Am. J. Trop. Med. Hyg., 95(5), 2016, pp. 1051–1053
doi:10.4269/ajtmh.16-0504

Case Report: Severe Anemia and Lung Nodule in an Immunocompetent Adopted Girl with *Strongyloides stercoralis* Infection

Dora Buonfrate,[1]* Federico Gobbi,[1] Anna Beltrame,[1] and Zeno Bisoffi[1]
[1]*Centre for Tropical Diseases, Ospedale Sacro Cuore Don Calabria, Negrar, Verona, Italy*

Abstract. *Strongyloides stercoralis* is a soil-transmitted helminth widely diffused in tropical areas. Chronic infection is usually characterized by absent or mild symptoms, but immunocompromised subjects are at risk of developing a severe syndrome that can be fatal if not promptly treated. We report a case of *S. stercoralis* infection causing severe anemia (hemoglobin 4.9 g/dL) and a lung nodule in a 14-year-old girl of Ethiopian origin adopted by an Italian couple. Severe anemia due to strongyloidiasis has been rarely reported, and mostly in severely ill patients, whereas our patient was immunocompetent and in good general conditions. Also, lung nodules have been only occasionally described in absence of respiratory symptoms. We discuss the management of patients with these findings, and we suggest to update the screening of immigrants from countries endemic for strongyloidiasis, including serology.

INTRODUCTION

Strongyloidiasis is the infection caused by the soil-transmitted helminth (STH) *Strongyloides stercoralis*. The worldwide prevalence of this nematode has been estimated to be around 370 million cases, distributed mainly in tropical and subtropical areas.[1] In Europe, autochthonous infection has been documented in elderly people who were presumably exposed to contaminated soil in their youth, when they used to walk barefoot in the country (and when sewage disposal was not adequate).[2–4] In fact, *S. stercoralis* is characterized by a peculiar autoinfective cycle that permits the infection to become chronic.[5] Only sporadic cases of possible current transmission have been reported in Europe.[6] In immunocompetent hosts, chronic strongyloidiasis tends to have subclinical, unspecific manifestations involving the abdomen, the respiratory tract, and the skin. In these people, eosinophilia is often the only clue of an underlying parasitic infection, and stool examination is frequently negative, due to an intermittent larval output. On the other hand, immunocompromised patients are prone to developing severe infection, with potentially fatal complications. In hyperinfection, larvae are generally easily detected by stool (and also other body fluids) microscopy, because of their increased number.[5] Other diagnostic tests, such as serology, stool culture (including agar plate culture [APC]), and real-time polymerase chain reaction (PCR) (quantitative PCR [qPCR], currently available in a few referral centers), demonstrated higher sensitivity than stool microscopy, so they are useful to achieve the diagnosis during the chronic phase.[7] However, a high index of suspicion is the first fundamental step leading to the diagnosis.

CASE REPORT

Since May 2015, a 14-year-old girl born in Ethiopia and adopted by an Italian couple at the age of 5, was admitted several times to a hospital in northern Italy for severe hypochromic microcytic anemia (lower hemoglobin value: 4.9 g/dL, mean corpuscular volume 54 fL, transferring saturation 5%) and mild abdominal pain. She underwent several investigations, among which the following resulted negative: screening for celiac disease, thalassemia and other hemoglobin disorders, hepatitis C virus and hepatitis B virus serology, fecal occult blood test, *Helicobacter pylori* antigen stool test, coproculture, abdominal ultrasound. The calprotectin was moderately increased (137 μg/g, normal values < 50). Neither gastroscopy (demonstrating mild gastritis) nor colonoscopy (showing eosinophilic colitis of the ascending colon) showed any bleeding source. She denied menorrhagia. She was prescribed iron and folic acid supplements, obtaining normalization of the hemoglobin levels. Eosinophilia (peak value 3,200/mm^3, 34.5%) was noticed too, so she was prescribed parasitological examination of three stool samples, plus *Entamoeba* and *Giardia* antigen test in stool. The latter resulted positive, so she received metronidazole for 7 days. Moreover, she was referred to a nutritionist to investigate possible alimentary allergies. However, both the eosinophilia and the abdominal pain persisted.

