CASE REPORT

Chronic strongyloidiasis with recurrent asthma exacerbations and steroid-associated 'hives'

Scott A Weisenberg

Department of Medicine, New York University School of Medicine, New York City, New York, USA

Correspondence to
Dr Scott A Weisenberg,
scottweisenberg@gmail.com

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SUMMARY

A 74-year-old man experienced worsening asthma for several years. Oral steroids were required on multiple occasions for asthma treatment. During his steroid courses, he developed a hive-like rash, which would resolve after completion of each steroid course. He was from Romania, and had lived in the USA for many years. Laboratory testing had shown eosinophilia. He was eventually diagnosed with strongyloidiasis by serology. Treatment with ivermectin led to marked improvement but not resolution of his long-term asthma. His hive-like rash, which was likely larva currens, did not recur with a subsequent steroid course. Improved recognition of strongyloidiasis, particularly in steroid-treated patients, is needed.

BACKGROUND

Strongyloides stercoralis is a geographically widespread¹ soil helminth which causes infection in humans via a complex life cycle. Filariform larvae in soil penetrate skin, migrate through the lungs and other tissues, and develop into adults in the human intestine.² In contrast to most other helminthic infections, autoinfection may occur within the human host, leading to both persistence of infection and clinical disease.

Symptoms of chronic infection reflect the life cycle and can include transient erythematous rashes, pruritus, bronchospasm, weight loss, nausea and diarrhoea.^{3,4} Many patients with chronic infection exhibit no obvious symptoms.² Subsequent immunosuppression including steroid use may lead to life-threatening hyperinfection⁵ and disseminated disease to other organs.

A case of chronic strongyloidiasis associated with worsened asthma, steroid-associated 'hives' is presented to highlight the chronic nature of the disease in some patients, as well as the continued underrecognition of this potentially fatal syndrome.

CASE PRESENTATION

A 74-year-old man presented with worsening asthma over several years. His symptoms included dyspnoea and chest pressure. He required courses of oral prednisone to improve his breathing. He originally developed asthma at age 48.

He also reported new-onset hives in the last few years. Interestingly, his hives only occurred while he was on prednisone. The hives would occur a few days after starting prednisone, then worsen and would gradually resolve after the prednisone

course. Often, the hives had a linear character. When he was later shown a picture of larva currens, he recognised it as his 'hives'.

He did not have fever or other unexplained symptoms. He also noted occasional diarrhoea, but could not say if it was associated with the respiratory symptoms or steroid use.

His laboratory testing had shown an elevated eosinophil count for years. A recent blood test showed an absolute eosinophil count of 1074/ μ L (normal 0–400).

Medical history included adult-onset asthma, gastro-oesophageal reflux, hypertension and history of knee arthroscopy.

He was born in rural Romania where he lived until he was 13. He was later a refugee in Italy.

Two brothers also had adult onset asthma.

Evaluation between episodes showed clear lungs with good air movement. Skin examination did not reveal any rashes.

INVESTIGATIONS

Laboratory investigations showed an absolute eosinophil count of 1074. Aspergillus antibodies were negative, as were Filaria and Toxocara antibodies. *Strongyloides* antibody was positive by a commercial laboratory. Stool ova and parasite testing was negative. Human T-cell lymphotropic virus serology was negative. Immune testing was normal. Pulmonary evaluation for asthma triggers suggested aspiration. Chest imaging did not show persistent infiltrates or masses, though he did have small lung nodules that did not change over time.

DIFFERENTIAL DIAGNOSIS

His combination of steroid-induced larva currens rashes and recurrent asthma made *Strongyloides* extremely likely even before serology.

TREATMENT

He was treated with two doses of ivermectin 200 μ g/kg.

OUTCOME AND FOLLOW-UP

His asthma improved markedly after ivermectin, though he still had mild asthma. His steroid-associated hives did not recur after the course of ivermectin. He was given a course of prednisone a year later in the setting of pneumonia, and did not have any hives or larva currens-like rashes.

Two brothers were subsequently diagnosed with steroid-requiring asthma. Each was diagnosed with

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strongyloidiasis after the case patient, and each improved on ivermectin.

