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Extreme Hypereosinophilia Revealing Disseminated Strongyloidiasis in a Critically Ill Patient

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Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
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Patient: Female, 63-year-old
Final Diagnosis: Extreme hypereosinophilia • *Strongyloides stercoralis* infection
Symptoms: Impaired consciousness • respiratory failure requiring mechanical ventilation via tracheostomy • severe malnutrition

Clinical Procedure: Bilateral frontal neurosurgical intervention • tracheostomy • mechanical ventilation • oxygen supplementation • supportive care and rehabilitation

Specialty: Critical Care Medicine • Infectious Diseases

Objective: Unusual clinical course

Background: Extreme hypereosinophilia is an uncommon but clinically important laboratory finding that may indicate serious underlying disease. In tropical regions, parasitic infections, particularly *Strongyloides stercoralis*, should be considered. However, the diagnosis may be overlooked in critically ill patients with multiple concurrent infections. Because disseminated strongyloidiasis carries high mortality when diagnosis is delayed, early recognition and empirical anti-helminthic therapy are essential in endemic settings.

Case Report: A 63-year-old Vietnamese farmer was transferred after 18 days of treatment for bacterial meningitis, intraventricular hemorrhage, *Corynebacterium striatum* pneumonia, and *Candida auris* infection. She remained critically ill and required respiratory support through a tracheostomy. Laboratory testing showed marked leukocytosis with extreme hypereosinophilia, severe anemia, profound hypoalbuminemia, acute kidney injury, electrolyte disturbances, and severe systemic inflammation. Arterial blood gas analysis confirmed hypoxemic respiratory failure. Given the extreme eosinophilia and endemic setting, disseminated strongyloidiasis was suspected, and empirical oral ivermectin was started before diagnosis. *Strongyloides*-specific IgG serology was positive, and *Strongyloides stercoralis* larvae were identified in sputum, confirming the diagnosis. The absolute eosinophil count declined from > 10 000 cells/μL to 450 cells/μL by the next day, 180 cells/μL by treatment day 3, and 140 cells/μL by day 5. Her systemic condition remained stable for approximately 2 weeks; however, she subsequently developed recurrent intracranial hemorrhage and died in hospital.

Conclusions: This case highlights that strongyloidiasis should be considered in patients with unexplained marked eosinophilia, even when severe bacterial or fungal infections dominate the clinical presentation. In endemic regions, early clinical suspicion and timely empirical anti-helminthic therapy may be crucial to prevent potentially fatal disseminated strongyloidiasis, particularly in malnourished and medically complex patients.

Keywords: Eosinophilia • Helminths • Hypereosinophilic Syndrome • Strongyloidiasis

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Introduction

Peripheral eosinophilia is a relatively common laboratory abnormality with a broad differential diagnosis. The most frequent causes include allergic diseases, drug reactions, parasitic infections, autoimmune disorders, and hematologic malignancies. Hypereosinophilia, usually defined as an absolute eosinophil count greater than 1500 cells/ μ L, warrants prompt clinical evaluation because persistent eosinophilia may indicate serious underlying disease and can lead to eosinophil-mediated organ damage [1]. In regions where parasitic infections remain endemic, helminthic infections represent an important and often overlooked cause of marked eosinophilia.

Strongyloides stercoralis is a soil-transmitted intestinal nematode endemic to tropical and subtropical regions and remains an important public health concern, particularly in low- and middle-income countries where sanitation and access to healthcare may be limited. Global epidemiological estimates suggest that the prevalence of strongyloidiasis in 2017 was approximately 8.1% (95% confidence interval: 4.2%-12.4%), corresponding to nearly 614 million infected individuals worldwide. Notably, the burden of infection is disproportionately concentrated in the Southeast Asian, African, and Western Pacific regions, which together account for approximately 76.1% of global strongyloidiasis cases [2].