On November 21, 2015, she was admitted to the Center for Tropical Diseases (CTD) in Negrar, Verona, which is a referral center for parasitic diseases in northeast Italy. Her general conditions were good, and physical examination was unremarkable, except for mild distension of the epigastric region. The full blood count showed 9,200/mm^3 white blood cells (WBC), eosinophils 1,900/mm^3 (21%), hemoglobin 12.9 g/dL, iron 4.1 micromol/L (normal values: 8.95–30.43), ferritin 8.3 μg/L (normal values: 10–120). Parasitological examination (with formol–ether concentration) of stool and urine resulted repeatedly negative, and so was serology for *Toxocara*, *Schistosoma* spp. (enzyme-linked immunosorbent assay [ELISA]), and filaria. qPCR for *Entamoeba histolytica*, *Entamoeba dispar*, *Cryptosporidium*, *Dientamoeba*, *Giardia*, *Blastocystis* spp., *Schistosoma* spp., and *Hymenolepis nana* resulted negative, too. Eventually, a diagnosis of strongyloidiasis was made by positive APC for *S. stercoralis*, qPCR on stool, and in-house immunofluorescence test anti-*S. stercoralis* IgG antibodies (immunofluorescence antibody test [IFAT] 1:1,280, positive ≥ 20). The patient received a single dose of 200 μg/kg ivermectin. Moreover, a chest X-ray showed interstitial thickening with a reticular pattern, and a left diaphragmatic pleural lesion. Hence, a pulmonary computed tomography (CT) scan was requested for a better definition of the radiological findings: the lesion revealed to be a nodular opacity with a maximum diameter of 19 mm (Figure 1), compatible with hamartoma. The radiologist suggested a close follow-up. The patient was discharged on November 28.

*Address correspondence to Dora Buonfrate, Centre for Tropical Diseases, Ospedale Sacro Cuore Don Calabria, Via Sempreboni 5, 37024 Negrar, Verona, Italy. E-mail: dora.buonfrate@sacrocuore.it

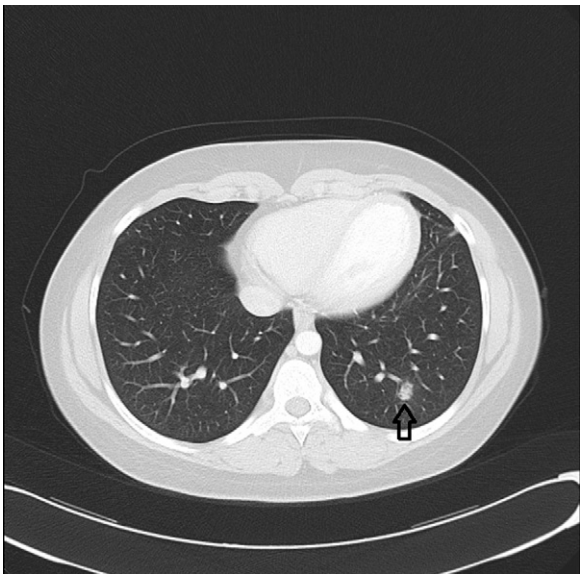

FIGURE 1 Computed tomography scan showing nodular opacity in the left lung.

On May 16, 2016, she went to another hospital for a follow-up pulmonary CT scan that documented the disappearance of the nodular opacity (images not available). On June 13, when the patient presented to the CTD for a follow-up visit, she was in good clinical conditions. She had not taken any medication at home, since last hospital admission. The blood tests showed 7,100 WBC/mm^3, eosinophils 200/mm^3 (3.2%), hemoglobin 11.2 g/dL, IFAT 1:40, negative qPCR and APC for *S. stercoralis*.

DISCUSSION

Abdominal pain and anemia are frequently caused by STH (hookworm in particular) in children/adolescents living in villages in sub-Saharan Africa.[8] In our case, the presence of eosinophilia was a further clue for a parasitic infection. Although the lifespan of STH is usually shorter than 9 years,[8] which is the time elapsed since our patient left Ethiopia, *S. stercoralis* could not be ruled out because of the autoinfective cycle. Actually, severe anemia has been only rarely reported in strongyloidiasis, and mostly in hyperinfected, severely ill patients, which was not our case.[9] Anemia was secondary to iron deficiency possibly due to malabsorption, as colonoscopy and gastroscopy did not show any bleeding foci and no other causes of blood loss were detected. Nodular pulmonary lesions caused by *S. stercoralis* have been rarely reported too, and in particular, there is no information on their frequency in asymptomatic patients.[10,11] They might derive from the migration of the larvae to the lungs, as suggested by Dogan and others, who found granulomas surrounding *S. stercoralis* larvae in the histological examination of lung biopsies performed in a patient.[10] We prescribed a chest X-ray for a general assessment of the patient, in absence of respiratory complaints. In our experience (and in line with other experts' opinion[12]), invasive procedures (such as pulmonary biopsy) can be avoided in the first assessment of a lung nodule in a patient with a parasitic infection, in particular, if the index of suspicion for other severe conditions is low. In fact, despite the lack of histological examination, the radiological follow-up showed resolution of the lesion, supporting the parasitic etiology.

IFAT was repeated about 7 months after treatment (because the titer decreases slowly through time[13]) and showed a 5-fold drop in titer, demonstrating the response to therapy, confirmed by the normal eosinophil count and the negative APC and qPCR. However, we have planned a further follow-up visit 1 year after treatment.

The mother reported that on her arrival in Italy, her daughter had undergone screening tests that included parasitological stool examination. However, this technique has low sensitivity for the detection of *S. stercoralis*, and a serology test (also considering the availability of commercial kits, easy to be used in average–equipped laboratories) should have been included in the screening. In fact, according to a diagnostic study, the sensitivity of serology is around 91–92% and 95% in case of commercial ELISA tests and our in-house IFAT, respectively,[14] making them good tools for screening.

