Neotrop. helminthol., 1(1), 2007

NOTA CIENTÍFICA / RESEARCH NOTES

STRONGYLOIDES STERCORALIS ASSOCIATED WITH NEPHRITIC SYNDROME IN A CHILD WITH INTESTINAL NEURONAL DYSPLASIA

STRONGYLOIDES STERCORALIS ASOCIADO CON SINDROME NEFRÍTICO EN UN NIÑO CON DISPLASIA INTESTINAL NEURONAL

Luis A Marcos[1,2,4], Daniel Lozano[3], Guillermo Calvo[3], Lenin Romani[1] & Angélica Terashima[4]

Fecha de recepción: 12 de abril del 2006, fecha de aceptación: 22 de setiembre del 2006.

Forma de citar: Marcos, L A, Lozano, D, Calvo, G, Romani, L & Terashima A. 2007. Strongyloides stercoralis *associated with nephritic syndrome in a child with intestinal neuronal dysplasia.* Neotropical Helminthology, vol. 1, no. 1, pp. 37-42

Resumen

La strongyloidiosis, causada por Strongyloides stercoralis, *es un serio problema de Salud Pública en el Perú. Reportamos a un niño de dos años de edad quien fue admitido en el Instituto Especializado de Salud del Niño en Lima con el diagnóstico de obstrucción intestinal asociado a 15 días de diarrea, fiebre y tos seca. El examen histopatológico del tejido necrótico del colon reveló displasia neuronal intestinal. Posteriormente, durante su hospitalización (12 días después) presentó hipereosinofilia (con 3,460 eosinófilos/mm³), tos, fiebre y una radiografía de tórax anormal, 5 días después el recuento de eosinófilos llegó hasta 34,286 células/mm³. Un día después se encontraron larvas de* S. stercoralis *en el examen directo de heces. La serología para HTLV-1 y HIV 1 fueron negativos. Cabe mencionar que nuestro paciente presentó hematuria microscópica e hipertensión arterial durante los más altos niveles de eosinófilos en sangre, por lo que se sospechó en una glomerulonefritis aguda. El tratamiento con tiabendazol se inició rápidamente, y fue administrado durante siete días. Los hallazgos clínicos desaparecieron y no se encontraron más larvas en los exámenes de heces. El paciente fue dado de alta asintomático. Este caso presenta fuertes indicios de ser una hiperinfección por* S. stercoralis *debido a la autoinfección desencadenada por la cirugía la cual intervino como factor estresante.*

Palabras clave: *Strongyloides stercoralis* – complications – glomerulonephritis – Peru.

Abstract

Strongyloidiasis, caused by Strongyloides stercoralis, *is a serious Public Health problem in Peru. We report the case of a two-year-old boy who was admitted at the Instituto Especializado de Salud del Niño in Lima with a diagnosis of intestinal obstruction associated with fifteen days of diarrhea, fever and cough. The histopathological examination of the necrotic tissue of colon showed intestinal neuronal dysplasia. During his hospitalization (12 days later) he presented hypereosinophilia (with 3,460 eosinophils/mm³), cough, fever and abnormal chest x-ray. Five days later, the eosinophil count reached up to 34,286 cells/mm³. One day later,* S. stercoralis *larvae were found in a direct stool smear. Serology tests for HTLV-1 and HIV were negative. Interestingly, our patient presented microscopic hematuria and high blood pressure during the highest levels of eosinophils in blood, therefore acute glomerulonephritis was suspected. Treatment with thiabendazole was readily started, and administered during seven days. After that, clinical findings disappeared and larvae were no longer detected in stool examinations. The patient was asymptomatic at discharged. This case presents strong evidence to be a hyperinfection of due to autoinfection triggered by the surgery as a stress factor.*

Keywords: *Strongyloides stercoralis* – complicaciones – glomerulonefritis – Perú.

