□ SHORT COMMUNICATION □

Serologically Diagnosed Toxocariasis with Hemophagocytic Syndrome in a Patient with Primary Biliary Cirrhosis

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Hemophagocytic syndrome (HPS) is a clinicopathological condition characterized by activation of macrophages or histiocytes with prominent hemophagocytosis in bone marrow and other reticuloendothelial systems (1). The clinical features include high fever, hepatosplenomegaly, lymphadenopathy, skin rash, coagulopathy, and cytopenia. Herein, we report a case of serologically diagnosed toxocariasis with manifestations similar to HPS lacking cytopenia. Although larvae were not found in the visceral organs by autopsy, visceral larva migrans (VLM) was strongly suspected based on the distinctly positive results in enzyme-linked immunosorbent assays (ELISAs) for *Toxocara (T.) canis*.

A 51-year-old man was diagnosed with primary biliary cirrhosis (PBC) (Scheur stage III) in 1995 based on symptoms (itching), biochemical data, and liver histology findings. The father of this patient was also diagnosed with asymptomatic PBC, and both cases were previously reported as PBC in a father and son (2). Since the time of that first study, the patient had been treated with ursodeoxycholic acid alone. Although endoscopic treatment was required for ruptures of esophageal varices, the patient remained in a stable compensated condition until the beginning of January 2005, when he developed a skin rash, fever, severe fatigue, and deteriorated liver function with ascites retention. At that time, laboratory data revealed prominent leukocytosis (WBC $25 \times 10^3/\mu\text{l}$, Hb 12.7 g/dl, Plt $12 \times 10^4/\mu\text{l}$) with marked eosinophilia (>80%) and elevated IgE (2100 U/ml, normal 0 less than 100 U/ml), while the ascites was found to contain a considerable number of eosinophils. A thoracic-abdominal

CT examination showed hepatosplenomegaly and lymphadenopathy in the para-tracheal and para-aortic areas. Bone marrow aspiration demonstrated an increase in eosinophils, but no malignant cells. Following serological screening for parasitoses using a multiple dot ELISA, toxocariasis was suspected, and a microplate ELISA assay against *T. canis* excretory-secretory antigens revealed a markedly high antibody titer in 1:900 diluted serum [optical density (O.D.) > 0.9, threshold O.D. 0.2]. Seropositivity against *T. canis* was further confirmed using a microplate ELISA with a recombinant *T. canis* antigen (3), which is highly specific for toxocariasis. A serum sample taken prior to development of the manifested symptoms and eosinophilia was unavailable, and the route of *T. canis* infection such as daily contact with dogs was not determined. Based on the marked seropositivity against *T. canis* shown in 3 different ELISAs, we made a diagnosis of infection with *T. canis*.

Prior to the introduction of antihelminthic therapy, the patient died of multiple complications, including pneumonia and disseminated intravascular coagulation, in February 2005. Autopsy results confirmed lymphadenopathy in the mediastinum and peritoneal cavity. Further, a histological examination showed hemophagocytic foamy cells in the lymph nodes (Fig. 1A, B) and bone marrow (Fig. 1C), though no neoplastic cells were observed. Erythrophagocytosis was also observed in Kupffer cells in the liver (Fig. 1D). Histological evidence of VLM such as the presence of larvae or eosinophilic granulomas could not be demonstrated in the visceral organs.

Toxocariasis presents various manifestations including multiple hepatic nodules, eosinophilic pneumonia, systemic vasculitis, and rheumatic arthritis-like symptoms. However, there is no known description regarding the development of HPS in toxocariasis. HPS is known to be associated with infections, mostly viral, as well as malignancy and autoimmune diseases. Although no specific viral infection, including cytomegalovirus and Epstein-Barr virus, or malignant cells were demonstrated in the present case, the possible role of underlying PBC could not be eliminated in the development of the HPS-like condition with eosinophilia in the present patient. Finkielman et al. (4) reported a case of HPS that developed in a patient with systemic lupus erythematosus complicated with strongyloidiasis. Since helminthiasis is known to affect the host immune system by activating T-helper 2 cell responses and macrophages (5), HPS might

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Figure 1. Microscopic examination of the para-tracheal lymphnode (A, B), bone marrow (C) and liver (D) (HE stain $\times 200$). Foamy cells with hemophagocytosis were prominently present in the lymph node (A, B). They were also found in the bone marrow (C, arrow). Kupffer cells phagocytosing erythrocytes in the liver were found in D (arrows).

result from a combination of autoimmune diseases and helminthiasis.

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