DISCUSSION

Strongyloidiasis is a geographically widespread helminth infection that occurs in tropical, subtropical and some temperate regions. Prevalence is likely underestimated due to difficulties in diagnosis.⁴ Steroid use is a well-recognised risk factor for *Strongyloides* hyperinfection and dissemination in patients with previously asymptomatic or mild clinical disease. These severe clinical syndromes can occur within days of starting steroids, or may occur only after months of steroid treatment. They may even begin days to weeks after completion of steroid treatment.⁶ Acute respiratory symptoms are commonly reported in case

reports of patients with disseminated disease or hyperinfection. These severe cases are often complicated by life-threatening acute respiratory distress syndrome, secondary bacterial pneumonia and pulmonary haemorrhage.⁷

Acute respiratory symptoms from *Strongyloides* may be confused with asthma in individual patients. New-onset asthma, along with worsening of stable asthma and worsening after steroid use, has been ascribed to *Strongyloides*.⁸ Steroids given for asthma or other conditions may worsen respiratory status through hyperinfection⁹ or lead to disseminated disease in other organs.¹⁰

Studies exploring the causative contribution of *Strongyloides* to asthma in at-risk populations have shown mixed results. The presence of *Strongyloides* in stool was not associated with

Patient's perspective

I grew up in a small village in Romania and lived there until I was 13 years old. The children in the village were barefoot all summer, running around in the dirt and the fields. The houses had dirt floors and the sanitation in the village was poor.

When I was in my late 40s, I had a stubborn case of pneumonia. Because my symptoms were mild in the beginning, it took several weeks before I was actually diagnosed and treated. Shortly after this episode, I developed asthma—which I had never had before. I was always a very healthy person, so this was scary and very new to me.

Over my 25+ years of asthma, I was on a rollercoaster with all types of inhalers. Some worked better than others; some did not work at all. I used nebulizers and rinsed my sinuses. I went to numerous allergists, pulmonologists and primary care physicians. I was determined to find out what was the trigger for my adult-onset asthma. My eosinophil level was elevated at five times the normal level, but every skin/allergy test was negative. At one point I even tried eliminating gluten and dairy products. I tried staying away from alcohol. The asthma symptoms were only getting worse and worse.

When an asthma crisis occurred, I had no choice but to take prednisone—sometimes starting with as much as 140 mg. I had to breathe and prednisone was the only thing that worked. By 2015 my asthma was so bad that I was taking a course of prednisone about once each month.

The last few years I noticed that I would get red rashes (I thought they were hives) around my abdomen and back (waist area). At first they would appear 4 days after I started prednisone, but then later they were coming sooner and were much more severe. They itched so badly I could not sleep; I was miserable. I asked the doctors about this, since prednisone is typically used to treat such rashes/hives. The answers were not helpful and varied from, 'that's strange' to 'that sounds paradoxical'.

The quality of my life was really suffering from the cycle of asthma crises, prednisone and then hives. I decided to try a new allergist and asthma specialist. Dr Matthew Loedwick ordered numerous blood tests, one of which was for *Strongyloides*. The blood work came back positive for *Strongyloides* and he advised me to see an infectious disease doctor for a diagnosis and treatment.

In October 2015, I met with Dr Scott Weisenberg. He listened carefully to every part of my history, questioned me thoroughly about my asthma symptoms and 'hives', and ordered additional blood tests. I recall that he showed me computer images of hives and also of larva, and the difference was clear; mine were not hives. Once the lab work reconfirmed the presence of *Strongyloides* he treated me with an aggressive course of ivermectin.

(Note: Also in October 2015, I went to a previously scheduled, thorough work-up at National Jewish Center in Denver because of my drive to find the cause/trigger to my asthma. All tests were negative. 'Challenge test'. Negative. Skin tests. Negative. Impedance test for acid reflux. Negative. Sleep Apnea test. Negative.)

Following the ivermectin treatment, I felt so much better that I thought I was cured of asthma. Although I had to accept that I still have asthma, it is immensely better and is well controlled with inhalers twice each day. The quality of my life is excellent. I am able to eat my regular, healthy diet (including bread and dairy) and enjoy a good glass of wine. Asthma crises are infrequent and I've only had to take prednisone twice in the last year since treatment. (The trigger was pneumonia, but now I know what to do when symptoms begin.) I keep ivermectin on hand and take it concurrently with the prednisone. No rashes. No hives. No itching.