1. Instituto de Medicina Tropical Alexander von Humboldt (IMTAvH), Universidad Peruana Cayetano Heredia (UPCH), Lima, Perú.
2. Internal Medicine Residency Program, University of Texas Health Science, Houston, Texas, USA.
3. Instituto Especializado de Salud del Niño, Lima, Perú.
4. Laboratorio de Parasitología, Instituto de Medicina Tropical Alexander von Humboldt (IMTAvH), Universidad Peruana Cayetano Heredia (UPCH), Lima, Perú.

INTRODUCTION

Strongyloidiasis is an intestinal parasitic disease caused by *Strongyloides stercoralis*, a soil-transmitted intestinal nematode. It has been estimated to infect up to 100 million people worldwide, mainly in tropical and subtropical regions (Genta, 1989; Genta, 2001; Grove 1989). It is one of the most important intestinal parasitic diseases in humans because it can produce a life-threatening illness in immunocompromised hosts (HTLV-1 co-infection, neoplasm, AIDS, radiation, severe malnutrition or chronic corticosteroids therapy) when larvae disseminate to multiple organs causing the hyperinfection syndrome. The complications in this stage are malabsorption, paralytic ileus, meningitis, gastrointestinal hemorrhage, gram-negative bacteremia, pneumonia and septic shock; the fatality rate can reach up to 77% (Rodriguez & Calderon, 1991; García-Godos *et al.*, 1992; Ma-hmoud, 1996; Nonaka *et al.*, 1998; Thomas & Costello 1998; Gotuzzo *et al.*, 1999; Chieffi *et al.*, 2000; Adedayo *et al.*, 2001)

In Peru, strongyloidiasis is a serious Public Health problem. There are many hyperendemic regions with prevalence rates up to 41% where children are mostly affected (Rodríguez & Calderón, 1991; Marcos *et al.*, 2002). The recommended treatment agents are ivermectin and thiabendazole (Náquira *et al.*, 1989; Datry *et al.*, 1994).

We report a case of human strongyloidiasis with intestinal neuronal dysplasia that developed clinical acute glomerulonephritis and then it was resolved with antihelmintic treatment. We suggest the possibility of *Strongyloides*-associated glomerulonephritis.

CASE REPORT

A 2-year-old male was admitted to emergency room at Instituto de Salud del Niño in Lima on September 25, 2002; transferred from Cusco with a 15-day history of bloody diarrhea, fever and cough. He was born and raised in a jungle region of Cusco and belonged to the Shipibo tribe.

Examination findings at admission revealed a pale and irritable infant with significant dehydration. His body temperature was 100 ºF (37.8 ºC), pulse 140/min, blood pressure 90/60 mmHg, and respiratory rate 32/min. In thorax, there were bilateral lung crackles and wheezing. The abdomen was distended, diffusely tenderness with peritoneal signs. No hepato- or splenomegaly were present. No peripheral edema was noted. The bowel sounds were hyperactive and a rectal examination revealed mucus and blood in stools. Stool examination (direct smear) showed from 7 to 15 red blood cells, 20 to 35 white blood cells per high power field and *Entamoeba coli* cysts.

Chest X-ray did not show any alteration. The white blood cell count was 22,600 cells/μL with 81% neutrophils, hematocrit 34%, erythrocyte sedimentation rate (ESR) 35 mm/h, blood urea 34 mg/dL, creatinine 1.25 mg/dL, serum potassium 1.82 mEq/dL. Other electrolytes were normal. The potassium was adequately corrected and the patient was hydrated, but abdominal distention and peritoneal signs persisted. An abdominal X-ray showed dilated intestinal loops. Therefore, the emergency team decided to operate the patient with the diagnosis of intestinal obstruction.

