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## CLINICAL VIGNETTE

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# Helminths Infection Presenting as Iron Deficiency Anemia

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### Case

A 53-year-old Filipino male presented to the emergency department with two months of intermittent dizziness and fatigue. He had no chronic illnesses and denied any chest pain, dyspnea, or jaundice. His exertional fatigue was worsening and associated with palpitations. There was a 15 pound weight loss over two months, without change in appetite or diet. The patient denied fevers, chills, cough, night sweats, diarrhea, hematemesis, bright red blood per rectum, or melena. He had no significant family history, specifically no blood dyscrasias, no use of alcohol and no chronic medications. He was originally from the Philippines and formerly worked in the coconut fields. He moved to the United States three years ago. He was initially seen at an outside clinic and told to come to the emergency room for evaluation of anemia.

In the ED the patient was afebrile with stable vital signs. He was in no distress without jaundice, petechiae or ecchymoses. His cardiovascular and pulmonary examinations were benign and his abdomen was soft and non-tender. Labs included hemoglobin of 3.3 g/dL, MCV of 50 and an eosinophilia of 18%. Chemistries included normal electrolytes and renal and liver function. Iron panel was consistent with iron deficiency anemia (iron 11 mcg/dL, transferrin 342 mg/dL, total iron binding capacity 439 mcg/dL, iron saturation 2%, ferritin <3 ng/mL). Vitamin B12, folate, lactate dehydrogenase, and haptoglobin were normal. Hemoglobin electrophoresis was consistent with iron deficiency anemia. Stool was negative for fecal occult blood. The patient was transfused three units of PRBC with repeat hemoglobin of 7.9 g/dL which remained stable above 8.0 g/dL throughout the hospitalization. Given the iron deficiency anemia, weight loss, and age, initial concerns included occult GI bleed or GI malignancy. Repeat CBCs showed persistent, increasing eosinophilia, up to 45% and stool testing for ova and parasites ordered. The first was negative and he was scheduled for outpatient EGD/colonoscopy and additional stool tests for ova and parasites. EGD/colonoscopy showed a sub-centimeter healing antral gastric ulcer, small deep ulcers in the duodenal bulb and a small rectal polyp, which was excised with a normal pathology. No active bleeding was noted. Three stool specimens for ova and parasites returned positive for hookworm and trichuris ova. He was prescribed mebendazole 100mg BID for three days and repeat stool tests for ova/parasites after treatment were negative.

### Discussion

In 2013, iron deficiency anemia affected around 1.2 billion people worldwide.<sup>1</sup> In high income countries, the leading etiologies for iron deficiency anemia include nutritional, such as vegan diets with inadequate intake of iron or pathologic conditions including chronic blood loss or malabsorption. In developing countries, iron deficiency is generally from insufficient dietary intake or chronic blood loss from intestinal worms.<sup>2</sup> Approximately 1.5 billion people globally are infected with soil transmitted helminthes, STH. STH include: Hookworms (*Necator americanus* and *Ancylostoma duodenale*), whipworms *Trichuris trichiura* and roundworms *Ascaris lumbricoides*.<sup>3</sup> This vignette will focus on hookworm infections.

Up to 740 million people globally are infected with hookworms. Infection rates are highest in the tropics and subtropics, especially in coastal regions, where temperature and sandy soils offers optimal conditions for survival and movement.<sup>4</sup> In the United States, hookworm infection was common over a hundred years ago (primarily in the rural South). Recognized as an obstacle for economic development, the Rockefeller Sanitary Commission (later known as the Rockefeller Foundation) was established in 1909 to eradicate hookworm infections.<sup>5</sup> Hookworm infection is strongly tied to socioeconomic and sanitary conditions. The prevalence of hookworm infection in the United States has decreased tremendously, although areas with continued poverty and open sewage still harbor pockets of infection. In 24 households in Lowndes County, Alabama, >40% reported exposure to raw sewage and more than one third of stool samples tested positive for hookworm.<sup>6</sup>

Human Hookworms infections usually begin when the filariform larvae in the environment penetrate the skin and enter the bloodstream. They then travel to the lungs, where they penetrate through the alveolar capillaries, migrate up the bronchi and trachea, over the epiglottis, and then are swallowed. They molt in the small intestine, where they then develop into adults. While in the small intestine, they survive by eating villous tissue and sucking blood through their attachment site in the small intestine. Female worms can start to lay eggs in forty days. The eggs are then passed in the feces and the larvae hatch and develop in the soil. *A. duodenale* adults live an average of one year and three to five years for *N. americanus*.<sup>5</sup>

Signs and symptoms may be present in only 10-30% of patients with high parasite burden. Clinical manifestations of hookworm infection may include dermatitis, pneumonia, abdominal pain, and iron deficiency anemia. Repeated infections can present as a pruritic papular vesicular rash at the point of larval entry, known as “ground itch”.<sup>4</sup> Heavily infected patients may develop a cough as the larvae migrate through the airways. This rarely can lead to pneumonitis that can last for more than a month as the larva continue to migrate out of the lungs.<sup>4</sup> Once in the GI tract, hookworms usually do not cause symptoms, but can be associated with abdominal discomfort.<sup>5</sup>

The most important clinical feature of hookworm infection is iron deficiency anemia. As part of their life cycle, they attach themselves to the intestinal wall and feed off villi and blood. Once they detach and move to a new location, blood loss at the previous site of attachment continues. *A. duodenale* adults can pull 0.1 to 0.2ml of blood per day, while *N. americanus* worms can suck 0.01 to 0.02ml per day. The amount of blood loss is proportional to the number of hookworms present. Signs and symptoms of iron deficiency anemia include pallor, fatigue, exertional dyspnea, and palpitations. In children, this can impair growth and intellectual and cognitive development. In pregnancy, it can lead to prematurity and low birth weight. In the elderly, it can result in congestive heart failure.<sup>5</sup>

Diagnosis of an infection relies on microscopic identification of the eggs in the stool. The different species of hookworm cannot be discerned visually from the eggs, but is done by examining the larvae or adult worms under the microscope. Stool samples will not be useful during the dermal, pulmonary, and early intestinal stages, as it can take from 8-38 weeks after skin penetration for eggs to appear in the feces.<sup>7</sup> A peripheral eosinophilia can also be seen and varies depending on the stage of the infection. In a group of infected volunteers, eosinophilia became apparent after two to three weeks, and peaked at five to nine weeks.<sup>8</sup> Treatment of hookworms consists of benzimidazole drugs, albendazole (400mg once) or mebendazole (100mg BID for three days). Pyrantal pamoate can be used as an alternative.

### Conclusion

While iron deficiency anemia in the United States is usually attributable to causes such as a selective diet and non-infectious gastro-intestinal blood loss, in developing countries, hookworm infection is still a major contributing factor. The prevalence of hookworm infection is heavily tied to poor socioeconomic status, sanitation, and hygiene. With improved socioeconomic conditions in the United States during the 20th century, hookworm infections decreased. But, areas with poor sanitation and sewage management still pose a public health risk for soil transmitted helminthes. Patients with iron deficiency anemia should be evaluated for parasitic infections if they are from an endemic country or have poor sewage sanitation, especially if evaluation for other causes of iron deficiency anemia are negative. Serial stool testing for O & P may be needed, until PCR assays become commercially available.

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