A distinctive feature of *Strongyloides stercoralis* infection is its ability to persist for decades through an autoinfection cycle, allowing the parasite to complete its life cycle entirely within the human host without the need for external reinfection. As a result, many infected individuals develop chronic infections that remain asymptomatic or manifest only with mild gastrointestinal or dermatologic symptoms. In such cases, peripheral eosinophilia may be the only detectable laboratory abnormality. However, in susceptible hosts, uncontrolled autoinfection can lead to hyperinfection syndrome or disseminated strongyloidiasis, conditions characterized by a marked increase in larval burden and widespread migration beyond the parasite's usual gastrointestinal and pulmonary life cycle. Severe strongyloidiasis is frequently complicated by secondary bacterial infections, including sepsis or meningitis caused by enteric organisms that are carried into the bloodstream during larval migration. Several conditions have been associated with an increased risk of hyperinfection, most notably glucocorticoid therapy and infection with human T-lymphotropic virus type 1 (HTLV-1). Additional predisposing factors include hematologic malignancies, solid organ transplantation, advanced HIV infection, and severe malnutrition. Anthelmintic agents, particularly ivermectin, are considered the treatment of choice and have been used successfully not only for the management of hyperinfection syndrome but also for prophylaxis in high-risk patients [3,4].

Despite available treatment, severe strongyloidiasis remains associated with substantial mortality, with reported case-fatality rates ranging from approximately 80% to 90%, particularly when diagnosis and treatment are delayed [5,6]. For this reason, early recognition of strongyloidiasis is critical, especially in endemic regions or in patients presenting with unexplained hypereosinophilia. Here, we describe a case of marked hypereosinophilia associated with *Strongyloides stercoralis* infection in a critically ill patient with multiple comorbid conditions, emphasizing the diagnostic challenges and the importance of early empirical anti-helminthic therapy.

Case Report

A 63-year-old Vietnamese woman, a farmer by profession, was transferred to our hospital from Cho Ray Hospital on March 6 for further management and rehabilitation after a prolonged severe illness. According to the referral documentation, she had been hospitalized at the tertiary center from February 17 to March 6 of the same year for bacterial meningitis, right intraventricular hemorrhage with postoperative status following bilateral frontal neurosurgical intervention, *Corynebacterium striatum* pneumonia, and *Candida auris* infection detected in sputum and urine. During that admission, she required respiratory support and received broad-spectrum antibiotics and antifungal therapy. At the time of transfer, her Glasgow Coma Scale score was 10, vital signs were stable, she was breathing spontaneously via tracheostomy with oxygen supplementation, and the neurosurgical wound was dry.

After transfer to our hospital, the patient remained critically ill and severely malnourished. Laboratory investigations revealed marked leukocytosis and extreme hypereosinophilia. The white blood cell count ranged from 21.72 to 23.56×10^3 cells/ μ L, while eosinophils accounted for 47.0% to 49.7% of circulating leukocytes, corresponding to an absolute eosinophil count between 10.22 and 11.70×10^3 cells/ μ L. Severe normocytic anemia was present, with hemoglobin levels of 6.8 to 7.6 g/dL. Additional laboratory findings included profound hypoalbuminemia (19.4 g/L), acute kidney injury with serum creatinine of 183.7 to 224.2 μ mol/L and estimated glomerular filtration rate of 21 to 26 mL/min/1.73 m², hypernatremia (153-154 mmol/L), hypokalemia (2.7-2.9 mmol/L), and marked systemic inflammation, with C-reactive protein of 193.48 mg/L (Table 1).

Arterial blood gas analysis demonstrated hypoxemic respiratory failure, with a pH of 7.475, PaCO₂ of 34.1 mm Hg, bicarbonate of 25.1 mmol/L, and PaO₂ of 58 mm Hg. Cardiac biomarkers were also elevated, including an NT-ProBNP level of 1420 pg/mL and high-sensitivity troponin I levels ranging from 71.88 to 77.61 ng/L without significant dynamic change.

Table 1. Serial laboratory results from March 6 to March 13 in the year of the patient's hospitalization.