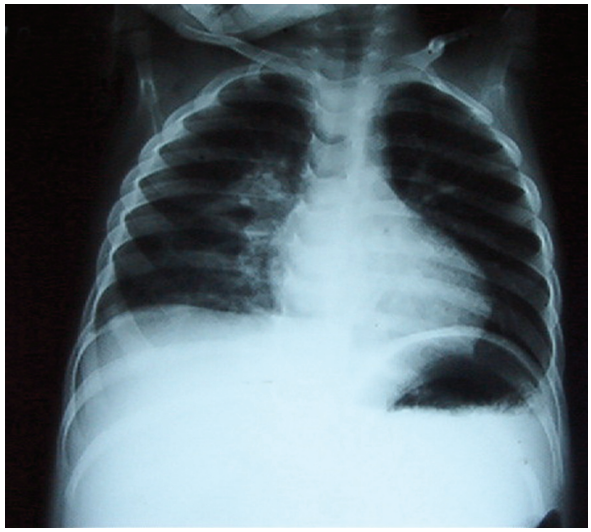
The surgical findings were dilated intestinal loops and narrowed descendent colon with signs of necrosis, so it was resected. After the surgery, the patient was admitted to The Intensive Unit Care (IUC) and was treated with wide-spectrum antibiotics, some results of blood analyses were: creatinine 0.79 mg/dL, serum potassium 3.23 mEq/dL and albumin 2.5 mg/dL. The histopathological examination of colon showed neuronal intestinal dysplasia. On September 29th, the patient had a functional colostomy, improved favourably and coursed asymptomatic. On October 6th, he presented with productive cough and tachypnea.

The following day high fever (38,8 ºC) and crackles in lower right thorax appeared. Chest X-ray revealed a parenchymal infiltrated in the right parahiliar region. The white blood cell count showed 17,300 cells/μL, 2% bands, 38% neutrophils and 20% eosinophils. Therefore, this was thought to account for nosocomial pneumonia and the treatment was started with broad-spectrum antibiotics. On October 10th, no clinical improvement was reported. A control chest X-ray showed infiltrative changes in the right lower lobe, parahiliar region and interstitial diffuse patron was observed, similar to the first chest X-ray.

The white blood cell count was 37,000 cells/μL, 1%

bands, neutrophils 20% and eosinophils 50%, ESR 25 mm/h. On October 15th, cough was persistent and physical examination was significant for diffuse roncus predominantly in lower right lung. The patient was clinically stable with low fever and cough. A control white blood cell count showed 55,300 cells/μL with 62% eosinophils. Stool examinations were repeated with direct smear technique and the results were negatives. A gastric aspirate was not obtained because the patient's father did not give consent.

Figure 1. Chest X-ray shows a persistent right parahiliar infiltrative during the highest eosinophilia level.



On October 19th, the patient clinically had a stable evolution. A stool examination (direct smear technique) revealed larvae of *S. stercoralis*. Chest X-ray revealed a persistent parenchymal infiltrated in the right parahiliar region (Figure 1).

He received a 7-day course of thiabendazole 250mg twice a day. HTLV-1 and HIV 1+2 ELISA's were negatives. On October 25th, a white blood cell count showed 25,600 cells/μL with 53% eosinophils. The previous urine examinations did not have any abnormal finding. However, the last urine examination showed between 8 and 10 red blood cells per high power field and also hemoglobin. Moreover, fever, poor appetite and dyspnea were reported.

On physical examination, his pulse was 160/min and blood pressure 170/100 mmHg. Cardiology recommended treating with captopril 1 mg/kg/doses to control the hypertension. A nephritic syndrome was suggested. A renal ultrasonography was performed but no alterations were described. A doppler ultrasonography was done showing normal renal arteries morphology. Antistreptolysin antibodies (ASO) were within normal values; and cells of Lupus Erythematosus test (LE cells test) were negatives.

On November 29th, a control of white blood cell count reported 12,400 cell/μL and 29% eosinophils. On December 1st, both stool examinations (direct smear) and gastric aspirate (after tutor's consent) were negatives. One week after beginning thiabendazole, a urinary test was normal. Further blood analysis were made, blood urea 30.7 mg/dL, creatinine 0.52 mg/dL, glucose 74.6 mg/dL, total proteins 7.3 mg/dL, albumin 3.7 mg/dL, globulins 3.6 mg/dL, serum sodium 136 mEq/dL and serum potassium 5.21 mEq/d.

