



Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.

vated inflammatory parameters (C-reactive protein: 259 mg/l and procalcitonin 60.71 ng/mL), normocytic anaemia (haemoglobin 116 g/l, mean corpuscular volume [MCV]: 80.9 fl), lymphopenia (730 lymphocytes/mm³), thrombocytopenia (30,900 platelets/ml) and coagulopathy (prothrombin activity 70%, INR 1.27 and D-dimer: 12,351 ng/mL).

The chest X-ray revealed a faint and predominantly peripheral bilateral interstitial infiltrate, and a swab test for detection of SARS-CoV-2 by polymerase chain reaction (PCR) in nasopharyngeal exudate yielded a positive result.

With the initial diagnosis of COVID-19, the patient deteriorated clinically and in tests, tending toward hypertension and vomiting. In this context, it was vitally important not to forget, even in spite of the COVID-19 diagnosis and clinical and radiological compatibility, that the patient had travelled from an area where malaria is endemic. Moreover, this was a febrile syndrome upon return from a tropical country, accompanied by anaemia, hyperbilirubinaemia and thrombocytopenia.

A rapid immunochromatographic test (Malaria Ag Pf/Pan, Standard Diagnostics, Inc.[®]) was performed urgently, with a positive result for detection of *Plasmodium falciparum* antigen and common antigen. Immediately following this, a smear test was performed in peripheral blood, identifying two ring stage *Plasmodium falciparum*-type intraerythrocytic parasites with eccentric localisation and multiple parasitisation in a proportion of 4.5%.

After an initial assessment by the intensive care unit concerning the severe clinical (prostration and hyperbilirubinaemia) and parasitological (parasitaemia >4% in a semi-immune person) criteria, the patient ultimately received treatment with weight-adjusted dihydroartemisinin–piperaquine for three days with very good tolerance.^{9,10} The follow-up smear at 24 h showed a reduction in parasitaemia to below 1% and no parasitaemia was visible at the end of treatment. The gradual clinical improvement was accompanied by a resolution of symptoms.

With regard to COVID-19, the patient remained asymptomatic with clinical and radiological resolution without requiring supplementary oxygen therapy or other symptomatic treatment. Serology testing for SARS-CoV-2 was performed using ELISA and CLIA with seroconversion on the eleventh day from the first SARS-CoV-2 PCR test in nasopharyngeal exudate, which remained positive at discharge. We do not know what impact SARS-CoV-2 had on the evolution of the severe malaria, nor the possible influence of the artemisinin-based antimalarial treatment the patient received. Gendrot et al.,¹¹ having demonstrated activity *in vitro*, propose that antimalarial combinations at high concentrations in lung parenchyma may be useful as prospective COVID-19 therapies.¹¹ Given the lack of reported cases of SARS-CoV-2 and *Plasmodium falciparum* co-infection in the literature, this hypothesis will need to be addressed by future research studies.

We must not let down our guard in the treatment of imported disease, even in pandemic times, as rapid action and early diagnosis is vital in a medical emergency such as malaria.