Laboratory test (unit)	06/03	07/03	08/03	09/03	10/03	11/03	12/03	13/03
CBC								
WBC (× 10 ³ /μL)	21.72	23.56	14.36	15.43	17.09	15.79	15.49	—
Neutrophils (× 10 ³ /μL)	8.46	8.08	9.69	10.53	11.12	10.92	10.77	—
Lymphocytes (× 10 ³ /μL)	2.30	2.40	2.38	2.89	3.35	2.79	2.67	—
Monocytes (× 10 ³ /μL)	0.68	1.25	1.36	1.78	2.46	1.81	1.87	—
Eosinophils (× 10³/μL)	10.22	11.70	0.45	0.18	0.08	0.14	0.10	—
RBC (× 10 ⁶ /μL)	2.38	2.58	3.10	3.11	3.12	3.00	3.09	—
Hemoglobin (g/dL)	6.8	7.6	9.1	9.3	9.4	9.2	9.4	—
Hematocrit (%)	20.7	22.3	26.9	27.1	26.8	26.0	26.7	—
Platelets (× 10 ³ /μL)	168	177	170	144	180	176	215	—
CRP (mg/L)	193.48	—	—	—	—	—	—	—
Renal function								
Creatinine (μmol/L)	183.7	224.2	—	266.9	235.0	—	148.7	128.8
eGFR (mL/min/1.73 m ²)	26	21	—	17	20	—	34	40
Urea (mmol/L)	—	24.70	—	—	—	—	—	—
Electrolytes								
Sodium (mmol/L)	154	153	149	149	148	141	—	142
Potassium (mmol/L)	2.7	2.9	3.5	3.1	3.3	3.9	—	4.5
Chloride (mmol/L)	110	110	109	108	104	101	—	105
Calcium (mmol/L)	1.46	1.39	1.25	1.25	1.16	1.04	—	1.09
Magnesium (mmol/L)	—	—	0.70	0.71	0.74	0.62	—	0.73
Liver								
AST (U/L)	—	—	—	—	—	189.5	—	—
ALT (U/L)	—	—	—	—	—	37.8	62.0	—
Albumin (g/L)	19.4	—	—	—	—	—	36.5	—
Total protein (g/L)	—	—	—	—	—	—	68.5	—
Direct bilirubin (μmol/L)	—	—	—	—	—	—	6.0	—
Total bilirubin (μmol/L)	—	—	—	—	—	—	18.2	—
Cardiac								
High-sensitivity troponin I (ng/L)	—	77.61	—	—	—	—	22.65	—
NT-proBNP (pg/mL)	1420	—	—	—	—	—	7289	—
Arterial blood gas								
pH (arterial blood gas)	—	7.475	—	—	7.618	7.564	—	—
PaO ₂ (mm Hg)	—	58	—	—	83	100	—	—
PaCO ₂ (mm Hg)	—	34.1	—	—	23.3	28.1	—	—

Table 1 continued. Serial laboratory results from March 6 to March 13 in the year of the patient's hospitalization.

Laboratory test (unit)	06/03	07/03	08/03	09/03	10/03	11/03	12/03	13/03
HCO ₃ ⁻ (mmol/L)	—	25.1	—	—	23.8	25.4	—	—
Base excess (mmol/L)	—	1.8	—	—	2.3	3.1	—	—
SaO ₂ (%)	—	92	—	—	98	98	—	—
Helminth								
Strongyloides IgG	—	—	—	Positive	—	—	—	—
<i>Strongyloides stercoralis</i> larvae (sputum)	—	—	—	Positive	—	—	—	—
Toxocara IgG	—	—	—	Negative	—	—	—	—
Filariasis IgG	—	—	—	Negative	—	—	—	—

CBC, complete blood count; WBC, white blood cells; RBC, red blood cells; CRP, C-reactive protein; eGFR, estimated glomerular filtration rate; AST, aspartate aminotransferase; ALT, alanine aminotransferase; NT-ProBNP, N-terminal pro-B-type natriuretic peptide; PaO₂, partial pressure of oxygen in arterial blood; PaCO₂, partial pressure of carbon dioxide in arterial blood; SaO₂, saturation of oxygen in arterial blood; IgG, immunoglobulin G.

The patient continued to receive mechanical ventilation, antibiotic therapy, and antifungal treatment at our institution. However, the extremely elevated eosinophil count (10 220–11 700 cells/μL), which could not be explained by the previously documented bacterial and fungal infections, raised early clinical suspicion of disseminated parasitic infection, particularly strongyloidiasis, given the endemic setting and the patient's severely debilitated condition. Based on this suspicion, empirical oral ivermectin 12 mg once daily (approximately 200 μg/kg/day) was initiated promptly before confirmatory test results became available.

