of the plant. The main problems are that it takes 2 to 4 months to reach a significant degree of hyposensitization, and one must remain on maintenance thereafter or the level of sensitivity will increase again. Also, side effects may occur when too much of the allergen is ingested before an adequate level of hyposensitization has been achieved. Resorcinols in cashew nut shell cross-react with urushiol and have been used to induce hyposensitization to poison oak and poison ivy (16,17).

Improvement of clinical nickel dermatitis after an initial flare-up of the lesions has been achieved by oral desensitization (18,19) and by subcutaneous application of nickel in combination with UVB treatment (20). While the mechanism of suppression of the disease still remains to be elucidated, oral hyposensitization and T cell vaccination using nickel-reactive T lymphocytes (21) open new area of investigations for the treatment of contact allergy.

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