

COVID-19–Associated Eosinopenia in a Patient With Chronic Eosinophilia Due to Chronic Strongyloidiasis

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Abstract: Eosinopenia was frequently encountered in patients with coronavirus disease 2019 (COVID-19). We describe a case of a 59-year-old man who was treated with high-dose corticosteroids and anti-interleukin 1 receptor antagonist therapy because of severe acute respiratory distress syndrome due to a so-called cytokine storm in COVID-19. He had chronic eosinophilia for many years due to an unknown *Strongyloides stercoralis* infection, proven by serology and a positive polymerase chain reaction test on a stool sample. COVID-19 led to a complete resolution of eosinophilia, even before immunosuppressive treatment was started. Eosinophilia returned after recovery from COVID-19 and started to decline under treatment with ivermectin. Our case confirms previous reports of eosinopenia in COVID-19, as it appears even in patients with chronic eosinophilia. Presence of eosinophilia should prompt screening for strongyloidiasis in all patients eligible for immunosuppressive therapy because of the risk of *Strongyloides* hyperinfection syndrome, especially if this treatment is empirical.

Key Words: SARS-CoV-2, *Strongyloides* hyperinfection syndrome, corticosteroid treatment

(*Infect Dis Clin Pract* 2021;29: e305–e306)

Coronavirus disease 2019 (COVID-19) is a recent human respiratory disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).¹ Previous reports discussed the presence of eosinopenia—defined as an absolute eosinophil count of less than 200 per milliliter—in patients with COVID-19.^{2–5} It is hypothesized that a low eosinophil count is associated with more severe respiratory disease, and rising eosinophil count can serve as a marker for disease recovery.^{4,5} Little is known about the effect of COVID-19 on the eosinophil count in patients with chronic eosinophilia.

CASE DESCRIPTION

A 59-year-old Ecuadorian man, known to have type 2 diabetes, presented at the emergency department with a 10-day history of asthenia, cough, and progressive dyspnea. He was a former smoker (less than 5 pack-years), had no known allergies, and has resided in Belgium for 7 years. The patient was tachypneic and had a peripheral oxygen saturation of 88% on room air. Bilateral crackles were heard on lung auscultation. Laboratory test showed an elevated white blood cell count of 12,000 per milliliter and a raised C-reactive protein level up to 208 mg/L. Arterial blood gas analysis was compatible with type 1 respiratory insufficiency: partial pressure of carbon dioxide, 32 mm Hg (reference range, 35–45 mm Hg); partial pressure of oxygen, 38 mm Hg

(reference range, >60 mm Hg). Chest radiograph revealed bilateral pulmonary infiltrates, confirmed by computed tomography pulmonary angiogram with exclusion of pulmonary embolism. Real-time polymerase chain reaction test for SARS-CoV-2 was positive, confirming COVID-19.

The patient was admitted to the intensive care unit, where he received high flow nasal oxygen therapy. His condition deteriorated, and he was intubated. Because of persistent hypoxemia while using lung-protective ventilation strategies (including prone ventilation), the decision to commence veno-venous extracorporeal membrane oxygenation was made. A trial of interleukin 1 receptor antagonist therapy (anakinra) and systemic corticosteroids (methylprednisolone 80 mg, tapered over 1 month) was given. Slow improvement was seen.

Forty-nine days after admission, the patient's condition allowed a transfer to the Department of Pulmonary Medicine. Corticosteroids were quickly tapered from a dose of 16 mg to stop over a period of 7 days. Follow-up blood work showed a rising number of blood eosinophils—the highest value being 2670 eosinophils per milliliter. Eosinophilia was absent at initial admission (before start of systemic corticosteroid therapy), during intensive care unit stay, and under treatment with corticosteroids. Review of the patient's medical records revealed chronic eosinophilia in the previous blood test results (Fig. 1). In search of an etiology, serologic testing for *Strongyloides stercoralis* was positive, confirmed by molecular diagnosis of *S. stercoralis* in fresh fecal samples using real-time polymerase chain reaction. Single-dose ivermectin led to a significant decline in eosinophilia after 1 week, after which he was discharged in good health.