On March 9, *Strongyloides*-specific IgG serology was positive, and the laboratory report documented *Strongyloides stercoralis* larvae in the sputum sample, confirming the diagnosis. The specific serologic assay platform and the detailed sputum-processing and microscopy protocol were not available in the transferred medical records. Following initiation of ivermectin, the absolute eosinophil count decreased from > 10 000 cells/μL at baseline to approximately 450 cells/μL by the next day, 180 cells/μL by treatment day 3, and 140 cells/μL by treatment day 5. The total white blood cell count also progressively decreased during this period.

The patient's systemic condition gradually improved, renal function improved compared with admission values, and liver function remained stable during treatment. She remained hospitalized and clinically stable for approximately 2 weeks. She then developed recurrent intracranial hemorrhage and died during the same hospitalization. The exact duration of intensive care unit-level care could not be reliably determined from the transferred records. No post-treatment parasitological

follow-up examination of stool or sputum was documented or available before death.

Timeline

17 February

The patient was admitted to Cho Ray Hospital for bacterial meningitis and intraventricular hemorrhage.

February to March

Treatment for severe infection, including *Corynebacterium striatum* pneumonia and *Candida auris* infection, was administered; specifically, broad-spectrum antibiotics and antifungal therapy.

06 March

The patient was transferred to our hospital for continued respiratory care and rehabilitation. The patient had a Glasgow Coma Scale score of 10 and was breathing through a tracheostomy. Marked leukocytosis and extreme hypereosinophilia (> 10 000 cells/μL) were detected. Portable chest radiography performed on admission showed a tracheostomy tube in situ. Bilateral patchy pulmonary infiltrates were present, predominantly in the perihilar and lower lung zones. The cardiac silhouette appeared mildly enlarged. No obvious pneumothorax or significant pleural effusion was identified. The findings were compatible with bilateral infectious lung disease (**Figure 1**).



Figure 1. Chest radiograph obtained on March 6 (hospitalization day 1) showing bilateral pulmonary infiltrates.

07 March

Empirical ivermectin therapy was initiated due to strong suspicion of disseminated parasitic infection.

08 March

Eosinophil count decreased to 450 cells/ μ L.

09 March

Eosinophil count decreased to 180 cells/ μ L. Confirmatory laboratory results became available:

Strongyloides-specific IgG serology was positive (the assay platform was not documented in the transferred medical records). Sputum examination provided additional confirmation: *Strongyloides stercoralis* larvae were observed in the patient's sputum (the detailed specimen-processing and microscopy protocol was not available).

10 March

Eosinophil count decreased to 80 cells/ μ L.

Subsequent Course

The patient's systemic condition and renal function improved, liver function remained stable, and respiratory support was continued. After approximately 2 weeks of clinical stability, she

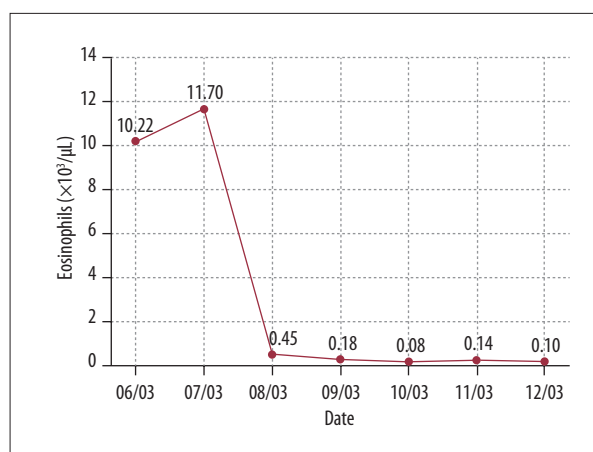


Figure 2. Eosinophil count by hospitalization day. Dates are in day/month (dd/mm) format.

developed recurrent intracranial hemorrhage and died in hospital. No repeat stool or sputum parasitological results were documented or available (Figure 2).

