ARQUIVOS DE ASMA, ALERGIA E IMUNOLOGIA

Review Article

Contact urticaria syndrome – a review

Síndrome da urticária de contato – uma revisão

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ABSTRACT

Contact urticaria syndrome (CUS), contact urticaria, and protein contact dermatitis (PCD) are entities described under the umbrella term of immediate contact skin reactions (ICSR). Generally, hives appear 20-30 minutes after contact with the offending substance, and disappear completely in a few hours, without leaving residual lesions. However, the CUS may be associated with severe systemic symptoms. A prevalence of 5-10% has been estimated among European workers; in the general population it is 1-3%. The mechanisms involved in CUS pathogenesis have not been fully elucidated. An initial approach to improving its understanding involves dividing this condition into non-immune and immune contact urticaria. The former does not require prior sensitization to the allergen, while the latter does. Diagnosis of CUS is established by a detailed history and physical examination, followed by skin tests with suspected substances. Removal of the triggering agent is the best treatment. This requires early proper diagnosis, occupational reporting, and development of preventive measures.

Keywords: Chronic urticaria, chronic inducible urticaria, angioedema, dermatitis, occupational dermatitis.

RESUMO

A síndrome da urticária de contato (SUC), a urticária de contato (UCO) e a dermatite de contato por proteínas (DCP) são entidades descritas sob o rótulo de reações cutâneas imediatas por contato. Geralmente as urticas surgem 20-30 minutos após a exposição por contato com uma substância, e desaparecem por completo em algumas horas, sem deixar lesão residual. Entretanto, a SUC pode apresentar sintomas generalizados graves. Estima-se uma prevalência, entre trabalhadores europeus, entre 5-10%, enquanto na população geral estima-se de que seja de 1-3%. Os mecanismos envolvidos na patogênese da SUC não foram totalmente elucidados. Uma abordagem inicial, para melhorar a sua compreensão, pode ser dividir esta condição em urticária não imunológica (UCNI) e imunológica (UCI). A primeira não necessita de sensibilização prévia ao alérgeno, enquanto a segunda necessita. O diagnóstico da SUC necessita de uma anamnese detalhada e exame físico seguido de teste cutâneo com as substâncias suspeitas. O afastamento do agente desencadeante é o melhor tratamento. Para isso é necessário o diagnóstico apropriado e precoce, a confecção de relatórios ocupacionais e o desenvolvimento de medidas preventivas.

Descritores: Urticária crônica, urticária crônica induzida, angioedema, dermatite, dermatite ocupacional.

Introduction

Contact urticaria syndrome (CUS), contact urticaria (CU), and protein contact dermatitis (PCD) are entities referred to as immediate cutaneous contact reactions.[1] All three of these conditions occur within minutes of exposure to an irritant that has penetrated the skin or mucous membranes.[1] Since Maibach and Johnson first described these diseases in 1975, a growing body of evidence has revealed multiple triggering factors and diverse clinical presentations. Triggers may include chemicals, foods, preservatives, fragrances, metals, and animal or plant products.[2-4] Overall, hives appear 20–30 minutes after contact with a substance

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and disappear completely within a few hours, leaving no residual lesions. However, CUS may present with severe generalized symptoms.[2,4] Hjorth and Roed-Petersen defined PCD as an immediate dermatitis induced after contact with proteins (e.g., meat, fish, vegetables, etc.).[5] Prognoses for these diseases are generally good, although there are reports of severe symptoms.[4,6] Therefore, early detection and prevention are essential in the management of these conditions.

CUS is thought to be underdiagnosed and/or inadequately diagnosed.[7] Therefore, dissemination of knowledge about this condition to allergists, dermatologists, and occupational health physicians is important.[1,7]

Epidemiology

Accurate data on the prevalence of CUS are not available, but it is estimated to be 5–10% in European workers and 1–3% in the overall population.[4]

The Finnish Register of Occupational Diseases (FROD) identifies CU as the second most common occupational skin disease (29.5%) after contact dermatitis (CD). FROD reports bovine hair, flour and grain, and latex as the three most common triggers.[8] An Australian study found the three most affected occupations were health care workers (exposed to latex), food handlers (exposed to food), and hairdressers (exposed to ammonium persulfate).[9] In Germany, cosmetics and latex were the most common triggers.[10]

Reports of CUS have increased in recent years due to the use of personal protective equipment (PPE) and hand sanitizers because of the COVID-19 pandemic. The use of legal cannabis products has led to an increase in occupational cases of CU to cannabis.[4,11]