On December 13th, eosinophilia decreased significantly (13,400 white blood cell/μL with 10% eosinophils), ESR 26 mm/h and hematocrit 35%. His urine examination by microscopy made on December 21st presented with mild glucosuria but on physical examination, he appeared well, and the vital signs were normal. Therefore, due to his favourable clinical evolution the clinical team decided to discharge for follow-up after a week. The day

following discharge, the patient with his father revisited institute complaining of nausea, vomiting, oral intolerance and watery diarrhea.

A presumptive diagnosis of osmotic diarrhea with significant dehydration was done and he was hospitalized again. In the next days, he did not present vomiting and diarrhea. Stool examinations done periodically with sedimentation cup technique and plate agar culture were negative for *S. stercoralis*. His basal blood pressure was 90/50 mmHg however, he presented peaks of hypertension up to 130/80 mmHg in two opportunities.

He was treated with antihypertensive drugs. He not presented hypertension since the two first episodes. A Captopril Renal Scan was carried out to rule out renal artery stenosis versus renovascular hypertension but it did not show any abnormality. Finally, we concluded that eosinophilia caused by *S. stercoralis* infection or the parasite by itself or immunological factors could be the causing of glomerulonephritis since clinical findings disappear after thiabendazole treatment. After two months, a urinary test was made and it was normal. Blood pressure

controls were normal until three months of follow-up.

DISCUSSION

We report a case of a child with neuronal dysplasia operated because an intestinal obstruction syndrome, who after the surgery developed a hyperinfection syndrome due to *S. stercoralis* infection associated with a nephritic syndrome during the highest peak of eosinophilia. Since antihelminthic treatment was started, improvement of renal impairment was observed and a decrease of eosinophils counts as well. Involvement of the kidney, glomerulonephritis, has been described in association with *S. stercoralis* disseminated infection (Wong *et al.*, 1998; Mitsunaga *et al.*, 2003).

In fact, symptoms usually respond promptly, as in our case, to appropriate antihelminthic therapy. However, *Strongyloides*-related glomerulonephritis has not been demonstrated *in situ* yet.

The development of nephritic syndrome in our patient could have been caused by many possible factors such as previous bacterial infection, autoimmune disorder; high eosinophils count in blood or *S. stercoralis* larvae *per se*. However, a decrease of blood pressure was observed after antihelmintic treatment, as well as absence of red blood cells in urine, along with a decreasing of eosinophils in blood. Moreover, the following laboratorial tests were negatives or within normal values: ASO, LE cells, renal ultrasonographic doppler, captopril renal scan and ESR. Thus, a possible cause of acute glomerulonephritis in our patient could be *S. stercoralis* infection. Immunological disorders, eosinophils or the parasite itself can be involved. A kidney biopsy could have been contributory to our hypothesis, but this invasive method was not necessary in the patient, since the clinical picture improved notoriously and the evolution was favorable.

During the hospitalization, a high suspicion of the infection by this nematode in the patient was the high number of eosinophils observed in the blood smear. However, a presumptive diagnosis of nosocomial pneumonia was done initially two weeks after the surgery. Despite the fact that he was started on antibiotics, there had neither a clinical nor laboratory analysis improvement. By contrast, a significant increased of eosinophils count up to 34286 cell/μL appeared. These findings, a progressive eosinophilia and pulmonary infiltrates, bring to mind a spectrum of parasitic diseases, mainly in their migratory stages, including differential diagnoses such as *Ascaris lumbricoides*, hookworms, *S. stercoralis* hyperinfection, toxocariasis and *Paragonimus* spp. (MacLean *et al.*, 1999). However, the last is not endemic from the region where the patient came from, and because of the hypereosinophilia (>1,500 cell/μL), the first option thought was strongyloidiasis. In the following days, there were larvae of *S. stercoralis* found in feces and the suspected diagnosis was confirmed.