Discussion

This case illustrates several clinically important points. First, the patient presented with extreme hypereosinophilia, with an absolute eosinophil count exceeding 10 000 cells/ μ L (approximately 50% of total leukocytes). Such marked eosinophilia is uncommon in routine clinical practice and substantially narrows the differential diagnosis. While allergic disease, drug reactions, autoimmune conditions, and hematologic malignancies must be considered, parasitic infections remain among the most important causes of eosinophilia in tropical regions. This is particularly relevant in our patient, a 63-year-old farmer residing in Dong Thap Province in the Mekong Delta of southern Vietnam, an area where soil-transmitted helminth infections remain endemic.

The clinical context further supported this consideration. At the time of evaluation, the patient was critically ill with multiple severe conditions, including bacterial meningitis, pneumonia with respiratory failure, and invasive fungal infection, raising concern for ongoing systemic infection despite broad-spectrum antibiotics and antifungal therapy. Laboratory findings demonstrated persistent leukocytosis (21 720 up to 23 000 cells/ μ L) and markedly elevated inflammatory markers (C-reactive protein, 193 mg/L), indicating ongoing severe systemic inflammation. In addition, the patient had several conditions known to predispose to severe parasitic disease, including profound malnutrition, severe anemia, electrolyte disturbances, and acute kidney injury related to critical illness and intensive antimicrobial therapy.

Among parasitic infections, *Strongyloides stercoralis* is of particular concern because of its unique autoinfection cycle, which

allows the parasite to persist for years within the host. In the setting of severe illness or impaired immunity, uncontrolled larval proliferation may lead to hyperinfection syndrome or disseminated strongyloidiasis [7]. During larval migration, enteric bacteria may be carried transmurally into the bloodstream, resulting in secondary bacteremia, sepsis, or meningitis. This pathophysiologic mechanism could plausibly contribute to the severe infectious manifestations observed in our patient.

Alternative causes of marked eosinophilia were carefully considered. Hypereosinophilic syndrome is characterized by persistent hypereosinophilia exceeding 1.5×10^9 cells/L on at least 2 complete blood counts obtained more than 1 month apart, accompanied by evidence of organ or tissue damage attributable to eosinophilic infiltration. Additional diagnostic criteria may include bone marrow eosinophilia exceeding 20% of nucleated cells, histopathologic evidence of extensive eosinophilic tissue infiltration or deposition of eosinophil granule proteins, and the exclusion of other secondary causes of eosinophilia [8]. In the present case, these criteria were not fulfilled. The marked eosinophilia was newly detected during the current acute illness, and there was no prior evidence of persistent eosinophilia. Furthermore, the clinical presentation was dominated by severe systemic infection rather than organ dysfunction attributable to eosinophilic tissue infiltration.

Hematologic malignancies associated with eosinophilia, including eosinophilic leukemia and lymphoma, were also considered in the differential diagnosis. However, these conditions typically present with sustained or progressively increasing eosinophil counts unless treated with disease-specific therapy. In contrast, our patient demonstrated a rapid and marked decline in eosinophil levels following the initiation of anti-helminthic treatment. The absolute eosinophil count decreased dramatically from more than 10 000 cells/ μ L at presentation to approximately 450 cells/ μ L after 2 days of therapy, 180 cells/ μ L after 3 days, and 140 cells/ μ L by the fifth day (Figure 2). Such a rapid normalization strongly supports a secondary reactive process rather than a primary hematologic disorder.

The diagnosis was confirmed by positive *Strongyloides*-specific IgG serology and detection of *Strongyloides stercoralis* larvae in sputum. These findings, together with the epidemiologic background, extreme eosinophilia, and rapid hematologic response to ivermectin, support severe strongyloidiasis in this critically ill patient. This case underscores the importance of considering strongyloidiasis in patients presenting with unexplained extreme eosinophilia in endemic regions and highlights the potential benefit of early empirical anthelmintic therapy when severe infection is suspected.