Pathogenesis

The mechanisms involved in the pathogenesis of CUS are not yet fully understood. A first approach to a better understanding of this disease may be to divide it into nonimmunologic contact urticaria (NICU) and immunologic contact urticaria (ICU). The former does not require prior sensitization to the allergen, whereas the latter does.[12]

ICU is a type I hypersensitivity reaction that occurs in patients with specific immunoglobulin E (IgE) against a particular trigger. Thus, ICU requires prior sensitization and only after repeated exposure to the offending agent will patients exhibit symptoms. Confirmation of this mechanism is seen when skin tests are performed, as positive tests are observed in affected patients and negative in controls. ICU can be caused by two types of agents. The first group includes high molecular weight proteins (10,000 kD or more), while the second group includes low molecular weight chemical haptens (less than 10 kD).[4] Table 1 displays a proposed classification of agents causing ICU.

Table 1
Classification of ICU triggering agents

Group I	Plant proteins
Group II	Animal proteins
Group III	Grains
Group IV	Enzymes

Modified from Giménez-Arnau AM, et al.[4]

Latex is the primary example of ICU. The reaction can range from hives to anaphylaxis. Thirteen different allergenic proteins have been described, named hevein (Hev) b1 to b13.[7] Latex allergy has broader implications for patients, as those allergic to latex have a high degree of cross-reactivity with other antigens, particularly those found in fruits (banana, kiwi, avocado, chestnut), sometimes referred to as "latex-fruit syndrome".[13] Plant dyes (e.g., henna, cassia, and indigo), usually used in powder form, are potential causes of ICU in hairdressers. In addition, oxidative hair dyes are possible causes of ICU in hairdressers, particularly due to the presence of para-phenylenediamine (PPD) and its derivatives.[14-16]

NICU appears to be more common than ICU, but without the presence of systemic symptoms. Among the substances that may induce NICU are cinnamaldehyde, benzoic acid, sorbic acid and nicotinic acid esters.[4,7] In all, 10% of hairdressers in a recent study reported CU from "blonde" hair dyes.[17]

The pathogenesis of PCD is thought to involve a coexistence of type I and type IV hypersensitivity reactions to proteins, usually with high molecular weight or even low molecular weight haptens, as described for ICU. Various foods such as fruits, vegetables, meat, and seafood or nonfood proteins have been reported to be responsible for PCD.[18]

Clinical manifestations

Symptoms of CUS are determined by the nature of exposure (form, duration, and extent), the characteristics of allergen, and the individual's susceptibility.[7]

CU typically occurs within 10–30 minutes of skin contact with the inciting agent and disappears within minutes or hours (< 24 hours). It affects areas of the body that come into contact with the inciting agent, usually exposed areas.[7] Late-onset CU has occasionally been described after repeated applications of the trigger.[19] Patients present with hives, rarely angioedema, associated with itching, burning, stinging and/or pain at the site of contact with the inciting agent. The clinical appearance of the primary lesions does not differ from other types of urticaria.[7]

Volatile proteins (e.g., flour) may cause conjunctivitis, rhinitis, or asthma if they come into contact with the conjunctival mucosa or respiratory tract. Systemic symptoms, such as abdominal pain, oral itching after ingestion (oral allergy syndrome [OAS]), and diarrhea, may occur upon contact with the mucosa of the gastrointestinal tract.[7] OAS is a form of contact urticaria that occurs minutes after ingestion and presents as itching, burning, and swelling of the lips, tongue, palate, or throat and is particularly associated with hypersensitivity to fresh fruit.[7,20]

A staging system was described by Amin & Maibach in 1997[21] and is described below.

Cutaneous reaction only (stages 1 and 2)

Stage 1: Localized hives, eczema, and nonspecific symptoms (itching, tingling, and burning).

Stage 2: Generalized hives.

Extracutaneous reactions (stages 3 and 4)

Stage 3: Asthma (wheezing); rhinitis, conjunctivitis (runny nose and watery eyes), oropharyngeal symptoms (lip edema, hoarseness, dysphagia), and gastrointestinal symptoms (nausea, vomiting, diarrhea, cramping).

Stage 4: Anaphylactic reactions (shock).

