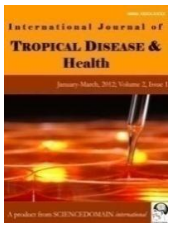

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Ascaris lumbricoides Beyond Intestinal Obstruction

Henrique Pott-Junior[1*] and Alberto Pereira Ferraz[2]

[1]Division of Infectious Diseases, Federal University of São Paulo–UNIFESP, São Paulo, Brazil.
[2]Division of Internal Medicine, Federal University of São Paulo–UNIFESP, São Paulo, Brazil.

Authors' contributions

This work was carried out in collaboration between all authors. All authors read and approved the final manuscript.

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Case Study

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ABSTRACT

Ascaris lumbricoides infestation remains the most common cause of eosinophilia. In addition, in cases of severe eosinophilia due to helminthinfestation, eosinophilic infiltration of several tissues may occur, and most likely to be clinically underestimated. If not early diagnosed, it can be severe and fatal. We describe the case of a 33 year-old man from Brazil, a unique case of *Ascaris lumbricoides* hipereosinophilia with systemic involvement including the heart, kidneys, and bone marrow, without symptoms. Transthoracic echocardiography revealed a dilated left ventricle with an endocardial thickening. A percutaneous renal biopsy revealed diffuse global glomerulonephritis and tubulointerstitial nephritis with renal eosinophilic infiltration. Bone marrow biopsy revealed eosinophilic infiltration without any signs of malignant disorder. The patient was successfully treated and resulted in significant organ improvement. Early institution of empiric therapy may be the most effective approach while perform an extensive empirical evaluation for alternative causes of disease.

Keywords: Eosinophilia; Ascaris lumbricoides; glomerulonephritis; cardiomyopathies.

**Corresponding author: Email: henriquepott@gmail.com;*

1. INTRODUCTION

Ascaris lumbricoides is a nematode parasite that infects a quarter of the world's population depending on geographic location and is a well-recognized cause of illness among persons with poor socio-economic conditions. [1]

About one third of the population in the cities of some developing countries live in slums and shantytowns where the prevalence and intensity of *A. lumbricoides* is significantly increasing due to favorable conditions of transmission.[1]

In general practice, helminth infestation is the commonest identifiable cause of eosinophilia. However, there are multiple causes, both infectious and non-infectious, of a peripheral blood eosinophilia and patients may present to a range of specialities other than infectious diseases [2,3]. In severe eosinophilia, infiltration of several tissues may occur. [3]

Eosinophilic infiltration has been associated with disorders of the lung, heart, gastrointestinal and biliary tracts and gallbladder [2,3]. Although single-organ eosinophilic infiltration due to helminth infestation has been reported [2,4-6], multiple organ involvement is rare.

Herein we describe a unique case of multiple organ infiltration (heart, kidneys, and bone marrow) due to *Ascaris lumbricoides* hipereosinophilia successfully treated and review previously reported cases in the literature.

2. CASE REPORT

A 33-year-old single, black man admitted to the hospital for a multidisciplinary evaluation with a four-year history of open tibial fracture complicated by tibialpseudo arthrosis. Otherwise, he was asymptomatic and specifically denied any symptoms. He had no family history of illness. The patient was married. There was no history of alcoholism, use of recreational drugs, or smoking, although the patient admitted sexual promiscuity in the past. He kept one dog at home.

On physical examination, the patient was afebrile and appeared well. The pulse was 84 bpm, and the blood pressure 140x80 mmHg. Punctate, erythematous, non-palpable lesions were present on the pseudarthrosis area of right leg. No subcutaneous nodules were discovered. The lungs and heart were normal. There was pitting (+) edema of the right leg to the knee, without varicosities, palpable cords, local pain, or tenderness. No edema was present in the left leg; the peripheral pulses (+) were equal bilaterally.

