

Unusual reaction to hymenoptera sting: a case of Schönlein-Henoch purpura

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Key words: hymenoptera venom allergy; leukocytoclastic vasculitis; Schönlein-Henoch purpura.

Here is a case of Schönlein-Henoch syndrome, a secondary unusual reaction of allergy to the bite of a stinging hymenoptera. A 12-year-old patient has come under our observation for the appearance of nettle-rash papule and later on of palpable purpura with small bruises on the lower limbs and gluteuses, reporting nonspecific abdominal pains. After 3 days, we have observed association of arthralgias on both ankles and knees. A similar occurrence had already happened a year earlier and had been interpreted as secondary to acute streptococcal tonsillopharyngitis. To an accurate anamnesis following the second event, we found out that the patient had been stung by a bee just a few days earlier. The same thing had happened the year before but this detail at the time had not been considered important and therefore not studied more carefully. The patient though was normally tolerant to *Diptera* bites. The skin tests with hymenoptera dehydrated extract (1) have been proved positive to 0,1 mcg/ml, with a 3rd Class RAST, to *Apis mellifera*, but negative to *Vespula* sp, *Polistes dominulus* and *Tabanus* sp. The skin biopsy specimen revealed a leukocytoclastic vasculitis (Fig. 1). All these clinical data, their

A case of a 12-year-old girl who has come under observation for a Schönlein-Henoch syndrome after a bee sting.

follow-up and the bioptical result have enabled us to diagnose a Schönlein-Henoch (SHP) relapsing purpura.

The SHP is a form of vasculitis to hypersensitivity characterized by small-vessels inflammation, with a mainly cutaneous clinical interest, usually observed in children, with tissue depositing of immunocomplex (ICC) containing IgA. The main clinical manifestations are characterized by a symptomatological tetrad: (i) cutaneous purpura, a must criteria for the diagnosis, mainly on the lower limbs and gluteuses; (ii) arthralgia, occurring in 75% of the cases; (iii) abdominal pain colitis type (in 70%) with intestinal bleedings (in 40%); (iv) kidney alterations nephritis like (in 30%) with hematuria episodes. The aetiology is unknown, but it is considered as main unleashing factors, the role played by viral and bacterial infections, the use of medicines and drugs, coldness, some nonspecific toxins, systemic diseases, tumoural pathologies and insect stings.

A fundamental element of the damage because of ICC is the increasing vascular permeability, which allows their passage among the endothelium cells. Cochrane et al. (2) demonstrated that both histamine and serotonin are the chemical mediators responsible for the vessel-permeabilization process. They are also allowing to fix a considerable quantity of ICC. Furthermore, also mast cells, triggered eosinophils and basophiles are able to release externally a wide range of inflammation mediators such as vasoactive amines, metabolites of arachidonic acid, cytokines (3). The further activation of the complement amplifies the inflammatory process with the production of chemiotactic factors for neutrophils, which once triggered releases lysosomal enzymes. We believe that this vasculitis has been secondary to the release of mediators from mast cells in an individual allergic to hymenoptera venom and not secondary to the toxicity of the venom itself.

Our case is the third one reported in literature (4,5) of this unusual reaction triggered by an insect sting, but the first one reported after an hymenoptera sting in a patient allergic to *Apis m.* In fact, in our case, the urticaria has shortly preceeded the outbreak of petechial eruption connected to the vasculitis pathology development, representing therefore an initial stage of hypersensitivity of the III type more than an aspect of the IgE-mediated reaction, which acted as a trigger factor. Even the histological examination gave evidence of a vasculitis but void of a relevant eosinophil reaction. This is why our patient underwent only one pharmacological treatment but has not been addressed to any specific immunotherapy (6).

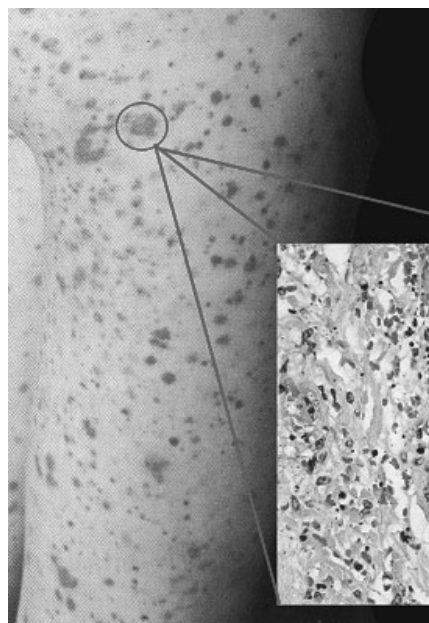


Figure 1. Cutaneous and histological aspect of Schönlein-Henoch

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Severe skin reaction due to excipients of an oral iron treatment

