

Pulmonary strongyloidiasis associated CD3+ large granular lymphocytosis

Muhammad A. Rishi, Saleha Z. Chaudhry¹

Rosalind Franklin
University of Medicine
and Science, North
Chicago, ¹Mercy
Hospital Medical
Center, Chicago,
IL, USA

Address for correspondence:

Dr. Muhammad A. Rishi,
757 W 14th Street,
Chicago, IL, 60607, USA.
E-mail: adeelrishi@yahoo.
com

Submission: 22-08-10

Accepted: 05-12-10

Abstract:

We report a case of pulmonary strongyloidiasis in a patient with large granular lymphocytosis. He was on short-term high dose immunosuppressant therapy. A 77-year-old white male presented to the emergency room with fever and shortness of breath for 10 days. The patient had been diagnosed about 3 months prior to this presentation with "large granular lymphocytosis" (LGL) after a workup for pancytopenia. Methotrexate and prednisone had been started 1 month ago for the treatment of LGL. Five days prior to the current presentation, he had been started on moxifloxacin as an outpatient but got progressively worse and came to an emergency room. Bronchial washings (bronchoalveolar lavage) demonstrated numerous filariform larvae of *Strongyloides stercoralis*. The patient was treated with ivermectin and improved. Pulmonary strongyloidiasis should be considered in the differential if X-ray findings show an interstitial or alveolar pattern and if the patient has visited the endemic areas, even in the remote past.

Key words:

Bronchoalveolar lavage, large granular lymphocytosis, strongyloidiasis

Strongyloidiasis is a parasitic disease that is usually caused by one of the two species (*Strongyloides stercoralis* and *Strongyloides fuelleborni*) of strongyloides, an intestinal nematode.^[1] It is widely distributed in the tropical and subtropical regions.^[2] The organism is endemic to former Czechoslovakia^[2] but not to Northeastern United States. In immunocompetent individuals, the infection may cause mild gastrointestinal symptoms.^[3] Untreated, the infection persists for many decades. Strongyloides hyper infection syndrome develops in patients who subsequently develop immunodeficiencies.^[2,3] Pulmonary strongyloidiasis is a common manifestation of strongyloides hyperinfection syndrome.^[4,5]

Case Report

This 77-year-old Czech man, previously a farmer, recently diagnosed with CD3+ LGL by bone marrow biopsy and flow cytometry, presented to the ER with a temperature of 104 °F and mild shortness of breath.

History of present illness showed that current symptoms had been present for 1 week. He was started on moxifloxacin as an outpatient without improvement of symptoms. The patient had been living in the Northeastern United States for the past 30 years and had never since traveled to areas endemic to strongyloides. The patient had worsening anemia over 2 months before current presentation secondary to LGL which prompted immunosuppressive therapy (prednisone 20 mg PO three times a day and methotrexate 20 mg

once a week) about 4 weeks before the current presentation.

His medical history was significant for CD3+ LGL and hypertension. The patient had a history of low-grade pancytopenia and had been followed by a hematologist as an outpatient. A bone marrow biopsy 3 months before this admission showed increased lymphocyte aggregates. Flow cytometry detected CD3+ T-cell population. T-cell clonality analysis was negative, and so secondary disease was suspected. Common etiologies of secondary LGL [Epstein Bar virus (EBV), Cytomegalovirus (CMV), Hepatitis B virus (HBV), Hepatitis C virus (HCV), Human immunodeficiency virus (HIV), Idiopathic thrombocytopenic purpura (ITP) and Rheumatoid arthritis (RA)] were ruled out and the cause of this nonclonal expansion of large granular lymphocytes remained elusive. Subsequently, the patient was started on immunosuppressive therapy. The patient had no history of dermatological or gastrointestinal manifestations of strongyloides infection.

Physical exam at the time of presentation was significant for a temperature of 101.4°F, a heart rate of 114/min, respiratory rate of 24/min and oxygen saturation of 94% on 2 L/min oxygen. The patient had a blood pressure of 110/60. Bilateral coarse crackles were heard at the bases of the lungs. Rest of the exam was within normal limits. Laboratory tests on admission are shown in Table 1. Imaging at admission included a CXR [Figure 1] showing increased interstitial markings and low lung volumes. Differential

Access this article online

Quick Response Code:



Website:

www.thoracicmedicine.org

DOI:

10.4103/1817-1737.78432

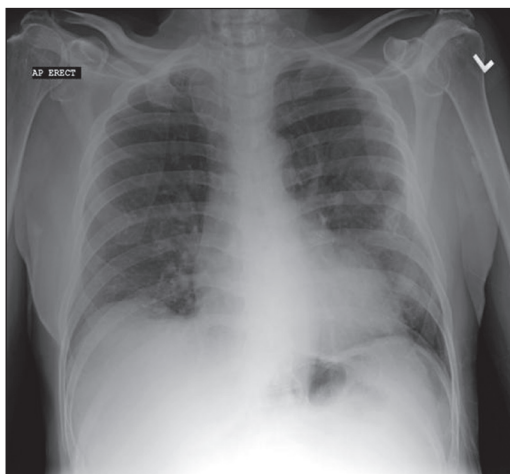


Figure 1: Chest X-ray on admission



Figure 2: Bronchoalveolar lavage photomicrograph showing *Strongyloides stercoralis*

Table 1: Admission labs

WBC	5.5	K	4.2
HB	7.9	Cl	97
HCT	32	HCO ₃	25
PLT	223	BUN	35
MCV	85.4	Cr	1.1
NEU%	67.5	GLU	124
LYM%	24.0	Ca	7.8
EOS%	3.5	PHOS	2.3
BAS%	0.1	ALB	2.3
BILI	0.4	AST	38
ALK PHOS	76	ALT	75

diagnosis included methotrexate-induced pneumonitis, atypical pneumonia (AP), and pneumocystis pneumonitis.

Hospital course was eventful. The patient was started on ceftriaxone, azithromycin, and bactrim. Prednisone was changed to hydrocortisone 30 mg four times daily after taking blood, urine, and sputum cultures. Methotrexate was stopped. The cultures remained negative over the next 48 h. However, the patient failed to improve. He continued to have persistent hypoxia and spiking fever. On day 3 post-admission, bronchoscopy with bronchoalveolar lavage (BAL) was done. It showed 5–20 *S. stercoralis* per high power field and atypical pneumocytes [Figure 2]. CD4/CD8 ratio was 0.8 (normal range, 0.8–2.1). HTLV 1/2 serology was negative. Tests for HIV also came back negative. Stool was negative for ova and parasites. Strongyloides antibodies were not obtained. The patient was started on Ivermectin 12 mg orally daily for 3 days and improved. The patient was discharged after 11 days of hospital course on a tapering dose of prednisone. Follow-up bronchoscopy was negative for strongyloides after 6 months. Repeat bone marrow biopsy done after 18 months which failed to show CD3+ LGL.

Discussion

This case is unusual in terms of possible association of pulmonary strongyloidiasis with CD3+ LGL. To our knowledge, this has not been described previously.

Large granular lymphocytes are morphologically recognizable subset of lymphocytes and have slightly basophilic cytoplasm with azurophilic granules. They represent 10–15% of the peripheral mononuclear cells. There are two phenotypes (CD- and CD3+ cells). CD3+ phenotype is the predominant form.^[6] A syndrome characterized by proliferation of large granular lymphocytes, i.e. LGL associated with neutropenia was initially reported in 1977^[7] and several studies have been published since.^[8,9] LGL can be primary or secondary and may be associated to a wide range of hematological and nonhematological disorders. Primary LGL shows clonal expansion and secondary LGL does not.^[8] Since the CD3- cells do not rearrange the T-cell receptor gene, and cytogenetic abnormalities are unusual in CD3-LGL expansions, clonality is hard to prove.^[10] This is not the case with CD3+ cells. Secondary LGL is considered reactive. EBV, CMV, HBV, HCV, HIV, ITP, connective tissue disorders such as rheumatoid arthritis, skin disorders such as pyoderma gangrenosum and hemophagocytosis syndromes have been described as potential causes of reactive LGL.^[8,11,12] One previous case report^[10] has described strongyloides as a potential cause of CD3-LGL.

Untreated, strongyloides may persist for many decades as a low-grade chronic infection. Immune suppression (due to corticosteroid therapy as in our patient, malnutrition, leukemia or lymphoma, and HTLV 1 infection) in patients with low-grade strongyloides infection may result in a hyperinfection syndrome.^[3,4] Pulmonary strongyloidiasis is one of the manifestations of the hyperinfection syndrome.^[5] Acute and subacute forms have been described. Prognosis is usually poor.^[13]

However, the diagnosis of pulmonary strongyloidiasis is often difficult and delayed since symptoms and laboratory findings are nonspecific. Chest imaging reveals nonsegmental patchy areas of consolidation diffuse a reticulonodular pattern and diffuse patchy opacities.^[14]

It is interesting to note that T/B cell clonality analysis in this patient was negative for any clonal rearrangements. This finding is suggestive of a reactive disorder. Common causes of reactive LGL were ruled out in our patient. Helminthes induce immunity by helper T-cell induced responses.^[15] It may be

suggested that chronic low-grade stimulation by a low-grade strongyloides infection over many years resulted in a reactive CD3+ large granular lymphocytosis (LGL) seen in this patient.

