Case Report: Hepatic Fascioliasis in a Young Afghani Woman with Severe Wheezing, High-Grade Peripheral Eosinophilia, and Liver Lesions: A Brief Literature Review

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Abstract. A 23-year-old recent emigrant from Afghanistan presented in August 2017 with severe wheezing and dyspnea that required hospital admission. Her illness was associated with marked peripheral blood eosinophilia (9,900–15,600/ μ L; 45.2–68%), as well as mild nausea, epigastric pain, and decreased appetite. She had lived until 3 months earlier in close proximity to cattle in her home in Kabul and did not recall eating watercress or other leafy plants associated with *Fasciola hepatica* transmission. Computerized tomography scanning showed bilateral ground-glass lung consolidations and multiple distinctive hypo-attenuating linear, tubuliform, and nodular liver lesions, including a large subcapsular hematoma. Numerous tests for rheumatological and malignant disorders were negative. *Fasciola hepatica* infestation was suspected on epidemiological, clinical, and radiographic grounds, and was confirmed by immunoblotting at the Centers for Disease Control (CDC). Multiple stool ova and parasite examinations were negative and endoscopic retrograde cholangiopancreatography did not identify trematodes. Her acute respiratory illness resolved with asthma-targeted therapies and her eosinophilia resolved with triclabendazole, which was obtained from CDC via an FDA Investigational New Drug application. Fascioliasis is uncommon in the United States, but the prolonged warfare and civil strife in Afghanistan and adjacent areas may lead to increased incidence outside the endemic region. Her case also demonstrates how hepatic imaging features of fascioliasis can be pathognomonic in clinical scenarios with eosinophilia and appropriate epidemiology and clinical features. We also highlight her relatively unusual presentation with symptoms of Loeffler-like syndrome alone.

CASE DESCRIPTION

A 23-year-old Pashto-speaking Afghani woman presented to the University of Colorado Hospital emergency department (ED) in November 2017 with 1 week of progressive shortness of breath, severe wheezing, dry cough, and chest tightness. Less prominent were mild myalgias, nausea, epigastric pain, and decreased appetite. She denied fevers, chills, jaundice, genitourinary symptoms, skin rash, localized swelling, or weight loss. She and her husband had moved from the Kabul region to Denver 4 months before presentation. In Afghanistan, the family housed cattle and sheep in rooms connected with the family living quarters. Their diet consisted of locally sourced vegetables, fruit, beef, lamb, chicken, and goat, but not fish or crustaceans. When queried via Pashto translators assisted with images of watercress, the patient and her husband did not recall eating this or other leafy plants growing in contact with standing water. Her husband and two small children were well. She had not traveled from Denver since arrival in the United States.

The patient reported at least four previous episodes of wheezing and shortness of breath in the past 2 years but was never treated for asthma. Two months earlier, evaluation by her primary care provider revealed major peripheral blood eosinophilia ranging (9,900–15,600/ μ L; 45.2–68%). She was asymptomatic at the time. Three stool examinations were negative for ova and parasites. She also tested negative for *Schistosoma*, *Strongyloides*, and *Toxocara* serum antibodies and a *Mycobacterium tuberculosis* interferon gamma release assay was nonreactive. Tests for autoimmune disorders were negative, specifically ANA, anti-DS-DNA, c-ANCA, p-ANCA, Sjogren's syndrome, anti-N-RNP, Smith IgG, anti-centromere.

A fluorescence in-situ hybridization test was negative for genetic rearrangements associated with hyper-eosinophilic syndrome and eosinophilic leukemia.

In the ED, she was afebrile. She did not have wasting or appear chronically ill. She required 2 L/minute of oxygen via nasal cannula. She was tachypneic and tachycardic, and auscultation disclosed prominent expiratory wheezing. The liver edge was not palpable. The physical examination was otherwise unremarkable.

Blood testing revealed an elevated WBC of 21,800/ μ L with high-grade eosinophilia (9,900/ μ L; 45%). There was minimal alkaline phosphatase elevation and the bilirubin, transaminases, and serum creatinine levels were normal. Multiplex upper respiratory PCR was negative for multiple viruses, as well as pertussis, Chlamydia, and Mycoplasma. HIV-1/2, urine Legionella, and Streptococcus antigen testing were also negative. Blood cultures, serum levels of *Aspergillus* spp. IgE allergen, *Aspergillus fumigatus* IgG, and *Aspergillus* galactomannan were negative.

A chest X-ray showed diffuse bronchial wall thickening without lung opacities. Computerized tomography (CT) of the chest, abdomen, and pelvis revealed bilateral upper lobe ground-glass consolidations (Figure 1A) and multiple distinctive hypo-attenuating linear, tubuliform, and nodular liver lesions (Figure 2A and B). A large hepatic subcapsular hematoma was noted (Figure 2). After treatment with corticosteroids, nebulized albuterol, and ipratropium, the patient's wheezing, shortness of breath, and eosinophilia temporarily improved, and the pulmonary infiltrates later resolved as assessed by a 10-day follow-up CT scan (Figure 1B).