In conclusion, strongyloidiasis can cause severe anemia and lung nodules also in immunocompetent subjects. Management of these patients can be based on laboratory and imaging follow-up after treatment, avoiding unnecessary invasive procedures. Screening of adopted children from low-resources countries, and more in general screening of immigrants from endemic areas, should include *S. stercoralis* serology test that is also a useful tool for monitoring the response to therapy.

Received June 20, 2016. Accepted for publication July 27, 2016.

Published online September 6, 2016.

Authors' addresses: Dora Buonfrate, Federico Gobbi, Anna Beltrame, and Zeno Bisoffi, Centre for Tropical Diseases, Ospedale Sacro Cuore Don Calabria, Negrar, Veneto, Italy, E-mails: dora.buonfrate@sacrocuore.it, federico.gobbi@sacrocuore.it, anna.beltrame@sacrocuore.it, and zeno.bisoffi@sacrocuore.it.

REFERENCES

1. Bisoffi Z, Buonfrate D, Montresor A, Requena-Mendez A, Munoz J, Krolewiecki AJ, Gotuzzo E, Mena MA, Chiodini PL, Anselmi M, Moreira J, Albonico M, 2013. *Strongyloides stercoralis*: a plea for action. *PLoS Negl Trop Dis 7:* e2214.
2. Abrescia FF, Falda A, Caramaschi G, Scalzini A, Gobbi F, Angheben A, Gobbo M, Schiavon R, Rovere P, Bisoffi Z, 2009. Reemergence of strongyloidiasis, northern Italy. *Emerg Infect Dis 15:* 1531–1533.
3. Roman-Sanchez P, Pastor-Guzman A, Moreno-Guillen S, Igual-Adell R, Suner-Generoso S, Tornero-Estebanez C, 2003. 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 69:* 336–340.
4. Buonfrate D, Baldissera M, Abrescia FF, Bassetti M, Caramaschi G, Giobbia M, Mascarello M, Rodari P, Scattolo N, Napoletano G, Bisoffi Z; CCM Strongyloides Study Group, 2016. Epidemiology of *Strongyloides stercoralis* in northern Italy: results of a multicentre case-control study, February 2013 to July 2014. *Euro Surveill 2016 Aug 4; 21(31)*. doi:10.2807/1560-7917.ES.2016.21.31.30310.
5. Nutman TB, 2016. Human infection with *Strongyloides stercoralis* and other related *Strongyloides* species. *Parasitology 16:* 1–11.
6. Duvignaud A, Pistone T, Malvy D, 2016. Strongyloidiasis in a young French woman raises concern about possible ongoing autochthonous transmission in Spain. *Int J Infect Dis 42:* 43–44.

7. Requena-Mendez A, Chiodini P, Bisoffi Z, Buonfrate D, Gotuzzo E, Munoz J, 2013. The laboratory diagnosis and follow up of strongyloidiasis: a systematic review. *PLoS Negl Trop Dis 7:* e2002.
8. Bethony J, Brooker S, Albonico M, Geiger SM, Loukas A, Diemert D, Hotez PJ, 2006. Soil-transmitted helminth infections: ascariasis, trichuriasis, and hookworm. *Lancet 367:* 1521–1532.
9. Rodriguez EA, Abraham T, Williams FK, 2015. Severe strongyloidiasis with negative serology after corticosteroid treatment. *Am J Case Rep 16:* 95–98.
10. Dogan C, Gayaf M, Ozsoz A, Sahin B, Aksel N, Karasu I, Aydogdu Z, Turgay N, 2014. Pulmonary *Strongyloides stercoralis* infection. *Respir Med Case Rep 11:* 12–15.
11. Mayayo E, Gomez-Aracil V, Azua-Blanco J, Azua-Romeo J, Capilla J, Mayayo R, 2005. *Strongyloides stercolaris* infection mimicking a malignant tumour in a non-immunocompromised patient. Diagnosis by bronchoalveolar cytology. *J Clin Pathol 58:* 420–422.
12. Kunst H, Mack D, Kon OM, Banerjee AK, Chiodini P, Grant A, 2011. Parasitic infections of the lung: a guide for the respiratory physician. *Thorax 66:* 528–536.
13. Buonfrate D, Sequi M, Mejia R, Cimino RO, Krolewiecki AJ, Albonico M, Degani M, Tais S, Angheben A, Requena-Mendez A, Munoz J, Nutman TB, Bisoffi Z, 2015. Accuracy of five serologic tests for the follow up of *Strongyloides stercoralis* infection. *PLoS Negl Trop Dis 9:* e0003491.
14. Bisoffi Z, Buonfrate D, Sequi M, Mejia R, Cimino RO, Krolewiecki AJ, Albonico M, Gobbo M, Bonafini S, Angheben A, Requena-Mendez A, Munoz J, Nutman TB, 2014. Diagnostic accuracy of five serologic tests for *Strongyloides stercoralis* infection. *PLoS Negl Trop Dis 8:* e2640.