Strongyloidiasis in the Allergology Service of A Tertiary Hospital in Valencia Province (Spain): A Retrospective Study (2010-2023)

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Strongyloides stercoralis (SS) is an intestinal parasite and nematode endemic to tropical and subtropical countries. Numerous cases of both imported[1-6] and autochthonous[2,4,6,7] infestation are diagnosed annually in Spain, especially in the Mediterranean area[2,5,7,8]. Chronic infestation is usually asymptomatic with persistent eosinophilia, but digestive, skin or respiratory symptoms may also appear, which lead to referral to our clinics[9]. It can also trigger hyperinfestation in immunocompromised patients, which is fatal in up to 80% of cases[10,11].

The diagnosis of *SS* infestation is based on the detection of larvae in faeces with specific methods of enrichment by culture/migration[1,12] but the sensitivity of these methods is very low and the support of determining specific IgG is been sucesfully used[12-14].

Our objective was to determine the profile of *SS-infected* patients who come to our clinics and thus contribute to the early detection and establishment of specific treatment, thus preventing the triggering of hyperinfestations, which can put their lives at risk.

Patients diagnosed with strongyloidiasis were retrospectively reviewed during the last 13 years (2010-2023) in the Allergology Service of the General University Hospital of

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Valencia, which cares for around 376,000 inhabitants, including a foreign population of 15%[15].

The diagnosis was by detection of *SS* in faeces by culture/migration of larvae on Mueller-Hinton agar plates for 7 days at room temperature, and/or via high diagnostic suspicion: Elevated total IgE and/or eosinophilia >500 cells/µL with specific IgG against positive *SS* (EIA *Strongyloides* IgG, DRG diagnostics, Marburg), who responded to treatment with ivermectin (200 µg/kg/day on 2 consecutive days). Patients with eosinophilia from other causes were excluded.

Demographic and epidemiological data and symptoms were compiled. Also physical examination, history of eosinophilia in peripheral blood, response to treatment, pre-treatment and post-treatment complete blood count, total IgE (ImmunoCAP®, elevated if >100 kU/L), skin tests (LETI®, positive if papules ≥3 mm) and specific IgE (ImmunoCAP®, positive if >0.35 kU/L) to aeroallergens and parasitological study in standard faeces. Cross-reactivity between *SS* and other helminths (*Anisakis* and *Ascaris*) was determined with skin prick tests with *Anisakis* (ROXALL®) and/or quantification of specific IgE to *Anisakis* and/or *Ascaris*.

The variables followed a normal distribution after the Kolmogorov test and were reported as a mean and standard deviation (SD). Categorical variables are expressed as count and percentage.

33 cases were recorded: 21 women (64%) and 12 men (36%), mean age 41 (SD 12 years); all foreigners: 30 South American (91%), 2 Pakistani (6%) and 1 Nigerian (3%). All reported possible previous contact with the parasite by walking barefoot in rural areas of their countries.

The patients were referred for evaluation due to eosinophilia, elevated IgE and/or various clinical manifestations: 25 (76%) had respiratory symptoms (recurrent cough

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or rhinitis with/without asthma); 21 (64%) had skin symptoms (urticaria, papules, recurrent pruritus); and 4 (12%) digestive discomfort (dyspepsia, changes in intestinal rhythm). Of these, 16 (48%) reported symptoms in a single shock organ: 10 (30%) respiratory and 6 (18%) skin. The rest of the patients, 17 (52%), had a combination of symptoms. Median delay time from the first reported eosinophilia was 4 years (SD 3). Mean total IgE was 1311 kU/L (SD 1379) and was elevated in 32 patients (97%).

Larval culture was performed in 26 patients (79%) and was positive in 9 (35%). 11 had other concomitant parasites, none of them by other nematodes. *Anis*akis sensitisation was tested in 14 patients (42%) and positive in 9 (64% of these).

IgG to *SS* was positive for all patients determined (32), and, after treatment, the levels were negative (21, 65% of these) or had decreased considerably (9, 28% of these) 3-9 months later. Repeat treatment was considered in 2 patients.

Mean eosinophilia decreased significantly ($p<0.01$) to 204 cells/μL (SD 108) from mean pre-treatment peak levels of 1376 cells/μL (SD 671). The decrease in the mean total IgE to 847 (SD 1158) was not statistically significant ($p=0.86$).

These retrospective study on strongyloidiasis cases diagnosed at our allergology clinics (all cases of imported origin, especially from South America) were in agreement with the results in Valerio et al.[2] via an *SS* infestation surveillance programme, with only 2.8% (2/70) autochthonous patients as well as Fernández et al.[4] with 1 of 9 cases (11%). Requena et al.[13] described a seroprevalence of almost 10% of the population from endemic areas, and it was higher in women. The results from our series of 33 patients (21 women and 12 men) differed from other studies in our Mediterranean environment[6], where the majority were men of a higher mean age of 61 years (SD 17) vs. 41 years (SD 12).

Similar to the series published by Fernández[4], 13 of the 24 patients (54%) with

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respiratory symptoms proved to be atopic with symptoms related to aeroallergens and remained, at least partially, after treatment with ivermectin.

The usual diagnosis was via serology against *SS*, while culture/migration was positive in only a third of cases. The serological determination is in our view a cost-effective intervention when we found patients with elevated IgE and persistent eosinophilia even when an allergological study is positive and partially explaine the symptoms referred[4]. Other authors, such as Salvador[1], also suggested serological testing was the most sensitive for screening in the population. Eosinophilia and serology monitoring will confirm the final elimination of the parasite or result in repeating the eradication treatment[14]—this occurred in 2 patients in our series.

SS infestation should be suspected in patients attending allergy clinics with persistent eosinophilia and elevated IgE, with or without respiratory/skin/digestive symptoms, even if they show sensitivity to allergens that partially explain them. This is especially so for foreign patients[1-6] but should not be ruled out for the native population[2,4,6,7]. Sensitisation to *Anisakis* could raise a reasonable suspicion of infestation by another nematode[4,9]. Treatment with ivermectin was well tolerated and very effective. We consider the detection of this pathology in allergy clinics to be of great importance since our patients are often candidates for treatment with corticosteroids for prolonged periods of varying length; this increases the risk of hyperinfestation, a serious complication associated with a very high mortality rate[10,11].

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Conflicts of Interest

The authors declare that they have no conflicts of interest.

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