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

de las Marinas Alvarez MD[1], Romero CS[2,3], Felix Toledo R[1], Alvariño Martín M[1], Martorell Calatayud C[1], Cerdá Mir JC[1], Navalpotro Rodríguez D[4], Martorell Aragones A[1]

[1]*Allergology Department, Consorcio Hospital General Universitario de Valencia, Valencia, Spain*

[2]*Anesthesiology Department, Consorcio Hospital General Universitario de Valencia. Valencia, Spain*

[3]*Research Methodology Department, European University of Valencia, Valencia, Spain*

[4]*Microbiology Department, Consorcio Hospital General Universitario de Valencia, Valencia, Spain*

J Investig Allergol Clin Immunol 2024; Vol. 34(3): 188-190
doi: 10.18176/jiaci.0955

Key words: Strongyloidiasis. Persistent eosinophilia. Early diagnosis.

Palabras clave: Estrongiloidiasis. Eosinofilia persistente. Diagnóstico precoz.

The nematode *Strongyloides stercoralis* (SS) is an intestinal parasite 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, although digestive, skin, and respiratory symptoms may also appear and lead to referral to clinics [9]. In immunocompromised patients, SS can also trigger hyperinfestation, which is fatal in up to 80% of cases [10,11].

The diagnosis of SS infestation is based on the detection of larvae in feces using specific enrichment methods based on culture/migration [1,12], although the sensitivity of these methods is very low and the approach has been successfully complemented by determination of specific IgG [12-14].

Our objective was to determine the profile of SS-infested patients who come to our clinics and are thus diagnosed early and prescribed specific treatment to prevent hyperinfestation, which can prove life-threatening.

Patients diagnosed with strongyloidiasis were retrospectively reviewed during 2010-2023 in the Allergology Department of General University Hospital of Valencia, Valencia, Spain, which cares for around 376 000 inhabitants, 15% of whom were born outside Spain [15].

Diagnosis was by detection of SS in feces through culture/migration of larvae on Mueller-Hinton agar plates for 7 days at room temperature and/or high diagnostic suspicion based on elevated total IgE and/or eosinophilia >500/μL with specific IgG against positive SS (EIA *Strongyloides* IgG, DRG Diagnostics). Patients had to have responded to treatment with ivermectin (200 μg/kg/d for 2 consecutive days). Patients with eosinophilia of other etiologies were excluded.

Demographic and epidemiological data and symptoms were compiled. We also performed a physical examination and recorded the following: history of eosinophilia in peripheral blood; response to treatment; pretreatment and posttreatment complete blood count and total IgE (ImmunoCAP, elevated if >100 kU/L); skin test results (LETI, positive if wheals ≥3 mm); specific IgE to aeroallergens (ImmunoCAP, positive if >0.35 kU/L); and a standard parasitological work-up in feces. Cross-reactivity between SS and other helminths (*Anisakis* and *Ascaris*) was determined using skin prick tests with *Anisakis* (ROXALL) and/or quantification of specific IgE to *Anisakis* and/or *Ascaris*.

The Kolmogorov-Smirnov test showed that variables followed a normal distribution. Variables are expressed as mean (SD). Categorical variables are expressed as count and percentage.

We recorded a total of 33 affected patients (21 women [64%] and 12 men [36%]; mean [SD] age, 41 [12] years), all of whom were born outside Spain (30 in South America [91%], 2 in Pakistan [6%], and 1 in Nigeria [3%]). All reported possible previous contact with the parasite by walking barefoot in rural areas of their home countries.

The patients were referred for evaluation owing to eosinophilia, elevated IgE, and/or various clinical manifestations, as follows: respiratory symptoms (recurrent cough or rhinitis with/without asthma), 25 (76%); skin symptoms (urticarial papules, recurrent pruritus) 21 (64%); and digestive discomfort (dyspepsia, changes in intestinal rhythm), 4 (12%). Of these, 16 (48%) reported symptoms in a shock organ: 10 (30%) in the respiratory tract and 6 (18%) in the skin. The remaining patients (17 [52%]), had a combination of symptoms. The median delay from the first reported eosinophilia was 4 (3) years.