The Infectious Disease service was consulted. The epidemiology, history, lung infiltrates, and distinctive liver imaging, as well as the degree of eosinophilia, focused our investigation on suspicion for helminths, and in particular fascioliasis, which is endemic in the Central Asian region that spans Iran, Afghanistan, and Pakistan,^{1–4} but can be found worldwide.^{2,5,6} Endoscopic retrograde cholangiopancreatography with bile duct aspiration

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FIGURE 1. Axial computerized tomography chest (A) demonstrating bilateral upper lobe ground-glass consolidations which resolved on a 10-day follow-up scan (B) after corticosteroid treatment.

was negative for trematodes or other helminths, ova, and parasites. The glutathione S-transferase (GST)-FhSAP2 recombinant antigen-based Western blot currently used by the Centers for Disease Control (CDC) to detect *Fasciola hepatica* total IgG and IgG4 antibodies was positive. The sensitivity and specificity of GST-FhSAP2 total IgG and IgG4 WB are similar at 94% and 98%, respectively.⁷ The optimal treatment for fascioliasis, triclabendazole,^{2,3,8–10} was requested through the FDA under an Investigational New Drug (IND) application and was then supplied by the CDC. Forty-five days after her ED presentation, the patient received treatment with two postprandial 750-mg doses (~10 mg/kg of body weight per dose). The doses were spaced 24 hours apart.⁸ At follow-up 6 weeks later, she reported complete symptom resolution. Her leukocytes had decreased to 7,500/ μ L from 16 to 20,000/ μ L and her eosinophils fell to 1,700/ μ L (23%) from 9,800/ μ L (45%). Three months later, further improvement in peripheral eosinophils was observed (800/ μ L; 9%). Screening of immediate family members for eosinophilia and stool ova and parasites is planned.

DISCUSSION

Respiratory symptoms in parasitic diseases may involve several mechanisms, including direct bronchopulmonary invasion (e.g., in paragonimiasis), transient bronchopulmonary migration of helminths (e.g., Loeffler's syndrome as with *Ascaris lumbricoides* or *Strongyloides stercoralis*), and, as is most likely in the present case of fascioliasis with symmetric CT-demonstrated ground-glass lung infiltrates, eosinophilia-associated hypersensitivity without parasite presence in the lung.^{11,12} Ectopic fascioliasis of the lung, with demonstrated

eggs in bronchial lavage, has been reported.¹³ The distinctive CT imaging findings in the liver, especially subcapsular hematoma, suggested fascioliasis as well.^{10,14,15} The patient was treated successfully with triclabendazole. This agent is preferred, as it is the only one known to kill both early and mature forms of this helminth, although resistance has been reported.¹⁶ In addition, unlike in Europe, triclabendazole is not currently FDA approved, which can lead to delays in treatment as the FDA IND approval process is pursued case by case.

Fasciola hepatica occurs predominantly in temperate climates where domesticated ungulates are raised. Afghanistan and the neighboring countries are high-prevalence areas, but worldwide acquisition including autochthonous transmission in the United States has been reported.^{1,2} There is a heavy presence in Andean countries such as Peru and Bolivia.^{6,10,17} Host species include sheep and cattle as definitive hosts, but other ungulates and rodents can also be infected. Snails are the intermediate hosts and humans can be infected by ingesting infected water or freshwater plants such as watercress that harbor encysted metacercariae.^{1,2,5,6} After the eggs are released into the environment with feces, they hatch out as miracidia, which invade the integument of snails. There, the parasites undergo several developmental stages, until cercariae are released. The cercariae then encyst as metacercariae on aquatic vegetation. After metacercariae are ingested by humans, they excyst in the duodenum and penetrate the intestinal wall, peritoneum, and liver parenchyma until they enter the biliary ducts where they mature into adult worms.^{2,5,6} Clinical manifestations include a transient liver phase, typically 6–12 weeks after ingestion, with fever, pain, hepatomegaly, jaundice, anorexia, nausea, vomiting, myalgia,

FIGURE 2. Post-contrast axial (A) and coronal (B) computerized tomography scan shows characteristic subcapsular hematoma (arrow) along with tortuous, hypo-attenuating tracts and nodules.

cough, and urticaria. Marked eosinophilia is almost always present. This phase can be complicated by hemobilia, and the distinctive subcapsular hematoma, and tubuliform tracts in the liver as we observed are consistent with this. There are also extrahepatic manifestations such as the Loeffler-like syndrome in this patient. Acute symptoms typically resolve within 2–3 months. A chronic biliary phase typically begins several months after ingestion and is often asymptomatic, although severe hepatobiliary sequelae can occur. It is important to emphasize that in the setting of significant eosinophilia and appropriate epidemiology, CT imaging of the liver can be nearly pathognomonic.^{10,14,15}

Warfare and civil strife in Afghanistan and the adjacent regions have potential to generate more imported cases of this disease. Easier access to *Fasciola* serology testing when supported by clinical evidence and characteristic liver imaging, as well as prompt ID consultation, could obviate costly, unnecessary other testing, such as those that our patient received (e.g., molecular probes for eosinophilic leukemia). Subcapsular hematomas along with tortuous or tubuliform, hypo-attenuating, and frequently subcapsular tracts occasionally coalescing into irregular nodules are the most characteristic features pointing toward hepatic fascioliasis.^{10,14,15}

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