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Case Report: Drug Hypersensitivity Syndrome Induced by Meglumine Antimoniate

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Abstract. We report a case of drug hypersensitivity syndrome (drug reaction with eosinophilia and systemic symptoms [DRESS]) induced by parenteral meglumine antimoniate (Glucantime) in a 40-year-old man who traveled to Bolivia and was treated for mucocutaneous leishmaniasis. Two weeks after starting therapy, the patient had fever, joint pain, a cutaneous eruption, and hypereosinophilia (1,358 cells/mm^3). These symptoms resolved after drug withdrawal but reappeared upon reintroduction of the drug. Pentavalent antimonials should be definitively withdrawn in patients with hypereosinophilia > 1,000 cells/mm^3 accompanied by systemic manifestations consistent with DRESS.

Although liposomal amphotericin B is now widely used in northern Mediterranean countries, pentavalent antimonials remain the first-line therapy for treatment of visceral, cutaneous, or mucosal leishmaniasis in many areas of the world.[1] Systemic administration of pentavalent antimonials has been associated with severe adverse events, i.e., sudden death, severe hepatitis, pancreatitis, and hematologic disorders.[2–4] To our knowledge, drug hypersensitivity syndrome, also referred to as drug reaction with eosinophilia and systemic symptoms (DRESS), has never been associated with antimonial drugs.[5]

A 40-year-old man with no pertinent medical history traveled to Bolivia in July and August 2007. After returning to France in September, he experienced night sweats and asthenia and showed a right maxillary, 2-cm adenopathy. All of these signs resolved spontaneously within one month. In October, a crusted rhinitis with nasal obstruction appeared, accompanied by painless ulcerations of the upper lip and hard palate. A diagnosis of cutaneous and mucosal leishmaniasis was confirmed by the observation of typical *Leishmania* sp. amastigotes in smears of tissue taken from the palate lesion.

Treatment with intramuscular meglumine antimoniate (Glucantime), 20 mg of pentavalent antimony/kg/day, was initiated. Results of weekly electrocardiograms and laboratory tests, including blood cell count, alanine aminotransferase, aspartate aminotransferase, bilirubinemia, gamma glutamyltransferase, blood amylase and lipase, urea, and blood creatinine, were normal until day 15. He had an eosinophil count of 222 cells/mm^3 on day 0; fever (39°C), joint pain, asthenia, anorexia, and night sweats appeared abruptly on day 15. Because these symptoms worsened, therapy was stopped on day 20. A complete blood cell count on day 26 showed 1,358 eosinophils/mm^3.

Because treatment had been interrupted before completion of the recommended 28-day course, meglumine antimoniate was reintroduced on day 28. However, a single injection led to an intense and abrupt recrudescence of all signs and symptoms. Results of a physical examination were normal, except for a weight loss of 3 kg and a macular and papular rash, predominant on the hands and forearms, comprising target-like papules (Figure 1). His eosinophil count was 2,740 cells/mm^3. Treatment was immediately stopped and symptoms and eosinophilia resolved within a week. The cutaneous and mucosal lesions healed one month after starting therapy, with no relapse observed at the six-month follow-up.

The appearance of intense systemic symptoms (maculopapular rash and eosinophilia greater than 1,000 cells/mm^3) two weeks after initiating therapy is suggestive of hypersensitivity syndrome.[6] Recrudescence of symptoms and eosinophilia upon reintroduction of the antimonial drug clearly points to a reaction induced by meglumine antimoniate (no other drugs had been simultaneously reintroduced).