Mean total IgE was 1311 (1379) kU/L and was elevated in 32 patients (97%).

Larval culture was performed in 26 patients (79%) and was positive in 9 (35%). Eleven patients had concomitant parasitic diseases, none of which was caused by other nematodes. Sensitization to *Anisakis* was tested in 14 patients (42%) and proved positive in 9 (64%).

IgG to SS was positive for all patients tested (32). After treatment, levels were negative (21 [65%]) or had decreased considerably (9 [28%]) (3-9 months later). Repeat treatment was considered in 2 patients.

Mean eosinophilia decreased significantly ($P<.01$) to 204 (108)/μL from pretreatment peak levels of 1376 (671)/μL. The decrease in the mean total IgE to 847 (1158) was not statistically significant ($P=.86$).

The findings of this retrospective study on strongyloidiasis diagnosed at our allergology clinics (all cases of imported origin, especially from South America) are consistent with the results of Valerio et al [2], whose SS infestation surveillance programme revealed only 2.8% (2/70) of autochthonous patients, and Fernández Rodríguez et al [4], who found that 1 of 9 cases (11%) was autochthonous. Requena-Méndez et al [13] reported seroprevalence in almost 10% of the population from endemic areas, with a higher percentage observed for women. The results from our series of 33 patients (21 women and 12 men) differed from those of other studies in the Mediterranean area [6], where most patients were men, with a higher mean age of 61 (17) years compared with 41 (12) years in our study.

Consistent with Fernández Rodríguez et al [4], 13 of the 24 patients (54%) with respiratory symptoms proved to be atopic. The symptoms were induced by aeroallergens and persisted, at least partially, after treatment with ivermectin.

The usual diagnosis was via serology for SS, while culture/migration was positive in only a third of cases. In our opinion, serological determination is a cost-effective intervention. We found patients with elevated IgE and persistent eosinophilia, even when an allergology study was positive, thus partially explaining the symptoms reported [4]. Salvador et al [1] also suggested that serological testing was the most sensitive screening technique in their study population. Monitoring of eosinophilia and serology testing confirm the final elimination of the parasite or indicate the need to repeat eradication treatment [14], as 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 are sensitive to allergens that partially explain them. This is especially so for foreign-born patients [1-6], although it should not be ruled out for the native population [2,4,6,7]. Sensitization 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 condition in allergy clinics to be of great importance, since patients are often candidates for treatment with corticosteroids over prolonged periods of varying length. This in turn can increase the risk of hyperinfestation, a serious complication associated with a very high mortality rate [10,11].

Funding

The authors declare that no funding was received for the present study.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

Previous Presentations

The data were partially presented in poster form at the XXXI Congreso Nacional "online" of Sociedad Española de Alergología e Inmunología Clínica (SEAIC), Zaragoza, 5-7 November 2020. Award for the best poster communication.

