Severe iron deficiency anemia and marked eosinophilia in adolescent girls with the diagnosis of human fascioliasis

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Human fascioliasis (HF), caused by the common liver fluke *Fasciola hepatica*, is an endemic infection in many parts of tropical countries. HF can also be seen in some of the non-tropical countries. This report describes two girls with severe iron deficiency anemia and eosinophilia, who were diagnosed as HF. The infection was successfully eliminated with the administration of triclabendazole. No side effects or recurrence was observed after the treatment. It should be kept in mind that marked eosinophilia with severe iron deficiency anemia should alert pediatricians to the possibility of *F. hepatica* infection.

Key words: Fasciola hepatica, iron deficiency anemia, eosinophilia, children.

Human fascioliasis (HF) is a parasitic disease caused by the fluke *Fasciola hepatica*. Generally, the disease is acquired by eating watercress or other vegetables or by drinking water contaminated with metacercariae. After ingestion of metacercariae, the larva penetrates through the gut wall into the peritoneal cavity, and passes into the liver through its capsule. In acute infection, fever and abdominal pain are common symptoms. After a few months, the young flukes migrate to the bile ducts, where they mature and begin to produce eggs. They may persist in the bile ducts for many years, resulting in the chronic stage of HF[1,2]. Human fascioliasis is a serious health problem in many tropical countries, whereas this infection has been reported rarely from the central and western regions of Turkey[3-6]. Two adolescent girls (10 and 14 years of age) who admitted to our hospital with severe iron deficiency anemia (IDA) and marked eosinophilia and were diagnosed as HF are presented in this report.

Case Reports

Case 1

A 10-year-old girl admitted to our hospital with the complaints of malaise and paleness for more than two months; however, the main reason for application to the hospital was fever for the last two days. On her physical examination, facial paleness and fine basilar crackles on her lungs were noted. Her laboratory studies revealed the following: hemoglobin (Hb) 4.8 g/dl; hematocrit (Htc) 14%; white blood cell (WBC) count 3100/mm^3 with 22% neutrophils, 48% lymphocytes, 10% monocytes, 20% eosinophils, and hypochromic-microcytic erythrocytes; mean corpuscular volume (MCV) 65 fL; red cell distribution width (RDW) 19%; platelet (Plt) count 155000/mm^3; and reticulocytes 0.8%. Biochemical parameters, direct and indirect Coombs' tests, and guaiac test of the stool were all negative. Serum iron (SI) level was 16 μmol/L, serum iron binding capacity (SIBC) 381 μmol/L, transferrin saturation (TS) 4.2%, ferritin level 1.5 ng/ml, vitamin B_{12} level 306 pg/ml, and folate level 11.6 ng/ml. Parasitic investigations were performed in blood and stool due to the high levels of eosinophilia observed in peripheral blood smears. No eggs or cysts were detected in formalin-fixed stool samples, whereas antibodies against *F. hepatica* by enzyme-linked immunosorbent assay (ELISA) with an optical density (OD) of 1.5 (cut-off B/0.3) and by immunofluorescence assay (IFA) titer of 1:320 (cut-off B/1:160) were detected positively in serum samples. Her immunoglobulin levels were not increased. Her abdominal ultrasonography and computerized

tomography (CT) were normal. Her chest radiography revealed bilateral infiltration. Thus, she was diagnosed as severe IDA, HF, and pulmonary infection. The patient was treated with oral triclabendazole (Egaten; Novartis, Switzerland) at a dosage of 10 mg/kg/dose, twice a day, for one day. The same dosage of triclabendazole was repeated after one week. Furthermore, iron (6 mg/kg/day; 3 months) and ampicillin sulbactam (50 mg/kg/dose, 3 times a day; 14 days) were given for IDA and pulmonary infection, respectively. She did not need transfusion, because she did not have any symptoms suggestive of heart failure. During the following weeks, her clinical condition improved, and she was discharged from the hospital two weeks later. Her eosinophil count had decreased to normal levels within two months. She has been followed for more than one year, and no recurrence was observed in this patient.