References

- Gascón J, Corachán M. Fiebre en el viajero internacional. *Medicina Integral*. 2001;37(8):354–6.
- Wilson ME, Weld LH, Boggild A, Keystone JS, Kain KC, von Sonnenburg F, et al. Fever in returned travelers: results from the GeoSentinel Surveillance Network. *Clin Infect Dis*. 2007;44:1560–8. <http://dx.doi.org/10.1086/518173>.
- Freedman DO, Weld LH, Kozarsky PE, Fisk T, Robins R, von Sonnenburg F, et al. Spectrum of disease and relationship to place of exposure in ill returned travelers. *N Engl J Med*. 2006;354:119–30.
- Hill DR. The burden of illness in international travelers. *N Engl J Med*. 2006;354:115–7.
- Wilson ME. The traveller and emerging infections: sentinel, courier, transmitter. *J Appl Microbiol*. 2003;94:1S–1S.
- World Health Organization. ISBN 978-92-4-156572-1; [Accessed 18 October 2020]. Available from: <https://www.who.int/publications/i/item/9789241565721>, 2019.
- Tatem AJ, Jia P, Ordanovich D, Falkner M, Huang Z, Howes R, et al. The geography of imported malaria to non-endemic countries: a meta-analysis of nationally reported statistics. *Lancet Infect Dis*. 2017;17:98–107. [http://dx.doi.org/10.1016/S1473-3099\(16\)30326-7](http://dx.doi.org/10.1016/S1473-3099(16)30326-7).
- Mischlinger J, Rönberg C, Álvarez-Martínez MJ, Bühler S, Paul M, Schlägenhauf P, et al. Imported malaria in countries where malaria is not endemic: a comparison of semi-immune and nonimmune travelers. *Clin Microbiol Rev*. 2020;33. <http://dx.doi.org/10.1128/CMR.00104-109>, e00104–9.
- Muñoz J, Rojo-Marcos G, Ramírez-Olivencia G, Salas-Coronas J, Treviño B, Pérez Arellano JL, et al. Diagnóstico y tratamiento de la malaria importada en España: recomendaciones del Grupo de Trabajo de Malaria de la Sociedad Española de Medicina Tropical y Salud Internacional (SEMSTI) [Diagnosis and treatment of imported malaria in Spain: Recommendations from the Malaria Working Group of the Spanish Society of Tropical Medicine and International Health (SEMSTI)]. *Enferm Infecc Microbiol Clin*. 2015;33:e1–13. <http://dx.doi.org/10.1016/j.eimc.2013.12.014>.
- Rojo-Marcos G, Cuadros-González J. Malaria y Protozoos Intestinales. *Enferm Infecc Microbiol Clin*. 2016;34(3):191–204. <http://dx.doi.org/10.1016/j.eimc.2015.12.009>.
- Gendrot M, Duflot I, Boxberger M, Delandre O, Jardot P, Le Bideau M, et al. Antimalarial artemisinin-based combination therapies (ACT) and COVID-19 in Africa: In vitro inhibition of SARS-CoV-2 replication by mefloquine-artesunate. *Int J Infect Dis*. 2020;99:437–40. <http://dx.doi.org/10.1016/j.ijid.2020.08.032>.

Sergio Ferra Murcia^{a,*}, Bárbara Hernández Sierra^b,
Esteban Alessandro Vogt Sánchez^b,
Antonio Ramón Collado Romacho^a

^a Unidad de Enfermedades Infecciosas, Servicio Medicina Interna, Hospital Universitario Torrecárdenas, Almería, Spain

^b Servicio de Medicina Interna, Hospital Universitario Torrecárdenas, Almería, Spain

* Corresponding author.

E-mail address: sergio.ferra.sspa@juntadeandalucia.es

(S. Ferra Murcia).

<https://doi.org/10.1016/j.eimc.2021.08.006>

2529-993X/ © 2020 Sociedad Española de Enfermedades Infecciosas y Microbiología Clínica. Published by Elsevier España, S.L.U. All rights reserved.

Eosinophilia and abdominal pain after severe pneumonia due to COVID 19[☆]



Eosinofilia y dolor abdominal tras una neumonía grave por enfermedad por coronavirus 19

Immunosuppressant treatments are being used frequently in the context of the coronavirus disease 2019 (COVID-19) pandemic.

[☆] Please cite this article as: Pintos-Pascual I, López-Dosil M, Castillo-Núñez C, Múñez-Rubio E. Eosinofilia y dolor abdominal tras una neumonía grave por enfermedad por coronavirus 19. *Enferm Infecc Microbiol Clin*. 2021;39:478–480.

These treatments can predispose to the reactivation of infections that had remained asymptomatic.

