

CONTACT POINT

Drug reaction with eosinophilia and systemic symptoms syndrome induced by benznidazole

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Chagas disease is caused by the protozoan parasite *Trypanosoma cruzi* and is endemic in South America. In recent decades it has been increasingly diagnosed in North America and many European countries, mainly because of population mobility. Benznidazole is the first-line treatment option for treating Chagas disease in Spain. Although the most frequent adverse events are cutaneous, few severe cutaneous adverse reactions have been reported.

CASE REPORT

A 30-year-old woman from Bolivia suffered from malaise, generalized oedema and exanthema with subsequent desquamation, without mucosal involvement. She was treated with corticosteroids and improved within 2 weeks. A biopsy specimen showed a moderate perivascular lymphocytic infiltrate in the papillar and superficial dermis. The patient was sent to our Allergy Department for work-up. Review of the clinical history showed that the patient had had cervical and inguinal lymphadenopathy, fever (38.6°C), high C-reactive protein (CRP) (30 mg/mL), elevated liver enzymes (glutamate-pyruvate transaminase (GPT) 103 IU/L), eosinophilia (>4000 eosinophils/mL), and desquamation. She had begun taking benznidazole for chronic Chagas disease 50 days before the rash appeared. Moreover, 3 days before the onset of the rash, she had been treated with paracetamol, cloxacillin, naproxen, and metamizole, owing to an injury. All drugs were discontinued.

Allergological work-up, including patch tests with Curatest adhesive strips (Lohmann & Rauscher, Rengsdorf, Germany) with readings taken on day (D) 2 and D4, and oral challenges, gave negative results with naproxen, paracetamol, cloxacillin, and metamizole. However, benznidazole 5% pet. gave positive patch test reactions on D2 (+++) and D4 (+++) according to ICDRG criteria. The patient was diagnosed with drug reaction with eosinophilia and systemic symptoms (DRESS) syndrome.

DISCUSSION

In 2017, Pacheco Coronel et al¹ reported the case of a Bolivian woman who developed erythematous, painful and itchy plaques, fever, malaise, gastrointestinal symptoms and impaired hepatic function 4 days after beginning treatment with benznidazole. The drug was stopped, and she was treated with antihistamines and corticosteroids, which led to improvement. González-Ramos et al² reported 2 cases of toxic epidermal necrolysis caused by benznidazole with consistent skin biopsies and positive lymphocyte transformation test results with benznidazole. Noguerado-Mellado et al³ described 6 cases of itchy maculopapular generalized rash, with positive benznidazole patch test reactions (10% in dimethylsulfoxide) in 5 of them. A case of acute generalized exanthematous pustulosis was reported by Álava-Cruz et al⁴ in a 32-year-old patient with Chagas disease who began treatment with benznidazole and 6 weeks later developed multiple pinhead-sized, sterile pustules with fever, elevated liver enzymes, and peripheral eosinophilia. The patient underwent patch testing with benznidazole 5% in dimethylsulfoxide, which gave a positive reaction.

In conclusion, we have shown, by a positive patch test reaction, a non-immediate hypersensitivity type IV mechanism in a patient with DRESS (Kardaun score of >5) caused by benznidazole. To the best of our knowledge, this is the first case of DRESS with a positive benznidazole patch test reaction to be reported. In the literature reviewed, a few severe cutaneous reactions have been reported, and patch tests with benznidazole gave positive reactions in only a minority of these. We recommend patch testing with benznidazole in patients with suspected DRESS, because this can help to establish the diagnosis.

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