For me, the discovery of strongyloides and the proper treatment led to a complete change in my asthma conditions. At the age of 76, and after 25 years of suffering, I feel like I finally have my life back. Regrettably, the medical professionals (at least the ones I saw prior to Drs Loedwick and Weisenberg) are not current with the fact that strongyloides occur not only in tropical and subtropical areas of the world, but also in Eastern Europe. The test for *Strongyloides* should be standard for all asthma sufferers. I have seen so many doctors, including ones at a leading university, and all they offered was the same old treatment. No one pursued why my eosinophil level was so high without allergies or why 'hives' would occur while taking prednisone. By the way, my eosinophil level is now normal for the first time in nearly three decades.

I not only credit Dr Weisenberg and Dr Loedwick and for saving my life: Two of my brothers developed severe coughing/asthma symptoms in the last 2 years. Each was getting progressively worse, even with taking prednisone. I told them to immediately request testing for *Strongyloides*; they did, and each tested positive. They each were treated with ivermectin and have gotten remarkably better since treatment. One no longer even needs inhalers.

Thank you again to both of these doctors who listened to me, were able to think out-of-the-box about my condition and provide me with the proper treatment.

asthma in an immigrant population, at least using one or more stools as the diagnostic criteria.¹¹ In another stool-based study, *Strongyloides* was found in 12 of 201 Canadian asthmatics, and no controls.¹² Among patients with asthma, the presence of *Strongyloides* is associated with a higher eosinophil count but otherwise similar disease.¹³

Regardless of its contribution to the prevalence of asthma on a population basis, *Strongyloides* may cause an asthma-like syndrome in individual patients. Boulware and colleagues comment on three immigrant patients with asthma-like syndromes who presented to primary care physicians and were treated with steroids. Two of these patients died from hyperinfection syndrome.¹⁴

Fortunately, the case patient never had a life-threatening episode despite his recurrent oral steroid courses. The marked improvement in long-term asthma control strongly suggests that *Strongyloides* was a significant contributing factor to his worsened adult-onset asthma in the years prior to diagnosis. He required a single course of steroids for asthma a year after treatment. He was given an additional treatment of ivermectin, and did not show any evidence of larva currens during that episode.

Despite the improvement in the case patient's asthma control, treatment of *Strongyloides* in patients with asthma does not lead to clinical improvements in some individual patients.^{13 15} Other reported patients have experienced least temporary improvement in individual asthmatic episodes.^{8 16–18} Thus, it appears that *Strongyloides* worsens asthma in some patients, but not in others.

Diagnosis of strongyloidiasis is confirmed by stool testing or serology. Stool testing by routine ova and parasites is relatively insensitive, but yield improves if up to seven stools are analysed. Negative stool tests do not exclude the infection.² Specialised incubation-based stool techniques may be done in experienced laboratories but are not available in most settings. ELISA tests² by commercial laboratories are available, though both false negative (particularly in immunocompromised patients) and false positive (via cross reaction) results may occur.

While retrospective case reports make clear the consequence of unrecognised infection in select patients, the busy individual clinician needs to understand when to consider, diagnosis, or treat *Strongyloides*. Most infected patients will be from tropical and subtropical regions. However, *Strongyloides* has been described in focal areas in the USA¹⁹ and Canada.¹² It is also occurs in Romania²⁰ and elsewhere in Eastern Europe.³ The case patient grew up in Romania, and likely acquired the infection in childhood.

The next question for the clinician is what to do after consideration of diagnosis. It is recommended to test for *Strongyloides* before starting chemotherapy, steroids or other immunosuppressants for at-risk patients.² However, in some clinical scenarios, the decision to start steroids needs to be made without delay. Empirical treatment of at-risk patients who are to receive steroids should be considered.¹⁰

Strongyloidiasis is a disease that all treating clinicians should have familiarity with, particularly if they prescribe steroids or immunosuppressants as part of their practice. Rather than being thought of as an exotic disease, it should be added to the list of imported silent chronic diseases such as tuberculosis and hepatitis B. Knowledge of strongyloidiasis is low in physicians-in-training,¹⁴ and should be improved. As the case patients course shows, recognition and treatment of *Strongyloides* infection can

Learning points

- ▶ Strongyloidiasis should be considered in all patients who will receive steroids or other immunosuppressants.
- ▶ *Strongyloides stercoralis* may contribute to worsened asthma control in some patients.
- ▶ *S. stercoralis* occurs in some non-tropical areas, including Romania.
- ▶ Steroid-associated rashes or hives should raise the possibility of larva currens as a symptom of strongyloidiasis.

lead to clinical improvement and avoid potentially catastrophic consequences of this underappreciated infection.

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