Two possible mechanisms are involved in this process. First, the surgery as a stress condition could have been the factor which triggered the mechanism of autoinfection. The time since larvae are carried to the lungs after enters systemic vessels are 2 weeks, and this was the time which the surgery was performed. Therefore, we think the surgery could be the triggering factor to develop the autoinfection. Second, under some circumstances such as chronic constipation (eg. intestinal neuronal dysplasia) larvae produced by the parasitic females could remain in the intestinal tract long enough to develop into infective stages. Such larvae will penetrate the tissues of the intestinal tract and develop as if they had penetrated the skin. Both mechanisms may explain the hyperinfection syndrome seen in the patient.

The importance of this parasitosis in Peru is noteworthy, there had been reported high prevalence rates in several regions mainly in the Amazonic Region (Gotuzzo *et al.*, 1999; Rodríguez and Calderón, 1991; Marcos *et al.*, 2002; Náquira *et al.*, 1989).

We have to mention that this parasitosis requires an adequate parasitological sedimentation test to detect larvae. In endemic areas, mostly in developing countries; a simple, economical and high sensitive parasitological test should be routinely done. However, the routine method in most of health centers is the direct smear test, whose sensitive is low in comparison with other sedimentation technique as Baermann's Modified in Cup Technique described by Lumbreras (1963), which is performed routinely in only a few health centers in Peru (eg. IMTAvH). The stool examination controls of our patient were made by this parasitological technique and with cultures. However, the first stool examinations done in the patient were carried out by direct smear, even though larvae were found in the analysis. It is probably the heavy burden infection increased the likelihood

to find them in feces by a direct smear.

The low level of suspicion for the diagnosis of strongyloidiasis can lead clinicians to delay the final diagnosis. We need more studies to evaluate the role of *S. stercoralis* infection and renal impairment in humans. The possibility of renal involvement should be carefully considered by physicians. This is the first case report of a nephritic syndrome probably associated to *S. stercoralis* infection in a non-immunocompromised patient in Peru; and despite its rarity in the clinical setting, it should be considered in the differential diagnosis of patients with glomerulonephritis, when associated with eosinophilia, or in patients who come from endemic areas.

ACKNOWLEDGMENTS

We thank Dr. Jessica N. Ricaldi, Institute of Tropical Medicine Alexander von Humboldt, Lima, Peru, for her assistance in the review of this manuscript.

REFERENCES

Adedayo, AO, Grell, GA & Bellot, P. 2001. *Case study: Fatal strongyloidiasis associated with human T-cell lymphotropic virus type I infection.* American Journal Tropical Medicine and Hygiene, vol. 65, pp. 650-651.

Chieffi, PP, Chiattone, CS, Feltrim, EN, Alves, RC & Paschoalotti, MA. 2000. *Coinfection by* Strongyloides stercoralis *in blood donors infected with Human T-Cell leukemia / Lymphoma Virus Type I in Sao Paulo City, Brazil.* Memórias do Instituto Oswaldo Cruz, vol. 95, pp. 711-712.

Datry, A, Hilmarsdottir, I, Mayorga-Sagastume, R, Lyagoubi, M, Gaxotte, P, Biligui, S, Chodakewitz, J, Neu, D, Danis, M & Gentilini, M. 1994. *Treatment of* Strongyloides stercoralis *infection with ivermectin compared with albendazole: results of an open study of 60 cases.* Transactions Royal of Society Tropical Medicine and Hygiene, vol. 88, pp. 344-345.

Gann, PH, Neva, FA & Gam, AA. 1994. *A randomized trial of single and two dose ivermectin versus thiabendazole for treatment of strongyloidiasis.* Journal of Infectious Diseases, vol. 169, pp. 1076-1079.

García-Godos, MC, Maco, V. & Lora, P. 1992. *Hiperinfestación por* Strongyloides*: un caso fatal.* Acta Médica Peruana, vol. 16, pp. 63-65.