The initial laboratory evaluation showed positive IgG but negative IgM antibodies for both cytomegalovirus and toxoplasmosis. Serology for human immunodeficiency virus 1 and 2, viral hepatitis and syphilis were negative. Hemagglutination for Chagas disease was non-reactive. The hematocrit was 25,7%; the white-cell count was 21.100/mm^3, with 18,5% neutrophils, 16,3% lymphocytes, 3,5% monocytes, and 61,3% eosinophils. The platelet count was 321.000/mm^3, and the total eosinophil count 12.934/mm^3. A complete 3 stool samples analysis revealed no abnormalities. A urinalysis showed clear, yellow urine with a specific gravity of 1.005, pH 5, 1 g/l of protein, 579.000 white and 1.189.000 red cells. The search for eosinophils cells in the urine was positive. Chest X-ray revealed cardiomegaly. The 12-lead electrocardiogram revealed atrial enlargement. Transthoracic echocardiography revealed a dilated left ventricle (LV) with an endocardial thickening in apex of LV, with diffuse hypokinesis in the both ventricular walls (left ventricular ejection fraction, 47%). The thickness was observed also in both the interventricular septum and posterior wall of the left ventricle, indicating left ventricular hypertrophy.

At the time of presentation, the main diagnosis was reactive eosinophilia due to an inflammatory reaction against the cutaneous fistulae, although other differential diagnoses needed to be considered due to other organ involvement (heart and kidneys).

Despite multiple organ involvement, the patient in this case remained asymptomatic. Based on the orthopaedic evaluation a surgical procedure was proposed, but the patient declined. We continued the investigation of the other organ dysfunctions. Percutaneous biopsy of the left kidney revealed tubulointerstitial nephritis full of eosinophilic cells, associated with an acute and global diffuse glomerulonephritis, also infiltrated by eosinophils (Fig. 1). Another complete 3 stool samples analysis revealed no abnormalities. Ultrasonographic examination of the abdomen revealed no abnormalities. Serum IgE levels was 524,8 IU/ml (reference:< 165,3 IU/ml). Serologic tests for *Toxocara*-specific were negative. A bone marrow biopsy revealed eosinophilic

infiltration without any signs of malignant disorder.

To enhance detection, 3 stool specimens were analyzed with >48 hours apart. The content of stool samples revealed *Ascaris lumbricoides* eggs. The diagnosis of *Ascaris lumbricoides* infestation causing eosinophilic organ infiltration (heart, kidneys, and bone marrow) was suggested by the results of the diagnostic workup coupled with the clinical scenario.

Twelve days after specific treatment with ivermectin (200 mcg/kg), the patient hematocrit was 26,3%; the white-cell count was 14.600/mm^3, with 51,5% neutrophils, 37,2% lymphocytes, 7,9% monocytes, and 2,7% eosinophils. The platelet count was 413.000/mm^3, and the total eosinophil count 394/mm^3. Several complete 3 stool samples analysis revealed no further abnormalities. Another transthoracic echocardiography revealed maintenance of left ventricular dilatation with mild diffuse hypokinesis, absence of endocardial thickening, left ventricular ejection fraction, 54%). Table 1 summarizes the laboratory evolution during hospitalization.

3. DISCUSSION

This is the first report of multiple organ damage (heart, kidneys, and bone marrow) due to *A. lumbricoides* hypereosinophiliin a previously healthypatient. Although single-organ eosinophilic infiltration due to helminth infestation has been reported until now [2,4-6], multiple organ involvement was only associated with idiopathic hypereosinophilic syndromes, and its frequency variable from one study to another depending on the clinical subspecialty of the authors [7,8].

Typically, reactive eosinophilia due to an inflammatory reaction against parasitic infestation varies with the developmental stages of the parasite. In ascariasis, eosinophilia increases in the first three weeks reaching levels of from 1,000 to 5,000 eosinophils/µl and then slowly decreases in subsequent weeks [9].