Given the extreme eosinophilia and epidemiological risk factors, *Strongyloides stercoralis* infection was strongly suspected. Considering the potentially fatal consequences of delayed

treatment for disseminated strongyloidiasis [9], appropriate diagnostic testing was requested and empirical ivermectin was initiated before confirmatory laboratory results became available. The subsequent positive serology and identification of larvae in sputum provided microbiologic confirmation of the diagnosis.

Second, the diagnosis occurred in a medically complex patient with multiple concurrent severe conditions, including bacterial meningitis, intraventricular hemorrhage, bacterial pneumonia caused by *Corynebacterium striatum*, and *Candida auris* infection. In such settings, the presence of overwhelming bacterial or fungal infection may obscure the significance of eosinophilia and delay investigation for parasitic disease.

Third, the patient had severe malnutrition, as reflected by profound hypoalbuminemia. Malnutrition may impair host immune responses and increase susceptibility to persistent or disseminated infections. In our patient, the combination of severe systemic illness, prolonged hospitalization, and nutritional depletion likely contributed to the atypical presentation.

An important aspect of this case was the early empirical administration of ivermectin based on clinical suspicion, even before definitive laboratory confirmation was available. This decision was supported by the magnitude of the eosinophilia and the absence of an alternative explanation. The patient demonstrated a rapid hematologic response, with eosinophil counts decreasing dramatically within several days. This response was consistent with effective treatment; however, normalization of eosinophil counts alone cannot establish parasite eradication.

Although the patient's systemic condition remained stable for approximately 2 weeks, she subsequently developed recurrent intracranial hemorrhage and died during the same hospitalization. No post-treatment parasitological results from stool or sputum were documented or available; therefore, microbiologic clearance could not be confirmed. In addition, the exact *Strongyloides* IgG assay platform and the sputum-processing and microscopy protocol were unavailable in the transferred records. These limitations should be considered when interpreting the treatment response. Nevertheless, the case emphasizes the need for a high index of suspicion and prompt treatment for strongyloidiasis in critically ill or malnourished patients with unexplained marked eosinophilia in endemic settings.

Conclusions

Positive *Strongyloides*-specific IgG serology and identification of *Strongyloides stercoralis* larvae in sputum confirmed the diagnosis. The rapid decline in eosinophil counts after

empirical ivermectin underscores the value of early recognition and treatment in critically ill patients with unexplained extreme hypereosinophilia in endemic settings. Because no post-treatment parasitological results were available, hematologic improvement should not be interpreted as confirmation of parasite eradication.

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References:

1. Kovalszki A, Weller PF. Eosinophilia. *Prim Care*. 2016;43(4):607-17
2. Buonfrate D, Bisanzio D, Giorli G, et al. The global prevalence of *Strongyloides stercoralis* infection. *Pathogens*. 2020;9(6):468
3. Keiser PB, Nutman TB. *Strongyloides stercoralis* in the immunocompromised population. *Clin Microbiol Rev*. 2004;17(1):208-17
4. Nutman TB. Human infection with *Strongyloides stercoralis* and other related *Strongyloides* species. *Parasitology*. 2017;144(3):263-73
5. CDC. Clinical overview of *Strongyloides*. Updated Feb 11, 2026. Accessed Sep 28, 2026. URL: <https://www.cdc.gov/strongyloides/hcp/clinical-overview/index.html>
6. Yeh MY, Aggarwal S, Carrig M, et al. *Strongyloides stercoralis* infection in humans: A narrative review of the most neglected parasitic disease. *Cureus*. 2023;15(10):e46908
7. Kassalik M, Mönkemüller K. *Strongyloides stercoralis* hyperinfection syndrome and disseminated disease. *Gastroenterol Hepatol (N Y)*. 2011;7(11):766-68
8. Mikhail ES, Ghatol A. Hypereosinophilic syndrome. In: StatPearls. Treasure Island (FL): StatPearls Publishing; January 11, 2024
9. López-Delgado DS, Narváez CA, Bonfante-Villalobos R, et al. *Strongyloides stercoralis* hyperinfection with thrombosis: A systematic review of case reports. *New Microbes New Infect*. 2025;68:101659

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Patient Permission/Consent Declarations

Written informed consent was obtained from the patient's legal representative for the publication of this case report and any accompanying images. All identifying information has been removed to ensure patient confidentiality.

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