Drug reaction with eosinophilia and systemic symptoms classically includes fever, macular or papular rash (the two most constant features), lymphadenopathies, arthritis, lymphomonocytosis, and eosinophilia.[7] It usually occurs 2–6 weeks after treatment onset and is potentially associated with hepatitis, nephritis, and pneumonitis.[8,9] Typically, drug hypersensitivity syndromes/DRESS are associated with anticonvulsants, sulfonamides, allopurinol, azathioprine, dapsone, terbinafine, minocycline, and anti-retroviral agents such as abacavir, efavirenz, and nevirapine.[6]

This is the first reported case of drug hypersensitivity syndrome/DRESS associated with meglumine antimoniate. Because most patients are treated in leishmaniasis-endemic areas without systematic follow-up of laboratory parameters, the incidence of this drug reaction may be underestimated.[10] Moreover, eosinophilia may have other causes in these countries where helminthic diseases are also endemic.[11] Nonetheless, it is important to recognize such reactions because their appearance justifies immediate and definitive withdrawal of pentavalent antimonial drugs to prevent potentially severe visceral complications.

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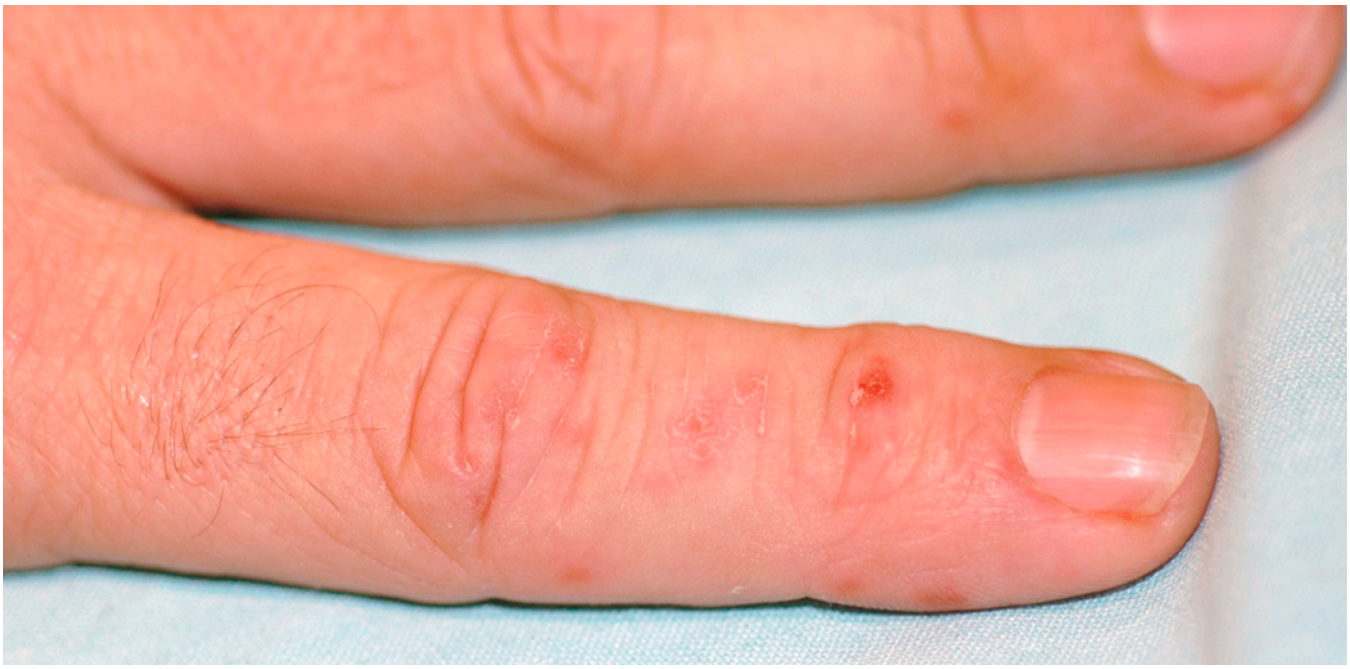

FIGURE 1. Cutaneous lesions in a 40-year-old man with a drug hypersensitivity reaction (drug reaction with eosinophilia and systemic symptoms) induced by a pentavalent antimonial drug (meglumine antimoniate). This figure appears in color at www.ajtmh.org.

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