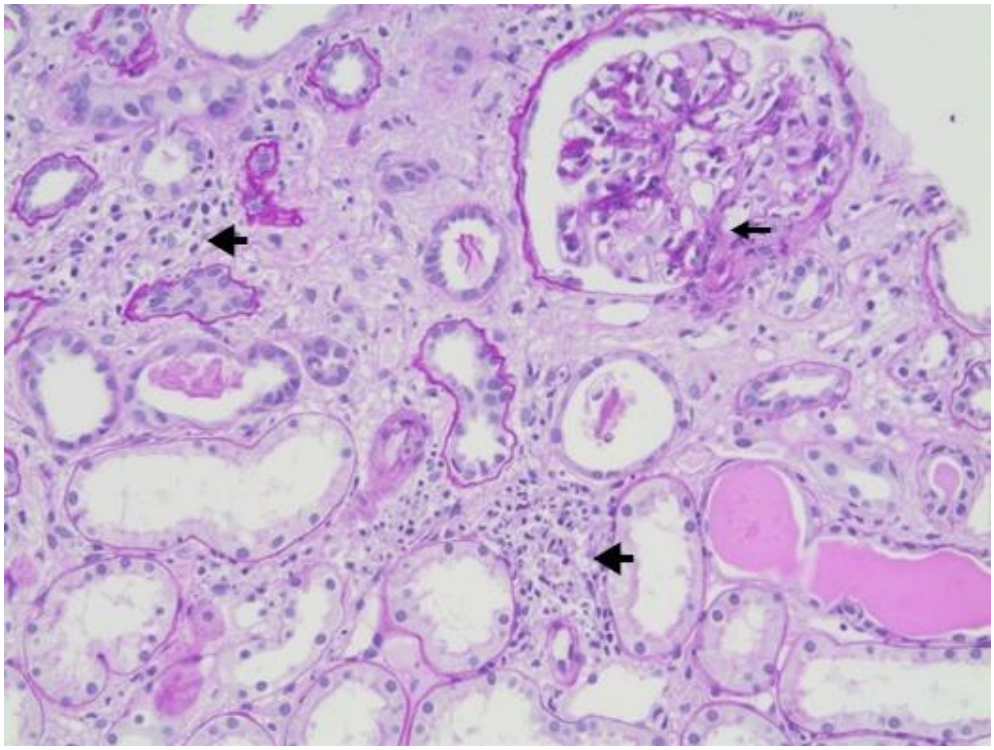

Fig. 1. Light microscopic view of kidney biopsy specimen (H&E, ×400): diffuse global glomerulonephritis (thin arrow) and tubulointerstitial (thick arrow) nephritis with renal eosinophilic infiltration

Table 1. Evolution of laboratory test results during hospitalization

Hematologic and blood chemical laboratory test results							
	1-year past record	**Hospital admission**	**5-day hospital admission**	**Ivermectin treatment**	**4-day post-treatment**	**8-day post-treatment**	**12-day post-treatment**
Hematocrit (%)	32	25,7	28	24	25,4	25,4	26,3
Leukocyte (/uL)	8020	21100	23700	20800	15100	11500	14600
Eosinophils (/uL)	24	12934	15761	13728	7173	4727	394
Creatinine (mg/dL)	0,68	1,24	1,25	1,32	1	1	0,84
Urine white cells (/uL)	9000	579000	-	-	98000	41000	20000
Urine red cells (/uL)	5000	1189000	-	-	143000	45000	8000
Urine eosinophils	Negative	Positive	-	-	Positive	Negative	Negative
Stool analysis		Negative	*A. lumbricoides*	*A. lumbricoides*	Negative	Negative	Negative

In 2002, Sakakivbara et al. [5] reported a case of organ eosinophilic infiltration due to helminth infestation. In this report, the authors describe a case of a Japanese man who had acute onset of severe cough from an unknown cause. On investigation, chest computerized tomography demonstrated multiple ground glass opacities in both lungs. Bronchoalveolar lavage showed abundant eosinophils. Abdominal computerized tomography demonstrated multiple low attenuation areas in the liver. Liver biopsy with ultrasonography revealed severe eosinophil infiltrations around the portal veins. Serologically, a multi-dot enzyme linked immunosorbent assay (DOT-ELISA) and ELISA inhibition test were positive for *Ascarissuum*. The findings disappeared after 6 month of treatment with albendazole.

In 2007, Kaji et al. [2] reported the case of a 28-year-old woman complaining of acute right hypochondrial pain and dyspnea associated with systemic eruption. Several imaging modalities revealed acute cholecystitis and pericarditis with massive pericardial effusion. A marked peripheral blood eosinophilia was observed and a high titer of antibody against *A. lumbricoides*. Treatment with albendazole drastically improved all clinical manifestations along with normalization of the imaging features and eosinophilia.