We present the case of a 70-year-old male patient who sought treatment at a tertiary hospital in the Community of Madrid in April 2020 in the context of the SARS-CoV-2 pandemic. The patient's only medical history was hypertension, in treatment with losartan-hydrochlorothiazide. The patient was of Ecuadorian origin, resident in Madrid since 2008, returning to his country for just a single visit in 2016. Specifically, the patient had lived in the rural Guayaquil area, and during his childhood had performed agrarian tasks and often walked barefoot. He later worked as a metalworker in a car factory, an occupation he currently continues in Spain. He came to the hospital presenting with a dry cough, fever, dyspnoea

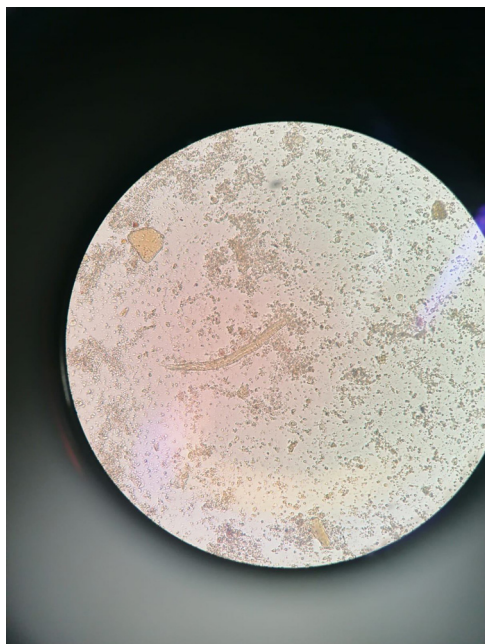


Fig. 1. *Strongyloides* larva in fresh stool.

and chest pain. The physical examination revealed constant dry rales up to the middle fields: RR: 34 bpm, baseline O2Sat: 92%. Blood tests were ordered, which most notably revealed: elevated transaminases, leukocytes 8690/ μ l, neutrophils 7680/ μ l (88.4%), lymphocytes 590/ μ l (6.8%), monocytes 360/ μ l (4.1%), eosinophils 10/ μ l (0.1%), basophils 10/ μ l (0.1%), haemoglobin 16 g/dl, platelets 244,000/ μ l. X-ray confirmed the presence of pneumonia and a nasopharyngeal swab PCR test was positive for SARS-CoV-2. For the first three days from admission he presented respiratory deterioration, developing adult respiratory distress syndrome, for which treatment was started with 250-mg boluses of methylprednisolone for five days. Tocilizumab was administered from day 6 to day 13, and anakinra on days 10–13 and 19–24. Following clinical improvement, the dose of corticosteroids was tapered, ending treatment at one month. The patient maintained a normal eosinophil count throughout his hospital stay. A Quantiferon test was ordered, with a negative result, as well as serological tests for HIV, syphilis, hepatitis B and C, *Leishmania* and *Trypanosoma cruzi* all negative. A serological test was also ordered for *Strongyloides stercoralis*, but the test was not available at the time.

At one month after discharge, the patient began to experience epigastric abdominal pain without nausea, vomiting, diarrhoea, fever, cutaneous pruritus, or loss of weight or appetite. The respiratory symptoms had resolved. The chest X-ray showed resolution of the pneumonia. Blood tests were ordered, returning the following leukocyte count: leukocytes 23,170/ μ l, neutrophils 3000/ μ l (12.7%), lymphocytes 5900/ μ l (25.3%), monocytes 900/ μ l (3.9%), eosinophils 13,300/ μ l (57.3%), basophils 200/ μ l (0.8%). Repeat serological tests were ordered, which were all negative except the one for *Strongyloides*, which was positive. The fresh stool analysis confirmed the presence of *Strongyloides* sp. larvae (Fig. 1). In view of the diagnosis, the patient received albendazole 400 mg/12 h for three days, with resolution of the digestive symptoms. Follow-up blood tests were performed several weeks later, with improvement of the eosinophilia. However, given that it did persist, new stool samples were requested, in which *Strongyloides* sp. larvae were once again observed. Given the treatment failure, treatment with ivermectin was initiated, with resolution of the clinical picture.