Genta, RM. 2001. *Strongyloidiosis. In Essentials Tropical Infectious Diseases,* ed. R. Guerrant, D. Walker & P. Weller, Churchill Livingstone Editorial, New York.

Genta, RM. 1989. *Global prevalence of strongyloidiasis: critical review with epidemiologic insights into the prevention of disseminated disease.* Reviews of Infectious Diseases, vol. 11, pp. 755–767.

Gotuzzo, E, Terashima, A, Alvarez, H, Tello, R, Infante, R, Watts, D M. & Freedman, DO. 1999. Strongyloides stercoralis *hyperinfection associated with human T-cell lymphotropic virus type-I infection in Peru.* American Journal of Tropical Medicine and Hygiene, vol. 60, pp. 146–149.

Grove, DI. 1989. *Historical introduction. In Strongyloidiasis: a major roundworm infection of man,* ed. D. I. Grove, Taylor and Francis, London.

Lumbreras, H. 1963. *Strongyloidosis: I. Evaluación de la técnica de Baermann Modificada en Copa en el estudio de la strongyloidosis.* Revista Médica Peruana, vol. 32, pp. 119-126.

MacLean, JD, Cross, J & Mahanty, S. 1999. *Liver, lung, and intestinal fluke infections. In RL Guerrant D, H Walker & PF Weller, (eds.). Tropical infectious diseases: principles, pathogens, & practice.* Churchill Livingstone, Philadelphia.

Mahmoud, AA. 1996. *Strongyloidiasis.* Clinical Infectious Diseases, vol. 23, pp. 949–952.

Marcos, LA, Maco, V, Machicado, A, Samalvides, F, Terashima, A, Quijano, C & Gotuzzo, E. 2002. *Diferencias de parasitosis intestinal en los Hospitales Militar y Regional de Iquitos.* Diagnóstico, vol. 41, pp. 185-187.

Mitsunaga, M, Miyauchi, N, Akiyama, Y & Saima, S. 2003. *A case of strongyloidiasis hyperinfection during oral corticosteroid therapy associated with a nephrotic patient infected with HTLV-1.* Nippon Ronen Igakkai Zasshi, vol. 40, pp. 397-401.

Naquira, C, Jimenez, G, Guerra, JG, Bernal, R, Nalin, DR, Neu, D & Aziz, M. 1989. *Ivermectin for human strongyloidiasis and other intestinal helminths.* American Journal of Tropical Medicine and Hygiene, vol. 40, pp. 304–309.

Nonaka, D, Takaki, K, Tanaka, M, Umeno, M, Takeda, T, Yoshida, M, Haraguch, Y, Okada, K & Sawae, Y. 1998. *Paralytic ileus due to strongy-*

loidiasis: case report and review of the literature. American Journal of Tropical Medicine and Hygiene, vol. 59, pp. 535–538.

Rodríguez, J & Calderon, J. 1991. *Intestinal parasitosis in pre-school children from Tarapoto.* Revista de Gastroenterología del Peru, vol. 11, pp. 153-60.

Thomas, CA & Costello, SA. 1998. *Disseminated strongyloidiasis arising from a single dose dexamethasone before stereotactic radiosurgery.* International Journal of Clinical Practice, vol. 52, pp. 520-521.

Wong, TY, Szeto, CC, Lai, FF, Mak, CK & Li, PK. 1998. *Nephrotic syndrome in strongyloidiasis: Remission after eradication with anthelmintic agents.* Nephron, vol. 79, pp. 333-336.

Autor para correspondencia/Author for correspondence:

Luis A. Marcos

Instituto de Medicina Tropical Alexander von Humboldt. Universidad Peruana Cayetano Heredia
Av. Honorio Delgado 430, Urb. Ingeniería. San Martín de Porres AP 4314, Lima 100.
Lima, Perú.

Correo electrónico/E-mail:
Luis.A.Marcos@uth.tmc.edu

Telefax: (511)-4823404