

An unexpected parasitic cause of hypereosinophilia: fascioliasis

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A six-year-old boy from Eastern Anatolia was admitted to our outpatient clinic with abdominal pain and hyperleukocytosis. His leukocyte count was $50 \times 10^9/L$ with an 80% eosinophilia. Serological investigation was positive at a titration of 1/2560 for *Fasciola hepatica*. Hepatomegaly with linear hypoechogenic strains, which is typical for *F. hepatica*, was seen on abdominal ultrasonography. He was successfully treated with triclabendazole, 10 mg/kg/day. He is now under follow-up without any complaints. Hypereosinophilia mimicking leukemia is not an expected finding. To our best knowledge, high leukocyte count with *F. hepatica* in a child has not been reported in the literature until now.

Key words: *Fasciola hepatica*, hypereosinophilia, hyperleukocytosis.

Eosinophilic leukocytosis may develop due to parasitic infections, allergic disorders, drug reactions, immunodeficiency syndromes, and connective tissue diseases. Allergy is the most common cause of eosinophilia in children, for example in the United States¹. However, parasitic infections, which are frequently observed in Anatolia, are the leading cause of hypereosinophilia in Turkey². *Fasciola hepatica* is known to be a rare parasite causing hypereosinophilia, especially in childhood³.

We report herein a six-year-old boy with eosinophilic leukocytosis who was infected by *F. hepatica*.

Case Report

A six-year-old boy presented with a complaint of abdominal pain for one week. He had been evaluated in a local hospital initially and was referred to our center with the presumptive diagnosis of leukemia based on leukocytosis. His grandfather and uncles were livestock-breeders. It was learned that he enjoyed swimming in a nearby lake. No similar complaints were detected in other family members.

He had no recent fever, diarrhea or weight loss. No pallor, icterus, petechia, or ecchymoses was

observed on physical examination. His body temperature, heart rate and blood pressure were appropriate for his age. On abdominal examination, hepatomegaly and splenomegaly were present at 3 cm and 1 cm below the costal margins on the midclavicular line, respectively. Lymphadenopathy was not present.

Complete blood count showed hemoglobin: 15.6 g/dl, leukocyte: $50.6 \times 10^9/L$ and platelet: $347 \times 10^9/L$. Peripheral blood smear revealed 80% eosinophilia, 16% neutrophils and 4% lymphocytes without any blasts. Hepatic and renal function tests were all normal. Serum lactate dehydrogenase level was 618 IU/L. No atypical cells were detected in the bone marrow aspirate evaluated by direct microscopy and flow cytometric studies. Analysis of RNA did not demonstrate FIP1-like-1/platelet-derived growth factor alpha fusion gene.

Auto-antibodies related to connective tissue disorders, including anti-nuclear antibody, anti-dsDNA, rheumatoid factor, p-ANCA, and c-ANCA, were all negative. Serum vitamin B12 and folic acid levels were 668 pg/ml and 5.94 pg/ml, respectively. Hypergammaglobulinemia was noted. Serum immunoglobulin (Ig)E, IgG and IgM levels were 1648 IU/ml, 2690 mg/dl and 312 mg/dl, respectively.

Echocardiographic investigation revealed normal endomyocardial thickness and systolic functions. Epidermal prick tests for house dust mite (*Dermatophagoides farinae*, *D. pteronyssinus*), pollen, molds, cockroach, cat, dog, and food were all negative. Stool examination for parasitic egg was negative twice.

Serological analyses by ELISA for *Toxocara canis*, *Trichinella spiralis* and *Echinococcus granulosus* were negative. No egg of *Ascaris lumbricoides* was detected in the stool, but a test by indirect hemagglutination (IHA) revealed positivity for *F. hepatica* at a titration of 1/2560. Moreover, abdominal ultrasonography showed hepatomegaly with linear hypoechogenic strains typical for the diagnosis of *F. hepatica* infection⁴. Doppler ultrasonography revealed splenic enlargement and increase in portal venous pressure.