Case 2

A 14-year-old girl admitted to our hospital with the complaints of malaise, paleness, and headache lasting for one week. On her physical examination, paleness and hepatomegaly 2 cm below the coastal margin were noted. Her laboratory studies revealed: Hb 7.1 g/dl; Htc 22%; WBC count 12000/mm^3 with 20% neutrophils, 24% lymphocytes, 6% monocytes, 50% eosinophils, and hypochromic-microcytic erythrocytes; MCV 58 fL; RDW 19%; Plt count 689000/mm^3; and reticulocytes 1.2%. Biochemical parameters, direct and indirect Coombs' tests, and guaiac test of the stool were all negative. Her immunoglobulin levels were within normal range. SI level was 12 μmol/L, SIBC 473 μmol/L, TS 2.5%, ferritin level 1.5 ng/ml, vitamin B_{12} level 288 pg/ml, and folate level 5.1 ng/ml. Parasitic investigations were performed in the blood and stool due to the high levels of eosinophilia. No eggs or cysts were detected in formalin-fixed stool samples, whereas antibodies against *F. hepatica* by ELISA with an OD of 1.8 and by IFA titer of 1:640 were detected in serum samples. Her abdominal ultrasonography revealed hepatomegaly and multiple, ovoid-shaped, 15x5 mm in diameter lymphadenopathies in the hepatic hilus. Her abdominal and thorax CT were normal. She was diagnosed as severe IDA and HF. The patient was treated with oral triclabendazole (Egaten; Novartis, Switzerland) at a dosage of 10 mg/kg/dose, twice a day. The same dosage was repeated after one week. Iron (6 mg/kg/day; 3 months) was also given for IDA. During the following weeks, she recovered promptly and was discharged from the hospital within one week. Her eosinophil count had decreased to normal levels within two months. She was followed for more than one year, and no recurrence was observed over this period.

Discussion

In this report, we present our experience in obtaining a better understanding of the current characteristics of HF infection and to identify the clinical pictures in which it should be suspected. Both of our patients were in the chronic phase of the infection because, other than marked eosinophilia, they did not have any symptoms, including no fever, urticaria, pain in the right hypochondrium, hepatitis, or hypergammaglobulinemia. Only one of our patients had mild hepatomegaly, though she had no fever or pain in the right hypochondrium. Both of our patients had marked eosinophilia. We are lucky that our patients did not develop either cholangitis or cholestasis, which might be seen during the chronic stage course of the infection.

Stool examination and ELISA can be used for the initial diagnosis of HF. Radiographic techniques including CT and ultrasonography, as well as magnetic resonance imaging are widely used for confirmation and follow-up of the disease. Invasive techniques, such as percutaneous cholangiography, endoscopic retrograde cholangiography, and liver biopsy may aid in the confirmation of the diagnosis but are not essential[7]. We used ELISA and IFA tests to diagnose HF in our patients. No eggs or cysts were detected in their stool samples. Radiologic imaging techniques were also used in our patients, though only lymphadenopathies and hepatomegaly were detected in one of the patients.

A study performed by Salem et al.[8] from Egypt showed that patients with chronic fascioliasis presented significant reduction in their Hb, Htc, mean corpuscular hemoglobin concentration (MCHC), SI, and TS levels when compared to those of the controls. The young fluke causes hemorrhage during their migration to the liver and within the liver. They may persist in the

bile ducts for many years in patients with chronic HF. Blood loss within the bile duct was suggested as a contributing factor for the development of IDA. Poor appetite and decreased iron uptake are also contributing factors for IDA in patients with chronic HF[8]. Thus, we considered that chronic HF was the cause of severe IDA seen in both our patients.

The treatment of HF has greatly improved in recent years, in contrast to other trematode infections requiring high or multiple doses of drugs with significant side effects. The failure of praziquantel in the treatment of HF has been reported by many authors[9,10]. Triclabendazole is a novel anti-helminthic and highly effective drug against adult and immature shapes of *F. hepatica* in sheep and cattle. It is regarded as the drug of choice for the treatment of HF[11,12]. Our patients with HF were also treated successfully with triclabendazole at a dosage of 10 mg/kg/dose, two doses per day, for one day. The same dosage was repeated after one week to prevent recurrence of the infection.

Human fascioliasis (HF) is a serious health problem in many countries; there are significant numbers of patients in Eastern Europe, Iran, Northern Africa, and South America[13]. However, the exact prevalence in Turkey is not known. The prevalence of HF was 1.8-2.7% in the eastern region of our country; however, there is no study about the prevalence of HF in the central and western regions. We found only one Turkish literature about the prevalence of HF, reported from İstanbul, the largest city in Turkey. According to this literature, a total of 27,664 stool samples from patients with suspicious intestinal parasitic infections admitted to İstanbul University between January 1999 and December 2009 were examined for intestinal parasites, and only one sample was found to be positive for *F. hepatica*. On the other hand, we expect that the exact incidence of HF in Turkey is higher than expected. To determine the exact prevalence of the disease, extensive serological investigations should be performed in different regions of Turkey[3-6].

In conclusion, all physicians, and especially pediatricians, should be familiar with the manifestation of HF to diagnose and treat the disease appropriately. It should be kept in mind that marked eosinophilia with severe IDA should alert the clinician to the possibility of *F. hepatica* infection. Triclabendazole is an effective, well-tolerated, easy to administer drug that should be considered in the treatment of HF.

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