Chronic Eosinophilic Pneumonia Due to Visceral Larva Migrans

Koji Inoue, Yoshikazu Inoue, Toru Arai, Yukifumi Nawa*, Yozo Kashiwa, Satoru Yamamoto and Mitsunori Sakatani

Abstract

A 38-year-old woman presented with worsening cough, blood eosinophilia, and pulmonary infiltrates. Bronchoalveolar lavage showed 96.4% eosinophils. The diagnosis of visceral larva migrans (VLM) was made based on the positive results in enzyme-linked immunosorbent assay for Toxocara canis together with clinical symptoms and laboratory data. Pulmonary infiltrates due to VLM generally manifest as a transient form of Löffler’s syndrome or simple eosinophilic pneumonia mainly in children. Here we report an adult case of VLM, with pulmonary infiltrates pathologically proven to be eosinophilic pneumonia, which persisted for 7 weeks before anthelmintic treatment with albendazole and manifested as chronic eosinophilic pneumonia.

Introduction

"Visceral Larva migrans" (VLM) is a term described by Beaver et al in 1952 (1). VLM results mainly from infestation by the common roundworms of dogs and cats, Toxocara canis (T. canis) and T. cati, respectively. A large proportion of dogs are infected, and the soil of public playgrounds is often contaminated with eggs of Toxocara. VLM occurs in all temperate and tropical areas of the world; it is found predominately in children since they frequently play with dogs or cats and sometimes eat with contaminated hands after playing in the sandbox of a public playground. VLM can also occur in adults although their route of infection remains unclear.

VLM begins by ingesting embryonated Toxocara eggs. The larvae which hatch from the eggs in the intestine invade into the intestinal wall and disseminate via the portal blood stream to the liver, and then to various organs, including the brain, heart, and lungs. Lung involvement is common and manifests as pulmonary infiltrates. Their presumptive mechanism is an allergic response to the larva in the lungs; eosinophilic infiltrates into the lungs. Most larvae seem able to remain dormant for many years. Eventually some larvae are encapsulated and destroyed by a host response, while others are seemingly protected by being walled off (2). Since humans are not suitable hosts for Toxocara larvae, they are unable to reach the intestine to lay eggs. Therefore, as the definition, the eggs or the mature adults are never seen in VLM. The definite diagnosis of VLM can be made only by proving the larvae. However, this means of the diagnosis is considerably unrealistic since the larvae are only 0.02 mm which is small a size to be obtained from extensive pulmonary infiltrates or other affected organs. For that reason, practically, the clinical diagnosis has been made by enzyme-linked immunosorbent assay (ELISA) using an antigen of T. canis. This method has been reported to have a 78% sensitivity and 92% specificity (3).

Pulmonary infiltrates due to VLM generally manifest as a transient form of Löffler’s syndrome (4) or simple eosinophilic pneumonia (5), and also have been reported to present as an acute form (6). And their histopathological changes may be eosinophilic pneumonia. This has been, however, little proven in the literature. Here we report an adult case of VLM, with pulmonary infiltrates histopathologically proven to be eosinophilic pneumonia, which did not make a spontaneous resolution within 1 month, persisted for 7 weeks before treatment, and manifested as chronic eosinophilic pneumonia (7).

Case Report

A 38-year-old woman had had non-productive cough for 5 months and went to another hospital on December 5, 2000. A radiograph of the chest showed small pulmonary infiltrates in the right upper field. Codein was administered. She was admitted to the hospital because of worsening cough and pulmonary infiltrates on December 28.

On admission to the hospital, a radiograph of the chest...
showed pulmonary infiltrates in the bilateral upper fields, and hematologic tests revealed leukocytosis and eosinophilia. Her condition did not improve despite antibiotics. The patient was referred to our hospital on January 9, 2001.

Except for subacute thyroiditis three years before referral, the patient had been well and never had had asthma or atopic diseases until she had developed non-productive cough. She had lived in an urban area of Osaka, Japan. She had worked at a factory, producing videocassette recorders under industrial dust-free conditions. She had never smoked. She had never owned a dog nor any pet. She did not remember eating food contaminated with soil that could have contained eggs of Toxocara.