The diagnosis of strongyloidiasis is established by visualising *Strongyloides* larvae. This infection is often underdiagnosed due to the low sensitivity of the diagnostic techniques, but serology is sufficient to rule out the diagnosis¹. Although in our setting such cases are usually imported, there is also endemic transmission in Spain². Most imported cases come from South America³, with Ecuador being one of the countries with the highest prevalence⁴.

Strongyloides is the only nematode capable of causing autoinfection in the host, leading to chronic parasitic infection lasting decades⁵. In immunocompetent patients, infection is often asymptomatic⁵. More than 80% of patients with imported strongyloidiasis present eosinophilia as the only manifestation. From this perspective, the presence of eosinophilia in a patient from South America should make us suspect *Strongyloides* infection, among other possible diagnoses³.

The symptoms, when they appear, are epigastric pain, skin lesions and/or eosinophilia⁶. In immunosuppressed patients, hyperinfection syndrome can arise, with multi-organ involvement and high mortality¹. The administration of glucocorticoids and other immunosuppressants is a risk factor for the development of symptoms^{6,7}. The treatment of choice⁸ is ivermectin (accessible on request as a foreign medicinal product not authorised in Spain), with albendazole being a less effective alternative (available in normal pharmacies). Given the exceptional circumstances, in our case albendazole was chosen as the first-line therapy because it was easy for the patient to acquire.

Our patient presented a reactivation of *Strongyloides* sp., probably in relation to prolonged corticosteroid administration. In clinical pictures of severe pneumonia due to COVID-19, other immunosuppressant drugs are also being used, such as tocilizumab or anakinra, which has been linked to an increase in the risk of opportunistic infections⁹. In general, a parasite study and eradication is recommended in those patients with a history of living in or travelling to endemic areas¹⁰. Moreover, screening needs to be carried out for latent infections (tuberculosis, hepatitis B) if immunosuppressant treatments are to be administered¹¹. Organ transplant guidelines¹² include the study of parasitic infections in patients from endemic areas. For these reasons, it would be interesting to carry out screening for latent infections in patients who are going to receive immunosuppression treatment in the context of this pandemic¹³.

Conflicts of interest

The authors declare that they have no conflicts of interest and received no funding to conduct this study.

References

1. Álvarez-Martínez MJ, Belhassen-García M, Flores-Chavez MD, Pérez de Ayala A, Sulleiro E. Diagnóstico de parasitosis importadas en España. In: Cercenado Mansilla E, Cantón Moreno R, editors. Álvarez-Martínez M, coord. Procedimientos en microbiología clínica. Sociedad Española de Enfermedades Infecciosas y Microbiología Clínica (SEIMC); 2020. p. 2020.
2. Barroso M, Salvador F, Sánchez-Montalva A, Bosch-Nicolau P, Molina I. *Strongyloides stercoralis* infection: a systematic review of endemic cases in Spain. *PLoS Negl Trop Dis.* 2019;13:e0007230, <http://dx.doi.org/10.1371/journal.pntd.0007230>.
3. Salvador F, Treviño B, Chamorro-Tojeiro S, Sánchez-Montalvá A, Herrero-Martínez JM, Rodríguez-Guardado A, et al. Imported strongyloidiasis: data from 1245 cases registered in the +REDIVI Spanish Collaborative Network (2009–2017). *PLoS Negl Trop Dis.* 2019;13:e0007399, <http://dx.doi.org/10.1371/journal.pntd.0007399>.
4. Buonfrate D, Mena MA, Angheben A, Requena-Mendez A, Muñoz J, Gobbi F, et al. COHEMI Project Study Group. Prevalence of strongyloidiasis in Latin America: a systematic review of the literature. *Epidemiol Infect.* 2015;143:452–60, <http://dx.doi.org/10.1017/S0950268814001563>.
5. Greaves D, Coggle S, Pollard C, Aliyu SH, Moore EM. *Strongyloides stercoralis* infection. *BMJ.* 2013;347:f4610.
6. Keiser PB, Nutman TB. *Strongyloides stercoralis* in the immunocompromised population. *Clin Microbiol Rev.* 2004;17:208–17.

