

An Elusive Diagnosis of *Strongyloides* Infection Masquerading as Daptomycin-Induced Eosinophilic Pneumonitis

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ABSTRACT

Daptomycin-induced eosinophilic pneumonitis, characterized by peripheral eosinophilia, bilateral pulmonary infiltrates and respiratory symptoms, is a recognized adverse drug effect. However, these findings overlap significantly with pulmonary strongyloidiasis, in which transpulmonary larval migration provokes a similar eosinophil-rich inflammatory response. Failure to distinguish between these entities carries serious consequences, as untreated *Strongyloides* infection can progress to hyperinfection syndrome with high mortality. We describe a middle-aged male with alcoholic liver cirrhosis who developed peripheral eosinophilia, bilateral pulmonary nodules, migratory consolidative opacities, and pleural effusions while receiving daptomycin for polymicrobial bacteremia. The findings were initially attributed to daptomycin-induced eosinophilic pneumonitis, and the drug was discontinued. However, given clinical suspicion for a parasitic etiology, *Strongyloides* testing was pursued. Stool ova-and-parasite examination and bronchoalveolar lavage were both negative; however, *Strongyloides* serology returned positive, confirming the diagnosis. The patient improved both clinically and radiographically following treatment with ivermectin and albendazole. The negative stool and bronchoalveolar lavage results further underscore the suboptimal sensitivity of conventional diagnostic methods and the essential role of serologic testing. Clinicians evaluating eosinophilia with pulmonary infiltrates in patients receiving daptomycin should systematically consider parasitic etiologies, including *Strongyloides* serology, before attributing findings solely to a drug-related cause.

KEYWORDS: *Strongyloides*; pneumonitis; daptomycin; eosinophilia

INTRODUCTION

Daptomycin is a cyclic lipopeptide antibiotic used for serious gram-positive infections, including bacteremia and endocarditis caused by methicillin-resistant *Staphylococcus aureus* and vancomycin-resistant enterococci.^{1,2} While generally well tolerated, daptomycin has been increasingly recognized

as a cause of eosinophilic pneumonia, characterized by fever, dyspnea, hypoxia, peripheral eosinophilia, and bilateral pulmonary infiltrates, typically occurring within two to four weeks of drug initiation.^{3,4} The diagnosis is generally made clinically after exclusion of alternative etiologies, and management centers on discontinuation of the offending agent, with or without corticosteroid therapy.^{4,5}

However, peripheral eosinophilia with concurrent pulmonary infiltrates has a broad differential diagnosis encompassing drug-induced reactions, allergic conditions, and parasitic infections.⁶ Among infectious etiologies, strongyloidiasis—caused by *Strongyloides stercoralis*—is particularly important, as transpulmonary larval migration provokes an eosinophil-rich inflammatory response producing pulmonary nodules, migratory consolidative opacities, and pleural effusions, frequently referred to as Löffler-like syndrome.⁷⁻⁹ The clinical features of pulmonary strongyloidiasis overlap substantially with daptomycin-induced eosinophilic pneumonia, creating a diagnostic pitfall. Failure to identify *Strongyloides* infection carries serious consequences, as untreated disease can progress to hyperinfection syndrome with mortality rates exceeding 70%.¹⁰

Severe strongyloidiasis has been predominantly described in patients with established immunocompromising conditions, including systemic corticosteroid use, solid organ transplantation, hematologic malignancies, HTLV-1 coinfection, and HIV/AIDS.^{10,11} The extent to which alcoholic liver cirrhosis predisposes to clinically significant infection remains incompletely understood.^{10,12} The diagnostic sensitivity of conventional methods is suboptimal; single stool examinations detect larvae in fewer than 50% of cases, and bronchoalveolar lavage may fail to identify organisms, making serologic testing essential.^{10,13}

We present a middle-aged male with alcoholic liver cirrhosis who developed peripheral eosinophilia and bilateral pulmonary infiltrates during daptomycin treatment. The eosinophilia was initially attributed to daptomycin-induced eosinophilic pneumonitis. However, *Strongyloides* serology later returned positive, reframing the clinical picture as pulmonary strongyloidiasis. This case highlights the overlapping presentations of these conditions and the importance of systematically evaluating for parasitic etiologies before attributing eosinophilic pulmonary disease solely to a drug-related cause.