References

1. Salvador F, Treviño B, Bosch-Nicolau P, Serre-Delcor N, Sánchez-Montalvá A, Oliveira I, et al. Strongyloidiasis screening in migrants living in Spain: systematic review and meta-analysis. Trop Med Int Health. 2020;25(3):281-90. doi: 10.1111/tmi.13352.
2. Valerio L, Roure S, Fernández-Rivas G, Basile L, Martínez-Cuevas O, Ballesteros ÁL, et al: North Metropolitan Working Group on Imported Diseases. Strongyloides stercoralis, the hidden worm. Epidemiological and clinical characteristics of 70 cases diagnosed in the North Metropolitan Area of Barcelona, Spain, 2003-2012. Trans R Soc Trop Med Hyg. 2013;107(8):465-70. doi: 10.1093/trstmh/trt053.
3. González A, Gallo M, Valls ME, Muñoz J, Puyol L, Pinazo MJ, et al. Clinical and epidemiological features of 33 imported Strongyloides stercoralis infections. Trans R Soc Trop Med Hyg. 2010;104(9):613-6. doi: 10.1016/j.trstmh.2010.06.001.
4. Fernández Rodríguez C, Enríquez-Matas A, Sanchéz Millán ML, Mielgo Ballesteros R, Jukic Beteta KD, Valdez Tejeda M, et al. Strongyloides stercoralis infection: a series of cases diagnosed in an allergy department in Spain. J Investig Allergol Clin Immunol. 2012;22(6):455-7.
5. de las Marinas MD, Martorell A, Felix R, Cerdá JC, García A, Navalpotro D. Strongyloidiasis: an emerging infectious disease that simulates allergic diseases. J Investig Allergol Clin Immunol. 2012;22(4):286-7.
6. Barroso M, Salvador F, Sánchez-MontalváA, Bosch-Nicolau P, Molina I. Strongyloides stercoralis infection: A systematic review of endemic cases in Spain. PLoS Negl Trop Dis. 2019;13(3):e0007230. doi: 10.1371/journal.pntd.0007230.
7. Lucas Dato A, Pacheco-Tenza MI, Borrajo Brunete E, Martínez López B, García López M, González Cuello I, et al. Strongyloidiasis in Southern Alicante (Spain): Comparative Retrospective Study of Autochthonous and Imported Cases. Pathogens. 2020;9(8):601-12. doi: 10.3390/pathogens9080601.
8. Román-Sánchez P, Pastor-Guzmán A, Moreno-Guillén S, Igual-Adell R, Suñer-Generoso S, Tornero-Estébanez C. High prevalence of Strongyloides stercoralis among farm workers on the Mediterranean coast of Spain: analysis of the predictive factors of infection in developed countries. Am J Trop Med Hyg. 2003;69(3):336-40.
9. Caraballo L, Llinás-Caballero K. The relationship of Parasite Allergens to Allergic Diseases. Curr Allergy Asthma Rep. 2023;23:363-73. https://doi.org/10.1007/s11882-023-01089-8.
10. Keiser PB, Nutman TB. Strongyloides stercoralis in the Immunocompromised Population. Clin Microbiol Rev. 2004;17(1):208-17. doi: 10.1128/CMR.17.1.208-217.2004.
11. Llagunes J, Mateo E, Peña JJ, Carmona P, de Andrés J. Hiperinfección por Strongyloides stercoralis [Hyperinfection caused by Strongyloides stercoralis]. Med Intensiva. 2010;34(5):353-6. doi: 10.1016/j.medin.2009.06.006.
12. Martín-Rabadán P, Martínez-Ruiz R, Cuadros J, Cañavate C. El laboratorio de microbiología ante las enfermedades parasitarias importadas [Clinical microbiology laboratory and imported parasitic diseases]. Enferm Infecc Microbiol Clin. 2010;28(10):719-25. doi: 10.1016/j.eimc.2010.03.013.

13. Requena-Méndez A, Salas-Coronas J, Salvador F, Gomez-Junyent J, Villar-Garcia J, Santin M, et al. High Prevalence of Strongyloidiasis in Spain: A Hospital-Based Study. Pathogens. 2020;9(2):107-19. doi: 10.3390/pathogens9020107.
14. Requena-Méndez A, Chiodini P, Bisoffi Z, Buonfrate D, Gotuzzo E, Muñoz J. The Laboratory Diagnosis and Follow Up of Strongyloidiasis: A Systematic Review. PLoS Negl Trop. Dis. 2013;7(1): e2002. doi: 10.1371/journal.pntd.0002002.
15. Informe de Gestió de la Conselleria de Sanitat Universal i Salut Pública 2022. Datos del Sistema de informacion poblacional (SIP). Fuente: Alumbra. Modulo SIP. Dici2022. (Pag 21). https://www.san.gva.es/documents/d/portal-estadistico/informe_de_gestion_2022_es Edita: Generalitat Valenciana. Conselleria de Sanidad Universal y Salud Pública © de la presente edición: Generalitat, 2023 Primera edición, junio 2023. Edición online Maquetada por: Publiprinters SL. 164 páginas.

Manuscript received September 25, 2023; accepted for publication October 23, 2023.

Maria Dolores de las Marinas Alvarez
Allergology Department
Consorcio Hospital General Universitario de Valencia
Av Tres Cruces nº 2
46014 Valencia, Spain
E-mail: ddelasma@yahoo.es/
delasmarinas_mar@gva