7. Fardet L, Généréau T, Poirot JL, Guidet B, Kettaneh A, Cabane J. Severe strongyloidiasis in corticosteroid-treated patients: case series and literature review. *J Infect.* 2007;54:18–27.
8. Henriquez-Camacho C, Gotuzzo E, Echevarria J, White AC Jr, Terashima A, Samalvides F, et al. Ivermectin versus albendazole or thiabendazole for *Strongyloides stercoralis* infection. *Cochrane Database Syst Rev.* 2016. <http://dx.doi.org/10.1002/14651858.CD007745.pub3>.
9. Morenab V, Milazzo L, Orenia L, Bestetti G, Fossali T, Bassoli C, et al. Off-label use of tocilizumab for the treatment of SARS-CoV-2 pneumonia in Milan, Italy. *Eur J Interl Med.* 2020;76:36–42.
10. Monge-Maillo B, Navarro M, Rodríguez E, Ramos Rincón JM, Chamorro Tojeiro S, Jiménez Sánchez S, et al. Affiliations expand Community screening campaign for *Strongyloides stercoralis* among Latin American immigrants in Spain. *Clin Microbiol Infect.* 2018;24:1220–1. <http://dx.doi.org/10.1016/j.cmi.2018.06.029>.
11. Winthrop KL, Mariette X, Silva JT, Benamu E, Calabrese LH, Dumusc A, et al. ESCMID Study Group for Infections in Compromised Hosts (ESGICH) Consensus Document on the safety of targeted and biological therapies: an infectious diseases perspective (Soluble immune effector molecules [II]: agents targeting interleukins, immunoglobulins and complement factors). *Clin Microbiol Infect.* 2018;24 Suppl 2:S21–40. <http://dx.doi.org/10.1016/j.cmi.2018.02.002>.
12. Schwartz BS, Mawhorter SD. AST Infectious diseases community of practice: parasitic infections in solid organ transplantation. *Am J Transplant.* 2013;13:280–303.
13. William M, Stauffer MD, Alpern JD, Walker PF. COVID-19 and dexamethasone. A potential strategy to avoid steroid-related strongyloid hyperinfection. *JAMA* Published online. 2020;324:623–4. <http://dx.doi.org/10.1001/jama.2020.13170>.

Ilduara Pintos-Pascual^{a,*}, Marcos López-Dosil^b,
Ciara Castillo-Núñez^c, Elena Múñez-Rubio^a

^a Servicio de Medicina Interna, Unidad de Enfermedades Infecciosas, Hospital Puerta de Hierro Majadahonda, Madrid, Spain

^b Servicio de Microbiología Clínica, Hospital Puerta de Hierro Majadahonda, Madrid, Spain

^c Medicina de Familia, Centro de Salud Brunete, Madrid, Spain

* Corresponding author.

E-mail address: ilduarapintos@gmail.com (I. Pintos-Pascual).

<https://doi.org/10.1016/j.eimce.2021.08.007>

2529-993X/ © 2020 Sociedad Española de Enfermedades Infecciosas y

Microbiología Clínica. Published by Elsevier España, S.L.U. All rights reserved.