Low-dose steroid therapy was initiated and continued for two days in order to prevent the complications of the leukocytosis. When the serological analysis revealed positive result for *F. hepatica*, steroid therapy was ceased and leukocyte count was decreased to $36.9 \times 10^9/L$. Triclabendazole treatment was started at the dose of 10 mg/kg. The drug was given as a single oral dose.

Discussion

The leading causes of eosinophilia, described as eosinophil count above $500/mm^3$, may change in different populations and regions of the world. In Turkey, allergic disorders are the major cause in large cities, whereas parasitic infections are more common in rural areas². Repetitive and prolonged antigen exposure to T lymphocytes by parasites is the cause of eosinophilic stimulation. T cells produce interleukin (IL)-5, IL-4 and IL-13, which stimulate proliferation and survival of eosinophils^{5,6}. Infections by certain parasites such as helminths cause greater degrees of eosinophilia than do others. Tissue granulomatous response to parasites is responsible for eosinophilia rather than the parasite itself. Thus, other parasites that do not reach the systemic circulation, such as *Giardia lamblia*, *Enterobius vermicularis* and *Trichuris trichiura*, do not cause eosinophilia. Repetitive stool analysis should be performed in the cases of eosinophilia, especially in those with suspected history, such as travel to tropical regions and rural lifestyle.

Fasciola hepatica is a trematode known as sheep liver fluke. Humans are incidental hosts. Although one-half of the patients are asymptomatic, fascioliasis is characterized usually by fever, eosinophilia and abdominal pain. According to the World Health Organization, more than 180 million people are at risk for *F. hepatica* infection and 2.4 million people are already infected by this parasite⁷. Risk factors for fascioliasis are ingestion of aquatic plants such as watercress, dog ownership and living in cattle- and sheep-breeding regions⁸. Our patient had all three of these risk factors. Laboratory studies generally demonstrate anemia and leukocytosis, but hyperleukocytosis ($>50 \times 10^9$) is very rare. In patients with eosinophilia, evaluation of past and present history in detail is of paramount importance in the diagnosis. In fact, it may decrease the requirement of laboratory studies.

Eosinophilia occurring in 14-82% of patients with *F. hepatica* may wax and wane during the chronic stage of infection⁹. Ig levels may be elevated, especially IgG and IgE, as observed in our patient. Ectopic presentation of *F. hepatica* may be seen rarely in different organs like the brain, eye and pancreas^{10,11}.

In the diagnosis, stool examination alone may not be enough for the diagnosis. In our case, detailed stool examination did not show any parasite or its eggs, whereas serologic examination by IHA yielded positive result for *F. hepatica* at Refik Saydam Hygiene Institute. Thus, in suspected patients, both stool and serological examination should be performed at the same time to establish the diagnosis.

In parasitic infections, mild to moderate eosinophilia is usually seen. However, hypereosinophilia mimicking leukemia is not an expected finding. In a previous study, leukocyte count range was recorded between $3.3 \times 10^9 - 16.1 \times 10^9/mm^3$ in patients infected by two parasites¹². In an other study, including 40 children with *F. hepatica* from Egypt, the eosinophil count was reported between 0.9 - $21 \times 10^3/mm^3$ ¹³. Prominent eosinophilia is usually recorded in patients with toxocariasis¹⁴. In our patient, leukocyte count was over $50 \times 10^9/L$ with 80% eosinophilia. We gave 0.5 mg/kg methylprednisolone treatment until the results of the parasitological analysis were obtained

because of the high risk of thromboembolic events caused by high leukocyte count. On the second day of the treatment, leukocyte count decreased to $36.9 \times 10^9/L$, and serological analysis for *F. hepatica* was found positive. Triclabendazole was started for the treatment and the steroid was stopped¹⁵. The symptoms disappeared and laboratory findings resolved after the treatment.

Fascioliasis can be prevented with public education and environmental precautions such as avoiding consumption of contaminated water and plants. Prognosis is excellent with appropriate treatment.

To our best knowledge, high leukocyte count with *F. hepatica* in a child has not been reported in the literature until now. Health care providers should keep in mind that *F. hepatica* can present with eosinophilic leukocytosis.

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