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RESEARCH LETTER

Possible DRESS syndrome in a child with borreliosis

To the Editor,

Antibiotic hypersensitivity reactions are a major health concern as they can be a significant cause of morbidity and mortality, limit therapeutic options, and increase socio-economic costs. Diagnosis can be challenging, as great number of drugs can elicit different immune-mediated reactions. A combination of clinical history and different tests is generally necessary to confirm the diagnosis, since none has sufficient sensitivity to be used alone.¹ In some non-immediate hypersensitivity reactions, the lymphocyte transformation test (LTT), which measures the *in vitro* proliferation of T lymphocytes in the presence of a suspected drug, can be the only tool to confirm the diagnosis.²

We report the case of a previously healthy 34-month-old girl who due to fever and odynophagia (interpreted as tonsillitis), was treated with amoxicillin without improvement. Three days later she began treatment with cefaclor, without result. She was then given two shots of penicillin, one in each buttock, with apyrexia after 48 h. Two weeks later, in the same location where penicillin was administered, two nodular inflammatory lesions appeared, with progressive worsening (Fig. 1). Due to the severity of these lesions, she was admitted to local hospital. Shortly after, she developed fever and was submitted to a surgical intervention at her buttocks for drainage of suspected abscess (not confirmed). Due to deterioration of her general status and suspected infectious panniculitis, she was transferred to our Central Hospital, and began flucloxacillin and clindamycin. Three days later, a diffuse exanthema (including both soles) appeared and an allergist was called. Flucloxacillin was stopped and the exanthema faded away, but a cutaneous *erythema migrans*, oedema of the left hand and both feet developed. After a careful and complete clinical history, a non-immediate hypersensitivity reaction to penicillin was suspected. The child began treatment with prednisolone (1.5 mg/kg/day). Buttock lesions began to disappear with objective improvement after third day of corticotherapy. Because of the *erythema migrans* lesion, a dermatologist was called.

Haemoglobin, platelets and creatinine results were normal. The white blood cells count showed leukocytosis with immature cells and eosinophilia (3000/ μ L), elevated AST (231 UI/L) and an aPTT time <20 s. IgG and IgA levels were

normal, IgM was slightly elevated (239 mg/dL), as well as total IgE (314 mg/dL). Parvovirus B19, Epstein Barr virus (EBV) and *Borrelia* IgM antibodies were positive, as well as Herpesvirus 6 (HHV-6) DNA on peripheral blood. The immunophenotyping and lymphocyte function *in vitro* study were normal. Auto-antibody screening revealed negative antinuclear and anticardiolipin antibodies. A skin biopsy at the site of one *erythema migrans* lesion showed dermis with inflammatory infiltrate, mainly lymphocytes, some neutrophils and eosinophils, with perivascular localisation and transendothelial migration, and the presence of DNA of *Borrelia burgdorferi*, Parvovirus B19 and EBV. At the same time, the result from the buttock lesion biopsy done a few days before became available, showing an unspecific inflammatory infiltrate with abundant eosinophils and scarce plasma cells. Prednisolone was maintained, with slow dose tapering.

Because allergy to penicillin was one of the most probable diagnosis, second line therapy with azithromycin for Borreliosis (14 days) was started, with clinical improvement and disappearance of the *erythema migrans*. The inflammatory lesions on both buttocks slowly disappeared. Specific IgE for penicillolyl G and V were both negative. A LTT was performed with penicillin, amoxicillin and cefuroxime. The stimulation index (SI) was calculated as proliferation with drug/proliferation without drug. The result was clearly positive to penicillin with a SI of 60.2 (considered positive when >3) at 100 μ g/mL, and indeterminate for amoxicillin and cefuroxime. DNA for all agents on peripheral blood was negative after five months.

Lyme borreliosis is the most commonly reported vector-borne disease in Europe and North America, and represents a major public health challenge. It is transmitted by ticks harbouring the infectious agent *B. burgdorferi*.³ The age distribution of lyme disease is bimodal, with the highest number of cases occurring in children with ages ranging from 5 to 14 years and adults from 55 to 74 years.⁴

This child developed a delayed hypersensitivity reaction to penicillin, with severe local manifestation, misinterpreted as panniculitis. She was successfully treated for Borreliosis (her basic illness) with a non-beta-lactam antibiotic. The diagnosis of beta-lactam allergy was confirmed by the LTT, which prove to be a useful tool to confirm the diagnosis of non-immediate drug hypersensitivity reaction. Several authors have suggested an association between severe drug hypersensitivity reactions, as is the Drug Rash with Eosinophilia and Systemic Symptoms (DRESS) syndrome, and reactivation of herpesvirus, including HHV-6 and EBV.^{5–7}



Figure 1 Lesions at sites of penicillin administration.

such as seen in this patient, and which might explain the leukocytosis with immature cells and eosinophilia, and the hepatic involvement.

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