HOSPITAL COURSE

A middle-aged Mexican male with alcoholic liver cirrhosis, esophageal varices, and diverticulosis presented with a progressive, diffuse, blistering rash of four days' duration. The patient had family in both the United States and Mexico, frequently travelling between the two countries. He had been recently discharged from a hospital in Mexico following treatment for infectious colitis, receiving intravenous antibiotics (patient did not remember which antibiotics he was taking) before transitioning to oral ciprofloxacin and metronidazole. Two days after completing antibiotics, he noted a rash initially involving the face and trunk, progressively spreading to the lower extremities with associated blistering, edema, and significant pain affecting the plantar surfaces. He endorsed oral and ocular discomfort but denied fever, chest pain, or shortness of breath.

The patient was admitted to the burn unit for suspected Stevens-Johnson syndrome. Punch biopsy from the left thigh demonstrated epidermal cell necrosis, a perivascular infiltrate of lymphocytes and eosinophils, and incidental dermatophytosis, consistent with severe drug eruption attributed to ciprofloxacin and metronidazole. Treatment with intravenous immunoglobulin was initiated with symptomatic improvement.

His course was complicated by severe sepsis and persistent fevers secondary to polymicrobial bacteremia. Serial blood cultures yielded *Klebsiella pneumoniae*, ESBL-producing *Escherichia coli*, *Lactobacillus rhamnosus*, and vancomycin-resistant *Enterococcus faecium*. Daptomycin and meropenem were initiated on day 18. Echocardiogram showed no evidence of endocarditis, and diagnostic paracentesis was culture negative. Blood cultures on days 22 and 24 were negative.

On hospital day 24, new peripheral eosinophilia was identified. CT chest on day 26 [Figure 1] demonstrated bilateral scattered ill-defined pulmonary nodules measuring up to 2 cm in the right upper lobe, left upper lobe subpleural consolidative opacities, bilateral pleural effusions with adjacent atelectasis, large-volume ascites, and cirrhotic liver morphology. Given the onset of symptoms coinciding with the initiation of daptomycin and with his recent history of antibiotic reaction, daptomycin-induced eosinophilic pneumonitis was the initial working diagnosis. The patient denied any history of autoimmune disorders, asthma, or malignancies.

Daptomycin was subsequently stopped after discovery of these findings. However, the patient's symptoms did not resolve, and he continued to meet criteria for sepsis (persistent fevers, leukocytosis, and tachycardia), with unresolving eosinophilia. After his clinical regression, suspicion for helminth infections began increasing, especially in the context of his frequent travel to Mexico. In particular, severe *Strongyloides* infection with suspected pulmonary involvement was entertained given eosinophilia, imaging findings

Figure 1. Axial view of initial CT chest on day 26, highlighting the 2cm right upper lobe pulmonary nodule.

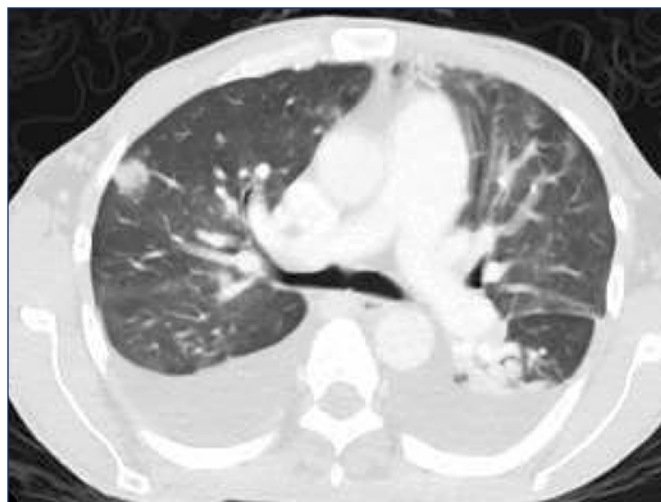


Figure 2. Axial view of follow-up CT chest one week after initiation of anti-parasitic therapy, showing complete resolution of the 2cm right upper lobe pulmonary nodule.