Actinotignum schaalii and genital ulcers in a pediatric patient[☆]



Actinotignum schaalii y úlceras genitales en paciente pediátrico

The diagnosis of genital ulcers in children is of particular importance, as they can be an indication of pathologies that are either non-infectious (Behçet's disease, inflammatory bowel disease, adverse drug reactions or Lipschütz ulcers) or infectious, and in some cases may be associated with sexual abuse. Of particular note are infections due to herpes simplex virus, cytomegalovirus and Epstein-Barr virus. Bacterial causes include streptococcus and staphylococcus infections, gram-negative bacteria and ecthyma gangrenosum due to *Pseudomonas aeruginosa*¹.

Actinotignum schaalii (*A. schaalii*) is a gram-positive, facultative anaerobic bacillus that resides in the urogenital mucocutaneous epithelium². Its true clinical significance has probably continued to be underestimated due to the difficulty of isolating it in routine cultures³. To date, just seven previous cases of paediatric infection have been described, primarily urinary and, less commonly, genital infections⁴, but never ulcers. We present the first case to be described in the literature of genital ulcers associated with isolation of this microorganism.

The patient was a seven-year-old boy who was seen following a telephone consultation during the COVID-19 lockdown. He presented with ulcers on the glans and balanopreputial region that had appeared 24 h earlier, without fever, history of trauma or recent use of new medications. The patient had been previously diagnosed with primary nocturnal enuresis and daytime wetting, with an increase in the preceding weeks, coinciding with increased anxiety due to the lockdown situation. This patient also had encopresis and Tourette's syndrome. There was no evidence of sexual abuse/assault.

During the examination, an ulcer of 4 mm was found on the glans (Fig. 1) and another of similar size but less deep, mirroring the first contralaterally, as well as others below the level of the balanopreputial frenulum, which was found to be erythematous. He did not present oropharyngeal lesions and the rest of the physical examination was normal. A sample of exudate was taken

from the ulcers for a microbiological study. The baseline blood test was normal, including C-reactive protein <0.2 mg/l, blood count: 11,890 leukocytes/mm³ (31% polymorphonuclear neutrophils, 54% lymphocytes, 7% monocytes, 7% eosinophils).

In the microbiological study, after 48 h' incubation in CO₂, a large number of very small (<1 mm) colonies had grown in pure, non-haemolytic, cytochrome-oxidase and catalase-negative cultures in a sheep blood agar medium (BD, Spain), which corresponded to gram-positive bacteria with a slightly curved morphology and traces of corynebacterium, with slow growth. They were correctly identified using MALDI-TOF mass spectrometry (Bruker Biotyper, Billerica, MA, USA) as *A. schaalii* (with a maximum score of 2.212). The antibiotic sensitivity study, in a blood agar medium in CO₂, found the following minimum inhibitory concentration values (mg/l) (interpreted at 48 h, according to the EUCAST criteria for anaerobic gram-positive bacteria and the CLSI 2020 criteria for anaerobic bacteria for tetracycline): ampicillin (0.064), clindamycin (0.023) and tetracycline (0.5) (sensitive), and metronidazole (>256) (resistant). Following isolation of the ulcer, a urine culture was taken to search specifically for *A. schaalii*, which was negative.

A serology test for *Chlamydia pneumoniae*, *Mycoplasma pneumoniae*, syphilis, *Toxoplasma gondii*, hepatitis C virus (HCV), hepatitis B virus (HBV) and human immunodeficiency virus (HIV) was negative. Only anti-cytomegalovirus and anti-Epstein-Barr virus IgG were detected. The antinuclear antibodies determination had a speckled pattern (1/160). Treatment was administered orally with amoxicillin (50 mg/kg/day, seven days) and topically



Fig. 1. Ulcers on the glans and the region below the balanopreputial frenulum.

[☆] Please cite this article as: Vázquez-Pérez Á, Santos-Pérez JL, Herrera-Goicoechea A, Gutiérrez-Fernández J. *Actinotignum schaalii* y úlceras genitales en paciente pediátrico. *Enferm Infecc Microbiol Clin.* 2021;39:480–481.