Diagnosis

Diagnosis of CUS requires a detailed history and physical examination, followed by skin testing for the suspected substances. Occupational history and habits are also very important to include in the history. Physical examination is crucial in assessing the nature of the lesions (if present). *In vitro* techniques are available for some allergens, such as latex allergy, which can be investigated by using basophil activation test (BAT), radioallergosorbent test (RAST), enzyme-linked immunosorbent assay (ELISA), or IgE for natural rubber components.[22]

Investigation with *in vivo* methods should be done cautiously, as severe systemic symptoms have rarely been described following testing.[4] A sequential order for skin testing procedures has been proposed (Figure 1).

Since patch tests are rarely positive, the diagnosis of PCD is made by means of the prick test.[24]

Many everyday cases require a differential approach, which may include tests such as patch testing and photopatch testing.[25]

Treatment

Treatment of CUS depends on identification and subsequent avoidance of the causative agent. In addition, therapies that prevent the release of mast cell mediators and possibly other mediators may suppress symptoms. Second-generation antihistamines are the drugs of choice for the treatment of hives.[26] High doses of antihistamines should be used before considering the use of alternative treatments. If eczema is present, topical immunomodulation with topical steroids and/or calcineurin inhibitors (tacrolimus and pimecrolimus) may be used. In severe cases of CUS, a short course of oral corticosteroids may be necessary.[4,23]

Antihistamines are not effective in cases of NICU, which leads to the use of nonsteroidal anti-inflammatory drugs (NSAIDs) and aspirin.[23]

Conclusions

CUS represents a significant challenge because of its occupational relevance, which is recognized in only a few countries. It may present as urticaria and/or dermatitis. Identification of CUS requires a high index of clinical suspicion, a detailed occupational history, physical examination, and ancillary testing (e.g., prick testing). Latex, cosmetics, plants, vegetables, and foods are the most common agents. Avoidance of the offending agent is the best treatment. This requires appropriate and early diagnosis, the preparation of occupational histories, and the development of preventive measures.

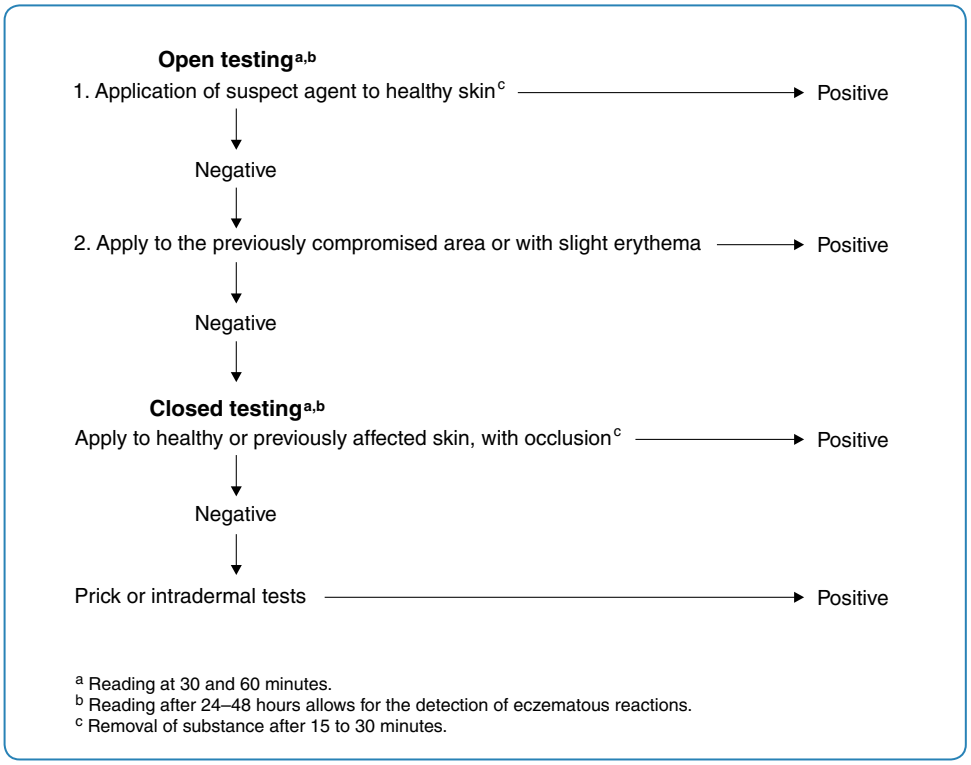

Figure 1
In vivo assessment of contact urticaria syndrome
Modified from França AT and Dortas Junior SD[23].

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