



Evaluation of eosinophilia in immigrants in Southern Spain using tailored screening and treatment protocols: A prospective study



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Summary Objective: To determine the etiology of eosinophilia in immigrant patients in Southern Spain.

Methods: Prospective study of immigrant patients with eosinophilia (>500 Eo/ μ L) attended in a reference Tropical Medicine Unit and evaluated through the implementation of a specific protocol structured in different levels meant to be accomplished depending on the findings of each previous level.

Results: Out of the 549 patients included in the study (89.6% from sub-Saharan countries), a diagnosis of helminthiasis was reached in 417 (75.9%), mainly by *Strongyloides stercoralis* (n = 190), *Schistosoma* (n = 33) and Hookworms (n = 126). 30 patients (5.5%) had a non-parasitic disorder (asthma, allergic rhinoconjunctivitis, skin conditions and drug-related eosinophilia). Multiple helminthic infections were very common: in 107 patients (19.5%) 2 helminth species were identified, three in 21 patients (3.8%), and four or more in 6 patients (1.1%). Eosinophilia was resolved in 31 of the 33 patients (93.9%) who received empirical treatment with ivermectin, albendazole and praziquantel as an etiological diagnosis was not reached after applying the whole protocol.

Conclusions: Diagnosis of helminthic infections in immigrant patients with eosinophilia can be improved by using tailored protocols based on geographical exposure. The implementation of

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these protocols may also save costs by systematizing diagnostic explorations. Empirical treatment with ivermectin, albendazol and praziquantel in sub-Saharan population when an etiologic diagnosis of eosinophilia has not been attained is an effective measure.

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1. Introduction

During last years, Spain has received a fairly high amount of immigrant population. Overall, in 2013 approximately 5,550,000 immigrants were living in Spain. The area of Poniente is a health area situated in Southeast Spain, holding a population near to 300,000 inhabitants, of which 21% are immigrants, the majority of them from Africa (Maghreb and sub-Saharan countries), Latin America and Eastern Europe. Usually, immigrant population consists of young and healthy people, although many of them may harbour a significant burden of infectious diseases as a result of disease prevalence in their countries of origin and exposures during migration [1–4].

An elevated eosinophil count is a frequent finding in immigrants and travelers returning from the tropics, and is often related to parasitic diseases, the majority of them being helminth infections [5–7]. Usually these infections are benign and self-limiting, but sometimes may lead to severe sequelae for the individuals.

The evaluation of unexplained eosinophilia in an asymptomatic individual is a challenging problem that requires knowledge about a wide variety of potential pathogens, their worldwide distribution and the utilization of a great number of complementary explorations. However, dealing with travelers and/or migrants with eosinophilia may often be a daunting experience. In some studies, up to 50% of patients never have a cause of their eosinophilia identified despite exhaustive evaluation [8–10], suggesting that we do not yet have a reliable algorithm to systematically identify the cause of eosinophilia in this population. The utilization of specific protocols could improve the diagnostic accuracy in this syndrome, as well as reduce the economic costs avoiding unnecessary examinations and tests.

We prospectively evaluated the causes of eosinophilia in adult immigrants through the application of a specific protocol designed in the Tropical Unit of the Poniente Hospital (Almeria, Spain).

2. Methods

Eosinophilia was defined as an increase of eosinophilic leukocytes to more than 500 cells per microliter (μL) in peripheral blood [11]. Patients with relative eosinophilia, defined as an elevated percentage of eosinophils ($>5\%$) in individuals whose peripheral blood eosinophilic leukocyte count remains <500 cells/ μL , were not considered.

In our health area, primary care physicians implement an immigrant patient care protocol that includes complete blood count and liver function tests, serology (HBV, HCV,

HIV and syphilis), as well as investigation of parasites in stools (three concentrated stool samples). Patients are referred to the Tropical Medicine Unit for several reasons, being one of the most frequent to study peripheral eosinophilia detected in this initial assessment.

A common protocol for the study of eosinophilia was designed to evaluate every patient. This protocol included (Fig. 1): medical history, epidemiological data, physical examination and several test distributed in three different levels:

First level: Full blood count, biochemical parameters including liver and renal function tests, iron metabolism and, only for patients from endemic areas, *Schistosoma* and *Strongyloides* serology testing (qualitative determination of IgG-class antibodies against *Schistosoma mansoni* by means of an enzyme immunoassay [Novalisa TM] and qualitative screening of serum IgG antibodies to *Strongyloides stercoralis* by means of an enzyme-linked immunosorbent assay [DRG® *Strongyloides* IgG]). Direct parasitological tests included examination of three concentrated stool samples –using Ritchie’s method – and, just for patients from endemic areas for schistosomiasis, optic microscopy of one concentrated urine sample (10 cc). Diagnosis of schistosomiasis was only considered when direct visualization of schistosome eggs was obtained. In all Sub-Saharan patients, Knott and/or saponin tests for microfilarias were performed too. Chest and abdominal X-ray were performed at this level as well.

In patients with symptoms or lesions suggestive of onchocerciasis, skin snips were taken.

If no etiologic diagnosis was obtained, the second level was accomplished. This second level included: new three stool and one urine samples for direct parasitological examination, a stool sample for *Strongyloides* culture (charcoal culture) and a pelvic and abdominal ultrasound exam for detection of urinary wall bladder alterations or signs of chronic hepatic disease. Mazzotti test was performed in patients with clinical suspicion of onchocerciasis but with negative skin snips.

Those patients that presented sonographic findings suggestive of schistosomiasis (such as focal and/or diffuse urinary bladder wall thickening) were administered empiric treatment with praziquantel.

If the etiology of eosinophilia continued unknown, the third level was carried out: a third new direct parasitological examination of three stool and one urine concentrated samples, serology testing for *Anisakis*, *Toxocara*, *Echinococcus*, *Fasciola* and *Trichinella* (although these tests may be performed at the first level of the diagnostic algorithm in the case of patients presenting with suggestive clinical data), cystoscopy and bladder biopsy (if presence of hematuria or persistence after praziquantel treatment of

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