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Iron deficiency is the most common cause of anaemia, at least in women and the administration of supplemental iron is the preferred approach to raise haemoglobin levels. Iron prepara-

Sunset yellow colorant as cause of hypersensitivity to iron replacement therapy.

tions (both oral and intravenous) have not an optimal tolerability profile, due to frequent local and systemic side effects, some of them also defined as hypersensitivity reactions (1). In this regard, it has been shown that, at least in part, drug reactions may be due to the excipients rather than to the active compound. In that case, patients are erroneously considered 'allergic' to the drug (2, 3) and do not receive the treatment. Colorants, which are commonly used as excipients in many drug formulations, are capable of evoking allergic reactions (4).

A 43-year-old female was referred to our clinic with the putative diagnosis of adverse reaction to iron oral treatment. The patient had a persistent iron deficiency anaemia and she had been on oral iron therapy with ferric propionate (Ferrofolin®; Farmades S.p.A, Rome, Italy) for at least 15 years, without significant problems. In April 2006, the GP replaced that drug with another preparation (ferrous sulphate, Ferrograd®, Abbott Italy S.p.A, Latina, Italy) that was considered more effective. Twenty-four hours after beginning this treatment, the patient developed a severe facial erythema with itching and skin oedema. The treatment was immediately stopped and systemic corticosteroid and antihistamines were given, this leading to disappearance of the lesions within 5 days. No episodes attributable to food or drug allergy was present in the clinical history, but on extensive questioning we ascertained that 10 years before she had to change her occupation (hairdresser) because of contact dermatitis. Nonetheless, no specific diagnostic test had been carried on in the past. We noticed that the two iron formulations had not only a different active principle but also a different excipient content. The ferrous sulphate is prepared as tablets containing Sunset Yellow FC&C No.6 (E110), Erithrosine (E127), Titanium Dioxide (E171), and methylmethacrylate as excipients. On the contrary, the previously tolerated ferric propionate is liquid, azodyes-free, and contains none of the mentioned excipients. When the patient was symptom-free, 2 weeks after discontinuation of steroids and antihistamines, a patch test was carried out with the European standard series of substances. The results were graded according to European

Society of Contact Dermatitis guidelines. Of note, an intense itching immediately appeared at the site of the patch and the patient reported the onset of slight facial erythema 6 h after the application. The test proved positive after 48 h for orange disperse 3 (3+), para-phenylenediamine (3+), and after 72 h for thimerosal (2+), gentamicin (3+), nickel sulphate (3+). Of these, only orange disperse was present in the iron formulation (as Sunset Yellow).

A single-blind, placebo-controlled oral challenge was then made, with ferrous sulphate eliciting facial itching and erythema and no reaction with ferric propionate. After the diagnosis of adverse reaction to orange disperse (Sunset Yellow) was established, the treatment with ferric propionate was resumed and the patient was advised to carefully check in the future the presence of the colorant in foods or drugs or cosmetic product.

The patient described was sensitized to some of the most common contact allergens and it is likely that she had become sensitized to these substances during her former occupation as a hairdresser. In fact, hairdressers and allied workers invariably handle cosmetics that contain colorants and preservatives (mainly para-phenylenediamine). In addition, in the past she had used gentamicin-containing ointments to treat her contact dermatitis. It has been shown that simultaneous patch positivity to paraphenylenediamine and disperse orange 3-like colorants is quite frequent (5), and studies reported a cross-reactivity between azo-dyes and paraphenylenediamine (6). The orange disperse colorants as Sunset Yellow are metabolized by the intestinal flora, with the production of sulfanilic acid (4-amino-benzene sulfonic acid) and 1-amino-2-naphthol-6-sulfonic acid. In turn, sulfanilic acid cross-reacts with para-phenylenediamine (7). This cross-reactivity is probably due to the production of common or similar oxidation products, particularly aromatic chemicals with an amino constituent in the para position.

The present case report highlights the importance of carefully studying the role of all components of a drug treatment, before diagnosing the patient as having hypersensitivity to the active principle.