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Letter to the Editor

Paracetamol-induced hypersensitivity vasculitis in a 10-year-old child

Dear Editor,

We report a 10 year-old child who came to our observation for an itching erythematous-purpuric rash arranged in a reticular form over the entire skin surface, which persisted since two months (Figure 1). Four days before its onset, the child experienced a flu-like episode with high fever, treated with paracetamol (usually administered for fevers in this child, without any adverse effects). The rash worsened becoming frankly vasculitic and resembling the pattern of livedo reticularis in one week. His parents noted that fever-related paracetamol administrations contributed to increase rash extension and severity. No gastrointestinal symptom or joint pain were reported in the two-month-period before our visit.

Child's past medical history did not reveal any relevant clue, with the exception of atopic dermatitis since he was 1 year-old, cyclically treated with antihistamines and emollient creams. Laboratory tests performed when we observed the patient for the first time revealed that blood cell count, kidney and liver function, C-reactive protein, and anti-O-streptolysin titer were all within normal limits. The assay for autoimmunity (anti-nuclear, anti-ENA, anti-DNAds, anti-cardiolipin, anti-beta$_2$ glycoprotein 1 antibodies, p/c-ANCA), immunoglobulins (IgA and IgE enclosed), cryoglobulins and serum complement were all negative.

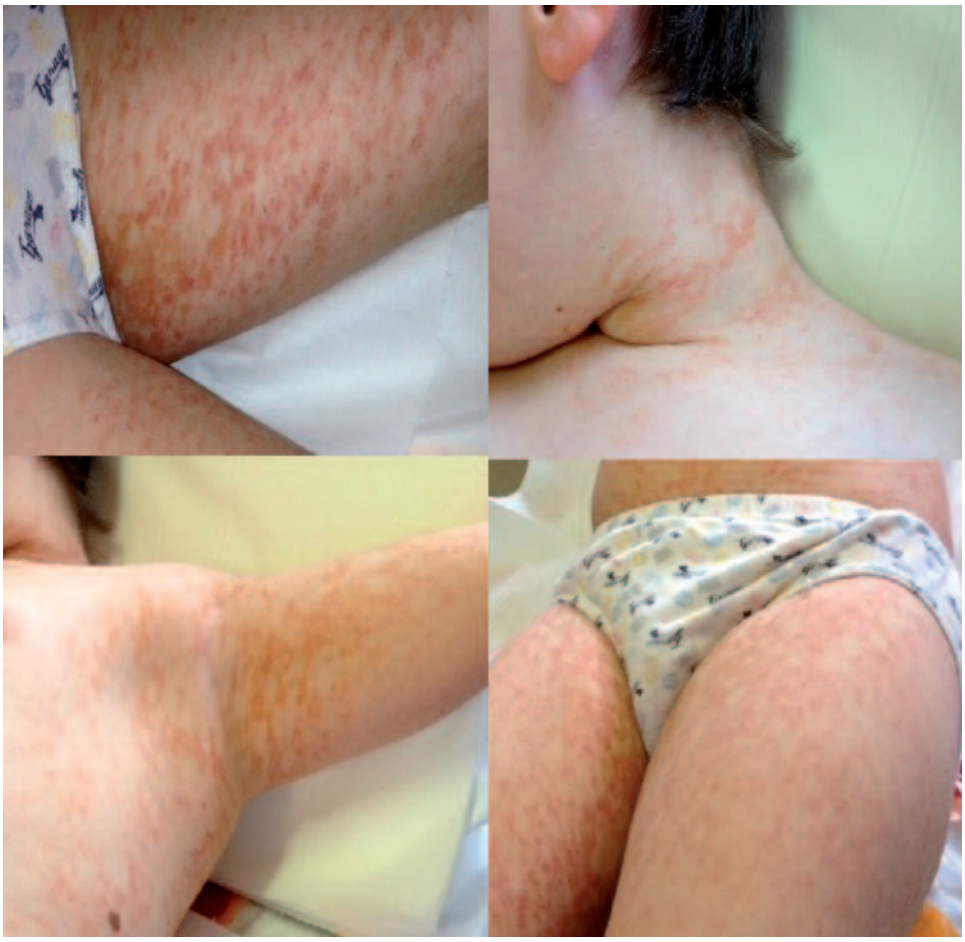

Figure 1. The pictures show the erythematous-purpuric rash, arranged in a reticular configuration over the limbs, trunk and neck of the child.