Also in 2007, Lau et al. [4] reported the case of a 27-year-old previously diagnosed HIV/AIDS male Vietnamese with *Ascaris lumbricoides*-induced eosinophilic pneumonitis. He presented with shortness of breath, chest tightness and a pruritic rash over his body and limbs. After 3 days of hospitalization, two worms of *Ascaris lumbricoides* were identified in his stool.

More recently, Sentürk et al. [6] reported a case of *Ascaris lumbricoides*-induced eosinophilic myocarditis presenting with symptoms resembling acute myocardial infarction with ST-segment elevation and cardiogenic shock. A diagnosis of acute myocarditis was made by the presence of normal coronary arteries, peripheral eosinophilia and stool examination for *Ascaris lumbricoides*. After corticosteroid treatment, the clinical status improved.

There are no pathognomonic clinical or radiological findings for the manifestations of organ eosinophilic infiltration. As seen on previous reports, the clinical manifestations of hipereosinophilia due to *A. lumbricoides* can be variable from one patient to another, depending on target-organ involvement by eosinophils.

The organ damage and/or dysfunction are the consequences of eosinophil-release of various mediators, whose nature and functions have been enumerated in great detail by Valent et al. [7]. Although virtually any tissue or organ can be affected, major tissue targets include the skin, lungs, digestive tract, heart and nervous system [7,10].

Heart damage encompasses tree stages: endo/myocardial damage by mediators released from tissue-infiltrated eosinophils leading to sterile microabscesses (usually clinically silent); soon, thrombi develop along these areas; most thrombi, however, become organized into fibrous tissue causing endomyocardial fibrosis. The fibrous tissue produces a restrictive cardiomyopathy and/or mitral or tricuspid valve regurgitation due to entrapment of the chordae tendineae. Similar findings could be found in our case by transthoracic echocardiography revealing endocardial thickening and diffuse left ventricular hypertrophy.

Kidney involvement can occur due to eosinophilic infiltration of the glomerulus and tubulointerstitial space. The histological analysis of renal biopsy in our patient revealed tubulointerstitial nephritis full of eosinophilic cells, associated with an acute and global diffuse glomerulonephritis, also infiltrated by eosinophils.

An increase of eosinophilic population in bone marrow has long been described by Stransky in case of intestinal parasites, particularly hookworm [11]. So, a bone marrow examination should be performed in patients in whom a clinical suspicion of bone marrow infiltration is present. Neoplastic disorders of the bone marrow can be easily differentiated from reactive bone marrow changes. In this case, the presence of anemia with hipereosinophilia led to a suspicion of malignancy. Bone marrow examination excluded this diagnosis.

Other causes of secondary eosinophilia are allergic conditions, such as dermatitis, rhinitis and asthma, but the values of eosinophils generally do not exceed 1,500/mm^3. There are other causes such as adrenal insufficiency, Churg-Strauss disease, atheroembolic and primary immunodeficiency syndrome, and among them hyperimmunoglobulinemia E, characterized by chronic dermatitis and recurrent infestation, were not compatible with the previous history of the patient. Regarding the primary causes of eosinophilia, the myeloproliferative and myelodysplastic syndromes constitute differential diagnosis. The diagnosis of idiopathic hypereosinophilic syndrome, finally, requires the exclusion of other causes of primary and secondary causes. The eosinophil count should be persistently greater than 1,500 mm^3 and there is evidence of target organ damage [7].

This case highlights the need for a high index of clinical suspicion among patients with poor socio-economic conditions with eosinophilia. Moreover, early institution of empiric therapy for helminthic infestation while waiting for a conclusive diagnosis.

4. CONCLUSION

In summary, helminth infestation is the commonest identifiable cause of eosinophilia. In some cases, however, eosinophilic infiltration of organs can occur, and most likely to be clinically underestimated. Yet, multiple organ involvement is rare and should be considered as a diagnosis of exclusion. Early institution of empiric therapy may be the most effective approach while perform an extensive empirical evaluation for alternative causes of disease.

CONSENT

All authors declare that 'written informed consent was obtained from the patient (or other approved parties) for publication of this case report and accompanying images.

ETHICAL APPROVAL

Not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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