DISCUSSION

We presented a case of a patient with chronic eosinophilia for 7 years caused by a chronic *S. stercoralis* infection in which COVID-19 counterbalanced the eosinophilic inflammation, leading to marked eosinopenia. As mentioned before, eosinopenia is a frequently encountered laboratory finding in COVID-19, present in around 50% to 70% of hospitalized patients with COVID-19.^{2,3} To our knowledge, this is the first case in which COVID-19 is responsible for a resolution of chronic eosinophilia. The reason why eosinopenia is observed in COVID-19 is not known to date but is probably multifactorial (inhibition of eosinophilic stimulation, apoptosis by interferon type 1, antiviral effect, etc).⁴

S. stercoralis is a soil-transmitted helminth that has the capability to autoinfect and is associated with different clinical entities: acute strongyloidiasis, chronic (mainly asymptomatic) strongyloidiasis, and *Strongyloides* hyperinfection syndrome (SHS).⁶ People are most frequently infected transcutaneously, from where larvae can migrate via the lungs and bloodstream to the small intestine. With an intact immune system, the host can regulate the population of the adult worms in the intestines. This may lead to chronic infection in which eosinophilia and raised immunoglobulin E levels are frequently encountered.⁶ Although *S. stercoralis* is endemic in the tropics and subtropics, an infection can also occur in other countries. Before moving to Europe in 2013, our patient

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The authors have no funding or conflicts of interest to disclose.

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ISSN: 1056-9103

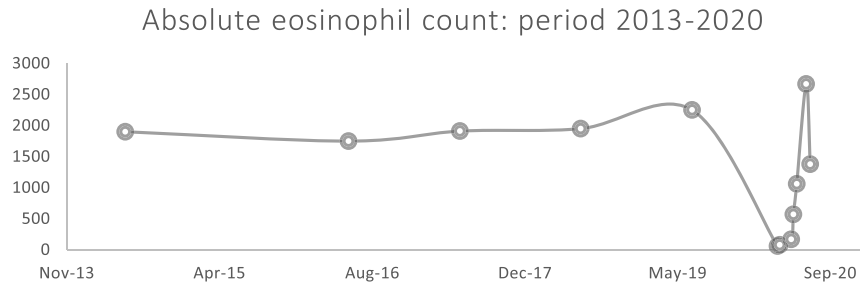


FIGURE 1. Evolution of absolute eosinophil count in the period between 2013 and 2020. Notice the absolute depletion of eosinophils during COVID-19, with rising eosinophils during recovery. Eosinophil count starts to decrease 1 week after treatment with ivermectin.

lived in Ecuador. A recent serological study in 1418 Ecuadorian people showed a seroprevalence of 20.7% in the general population, with a seroprevalence of 66.7% in some regions in Ecuador.⁷

The most serious clinical entity is SHS, which demands a high degree of suspicion in immunosuppressed patients and in patients who are candidates for immunosuppressive treatment.⁸ Geri et al⁹ published a case series of 133 patients with this potentially life-threatening condition caused by a disseminated infection with multiple organ involvement. Most frequent symptoms are fever, gastrointestinal symptoms, and respiratory symptoms including respiratory failure. Eosinophilia was only present in 34% of patients with SHS (in contrast to chronic infection in which eosinophilia is almost always present⁶). One should stay vigilant for other infectious (mainly parasitic) causes of eosinophilia with similar clinical presentation, like *Coccidioides*, *Trichinella*, *Ascaris*, and *Toxocara*. The most important risk factor for the development of SHS is immunosuppressive treatment because this alters the hosts' antiparasitic response. This is mainly the case with chronic corticosteroid treatment, which is often associated with a complete resolution of eosinophilia, but other forms of immunosuppressive treatments have been described.¹⁰ Screening for *S. stercoralis* has been recommended in immunocompetent patients with a high risk of exposure, as well as routinely in all immunosuppressed patients or candidates for immunosuppressive therapy with an increased risk.¹¹ In the latter group, ivermectin—which is still the treatment of choice for chronic strongyloidiasis⁶—should be provided if diagnostic testing is not available. A resolution of eosinophilia can be expected after 4 weeks of treatment.¹² The risk of SHS in patients with COVID-19 is rising, with the emerging use of systemic corticosteroids in these patients since the publication of the preliminary results of the RECOVERY trial¹³ showing a reduced 28-day mortality with the use of dexamethasone in patients receiving invasive mechanical ventilation or oxygen.

We can conclude that our patient had severe COVID-19 in combination with a quiescent chronic *S. stercoralis* infection with chronic eosinophilia for many years. He received high-dose immunosuppressive therapy to counter the cytokine storm described in COVID-19. This could potentially have increased the risk for SHS, but fortunately, our patient did not show any signs of this potentially life-threatening disease. This case illustrates that the presence of eosinophilia, now or in the past, should prompt screening for strongyloidiasis in all patients eligible for immunosuppressive therapy and especially when this treatment is empiric. Because of the COVID-19 pandemic, chronic (asymptomatic) strongyloidiasis and COVID-19 will not infrequently occur together, which can pose difficulties with the emerging use of systemic

corticosteroids—being the most important risk factor for the development of SHS. Finally, the case also confirms previous epidemiological studies in which eosinopenia can be an important feature of COVID-19, even in patients with chronic eosinophilia.

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