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A skin biopsy was performed in a purple macule on the right thigh. Histology showed dermal perivascular lymphocyte infiltration and red blood cell extravasation. No fibrinoid necrosis was detected. Direct immunofluorescence showed no immunoglobulin deposit.

Our final diagnosis was drug-induced hypersensitivity leukocytoclastic vasculitis, related to paracetamol administration. Betamethasone per os (0.1 mg/kg/day) and cetirizine (10 mg/day) were then started, with slow progressive improvement of skin lesions in about 3 weeks. The allergologic tests performed after one month were negative: paracetamol was deferred by allergologists in consideration of the recent adverse event experienced by the child. Paracetamol was then completely forbidden as antipyretic.

Leukocytoclastic vasculitis, characterized by the deposition of immune complexes in the vessel wall and polimorphonucleate infiltration around the vessels, is the most common skin vasculitis in children[1]. In the medical literature, hypersensitivity reactions with vascular involvement are mainly related to non-steroidal anti-inflammatory drugs (NSAIDs) and beta-lactam antibiotics, acting with pharmacological or immunological mechanisms[2]. Paracetamol is the most widely-used drug as a simple analgesic or antipyretic in children: as opposed to NSAIDs, which inhibit cyclo-oxigenase enzymes, paracetamol mechanism of action is still not perfectly known. Due to its weak anti-inflammatory activity and endocannabinoid reuptake blocking capacity, paracetamol is not generally classified as a NSAID[3].

Unlike Kawasaki syndrome, for which management recommendations are available[4], in other childhood vasculitides there are no guidelines, flow charts, or evidence-based studies to orient medical decisions. A case of leukocytoclastic vasculitis combined with arthritis following paracetamol administration was reported, in whom rechallenge with the drug was followed by the appearance of new similar lesions[5]. Our patient presented the vasculitic picture on the fourth day of paracetamol administration, and skin biopsy showed leukocytoclastic vasculitis: the rash was persistent for at least 2 months. Although most patients recover completely simply withdrawing paracetamol, some sensitized patients with history of atopic dermatitis, like ours, may require systemic corticosteroids. This report recalls attention to the occurrence of severe cutaneous manifestations associated with paracetamol, a drug largely used in pediatrics, as early diagnosis and drug withdrawal are crucial to the resolution of the vasculitis.

Conflict of Interest

The Authors declare that they have no conflict of interests.

Financial Disclosure

The Authors have no finantial relationships relevant to this article to disclose.

References

1) Weiss PF. Pediatric vasculitis. Pediatr Clin North Am 2012; 59: 407-423.
2) Doña I, Blanca-López N, Torres MJ, García-Campos J, García-Núñez I, Gómez F, Salas M, Rondón C, Canto MG, Blanca M. Drug hypersensitivity reactions: response patterns, drug involved, and temporal variations in a large series of patients. J Investig Allergol Clin Immunol 2012; 22: 363-371.
3) Graham GG, Davies MJ, Day RO, Mohamudally A, Scott KF. The modern pharmacology of paracetamol: therapeutic actions, mechanism of action, metabolism, toxicity and recent pharmacological findings. Inflammopharmacology 2013; 21: 201-232.
4) De Rosa G, Pardeo M, Rigante D. Current recommendations for the pharmacologic therapy in Kawasaki syndrome and management of its cardiovascular complications. Eur Rev Med Pharmacol Sci 2007; 11: 301-308.
5) Arad M, Weinberger A. Leukocytoclastic vasculitis after use of acetaminophen. J Clin Rheumatol 1997; 3: 108-111.

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