Resolution of the CD3+ LGL with treatment of strongyloides infection strongly suggests that the chronic strongyloides infection can result in a nonclonal expansion of LGL which resolves if the infection can be treated successfully.

References

1. Siddiqui AA, Berk SL. Diagnosis of *Strongyloides stercoralis* infection. Clin Infect Dis 2001;33:1040-6.
2. Genta RM. Global prevalence of strongyloidiasis: Critical review with epidemiologic insight into the prevention of disseminated disease. Rev Infect Dis 1989;11:755-67.
3. Milder JE, Walzer PD, Kilgore G, Rutherford I, Klein M. Clinical features of *Strongyloides stercoralis* infection in an endemic area of the United States. Gastroenterology 1981;80:1481-8.
4. Adedayo O, Grell G, Bellot P. Hyper infective strongyloidiasis in medical ward: Review of 27 cases in 5 years. South Med J 2002;95:711-6.
5. Namisato S, Motomura K, Haranaga S, Hirata T, Toyama M, Shinzato T, et al. Pulmonary strongyloidosis in a patient receiving prednisone therapy. Intern Med 2004;43:731-6.
6. Scott CS, Richard SJ. Classification of large granular lymphocytes and NK associated disorders. Blood Rev 1992;60:220-33.
7. McKenna RW, Parkin J, Kersey JH, Gajl-Peczalska KJ, Peterson L, Brunning RD. Chronic lymphoproliferative disorder with unusual, morphologic, ultrastructural and membrane surface marker characteristics. Am J Med 1977;62:588-96.
8. Loughran T. Clonal diseases of large granular lymphocytes. Blood 1993;82:1-14.
9. Oshimi K. Granular proliferative disorders: Report of 12 cases and review of literature. Leukemia 1988;2:617-27.
10. Myers B, Speight EL, Huissoon AP, Davies JM. Natural killer cell lymphocytosis and strongyloidosis infection. Clin Lab Haematol 2000;22:237-8.
11. Okuno SH, Tefferi A, Hanson CA, Katzmann JA, Li CY, Witzig TE. Spectrum of diseases associated with increased proportions or absolute numbers of peripheral natural killer cells. Br J Haematol 1996;93:810-2.
12. Imashuku S, Hibi S, Morinaga S, Takagi K, Chen J, Mugishima H, et al. Hemophagocytic lymphohistiocytosis in association with lymphocyte proliferation disorders in early childhood: Characteristic bone marrow morphology. Br J Haematol 1997;96:708-14.
13. Kinjo T, Tsuchioka K, Nakazato I, Ito E, Sato Y, Koyanagi Y, et al. Extensive alveolar hemorrhage caused by disseminated strongyloides. Int J Parasitol 1998;28:323-30.
14. Woodering JH, Harfhill H, Reed JC. Pulmonary strongyloidiasis: Clinical and imaging features. AJR Am J Roentgenol 1994; 162:537-42.
15. Niederkorn JY, Stewart GL, Ghazizadeh S, Mayhew E, Ross J, Fischer B. *Trichinella pseudospiralis* larvae express natural killer cell associated asialo- GMI antigen and stimulate pulmonary natural killer cell activity. Infect Immun 1988;56:1011-6.

How to cite this article: Rishi MA, Chaudhry SZ. Pulmonary strongyloidiasis associated CD3+ large granular lymphocytosis. Ann Thorac Med 2011;6:96-8.

Source of Support: Nil, **Conflict of Interest:** None declared.

Staying in touch with the journal

1) Table of Contents (TOC) email alert

Receive an email alert containing the TOC when a new complete issue of the journal is made available online. To register for TOC alerts go to www.thoracicmedicine.org/signup.asp.

2) RSS feeds

Really Simple Syndication (RSS) helps you to get alerts on new publication right on your desktop without going to the journal's website. You need a software (e.g. RSSReader, Feed Demon, FeedReader, My Yahoo!, NewsGator and NewzCrawler) to get advantage of this tool. RSS feeds can also be read through FireFox or Microsoft Outlook 2007. Once any of these small (and mostly free) software is installed, add www.thoracicmedicine.org/rssfeed.asp as one of the feeds.