potentially consistent with larval translocation, and otherwise unexplainable polymicrobial bacteremia. Bronchoscopy with bronchoalveolar lavage was negative. Stool ova and parasite examination was also negative. Nevertheless, given high clinical suspicion, *Strongyloides* serology was collected and returned positive. Empiric treatment was initiated with ivermectin 200 mcg/kg daily for four weeks and albendazole 400 mg twice daily for seven days. Follow-up CT demonstrated interval resolution of the right upper lobe opacity [Figure 2].

The patient improved steadily with resolution of fevers, normalization of white blood cell count, and improvement of the cutaneous eruption. He was transferred to step-down and subsequently to general medicine. Blood cultures on

days 26 and 31 showed no growth. At discharge on hospital day 56, he was afebrile and hemodynamically stable with improved leukocytosis. Outpatient follow-up was arranged with infectious disease, hepatology, dermatology, and podiatry.

DISCUSSION

Strongyloidiasis is a soil-transmitted helminthic infection with highest prevalence in tropical and subtropical regions.⁷ Published literature on clinically significant strongyloidiasis focuses on hyperinfection syndrome in classically immunocompromised hosts, particularly those receiving corticosteroids, organ transplant recipients, patients with hematologic malignancies, those with HTLV-1 or HIV co-infection, and those with hypogammaglobulinemia.¹⁰ Notably, our patient carried none of these established risk factors. While his alcoholic liver cirrhosis may have contributed to immune dysregulation, the extent to which hepatic cirrhosis alone confers susceptibility to *Strongyloides* hyperinfection remains poorly characterized.¹⁴ This case adds to limited evidence suggesting clinically significant pulmonary strongyloidiasis can occur in hosts lacking classically defined immunocompromising conditions.

In patients with *Strongyloides* hyperinfection, providers typically expect serial stool and BAL studies to be positive, given the immense parasitic load. In our patient, however, both modalities were negative throughout hospitalization. Treatment was guided by high clinical suspicion and confirmed by serological testing. Initial negative BAL and stool testing should not preclude treatment initiation when clinical suspicion remains high.

The pulmonary manifestations observed—bilateral pulmonary nodules, pleural effusions, and migratory consolidative opacities—are consistent with transpulmonary larval migration characterizing the *Strongyloides* life cycle, provoking an eosinophil-rich inflammatory response reminiscent of Löffler-like syndrome. The clinical presentations of pulmonary strongyloidiasis are nonspecific, encompassing cough, dyspnea, wheezing, and hemoptysis, mimicking asthma, community-acquired pneumonia, or acute respiratory distress syndrome.^{8,9} The interval evolution of CT findings—initial right upper lobe nodularity resolving with new left upper lobe consolidative opacities—was particularly suggestive of the migratory inflammatory process characteristic of larval transit.

A particularly instructive aspect was the initial attribution of eosinophilia to daptomycin rather than parasitic infection. Given the temporal relationship between daptomycin administration and development of eosinophilia with pulmonary findings, initial suspicion of daptomycin-induced eosinophilic pneumonitis was understandable.^{3,4} However, substantial clinical overlap created a diagnostic pitfall. Only upon further evaluation prompted by persistent eosinophilia

was *Strongyloides* serology obtained and found positive. This sequence underscores the importance of comprehensive diagnostic workup for eosinophilia, including serologic testing, before attributing eosinophilic lung disease solely to pharmacologic causes. Failure to identify the parasitic etiology could have resulted in omission of antiparasitic therapy and progression to hyperinfection.

This case reinforces several principles. First, the absence of classic immunocompromising risk factors should not preclude consideration of strongyloidiasis in patients with compatible findings.^{7,10} Second, the nonspecific nature of pulmonary strongyloidiasis demands high clinical suspicion when peripheral eosinophilia accompanies unexplained infiltrates.^{8,9} Third, clinicians must systematically evaluate both drug-induced and infectious etiologies of eosinophilic pneumonia to avoid diagnostic anchoring.^{3,4}

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