On admission, the body temperature was 36.6 degrees Celsius, the pulse was 76 per minute, and the respirations were 10 per minute. The blood pressure was 110/70 mmHg. By auscultation, crackles were heard over the upper lungs.

Hematologic tests showed a hematocrit of 31.6%, erythrocyte sedimentation rate of 83.6 mm/h, platelet count of 326,000/mm³, and white blood cell count of 14,500/mm³ with 58.5% eosinophils, 23.1% neutrophils, and 14.0% lymphocytes. Analyses of blood chemistry and enzymes were as follows: urea nitrogen of 7 mg/dl, creatinine of 0.5 mg/dl, lactate dehydrogenase of 478 U/l, aspartate aminotransferase of 16 U/l, alanine aminotransferase of 11 U/l, bilirubin of 0.2 mg/dl.

Immunologic tests showed an immunoglobulin G (IgG) of 1,271 mg/dl, IgA of 156 mg/dl, IgM of 182 mg/dl, and IgE of 438 mg/dl. Neither MPO-ANCA nor PR3-ANCA was detected in her serum. Analysis of arterial blood gas under breathing room air showed a PaO₂ of 81.8 mmHg and PaCO₂ of 38.3 mmHg. An electrocardiogram revealed no abnormalities. A tuberculin test was negative.

A radiogram of the chest on referral to our hospital showed pulmonary infiltrates in the left upper and middle fields (Fig. 1A). High-resolution computed tomography on referral revealed peripheral consolidation and ground-glass opacities in the left upper and middle fields (Fig. 2). In addition, a chest radiogram just before treatment on January 25 showed migration of pulmonary infiltrates from the upper and middle fields to the middle and lower fields. Analysis of bronchoalveolar lavage fluid (BALF), obtained from the lingual, showed that its total cell count was 38.4x10⁵/ml with 96.4% eosinophils, 0.8% macrophages, 1.8% lymphocytes, and 1.0% mast cells. Specimens of transbronchial lung biopsy (TBLB) demonstrated eosinophilic pneumonia (Fig. 3).

No larvae were identified in the BALF or TBLB specimens.
There were no eggs in her stool. In her serum, anti-IgG to *T. canis* was detected by a commercial multiple-dot ELISA kit (SRL, Tokyo), which contains 12 different parasite antigens including *T. canis*. The positive results of anti-IgG to *T. canis* were further confirmed by microplate ELISA using an excretory-secretory antigen derived from *T. canis* larvae, at the Department of Parasitology, Miyazaki Medical College, Japan. This test revealed an A<sub>405</sub> of 0.35 (cut-off, 0.2). Based on the positive results of anti-IgG to *T. canis* and clinical findings, we diagnosed this case as CEP due to VLM.

As anthelmintic treatment, albendazole (600 mg per day) was administered on January 25. Her cough had lasted 7 months and dissipated 2 weeks after the treatment. Moreover her pulmonary infiltrates that had persisted for 7 weeks cleared 3 weeks after the treatment (Fig. 1B). In addition, her elevated white blood cells, blood eosinophils and IgE values fell to within the normal level, 2 weeks, 6 weeks, 1 week after the treatment, respectively (Table 1). Albendazole was continued for 8 weeks. During the 8 weeks of the treatment, slight skin eruptions were transiently developed as a mild adverse effect.

### Discussion

Patients with VLM most commonly present with pulmonary symptoms. In a series of 51 children cases with VLM, cough occurred in 80% cases, wheezing in 63%, and fever in 80% (8). The present adult patient presented with cough lasting 6.5 months.

In a series of 17 children cases with VLM, pulmonary infiltrates occurred in 42% cases (9). Pulmonary infiltrates due to VLM are presumed to be an allergic response to the larvae migrating through the pulmonary circulation; eosinophilic infiltrates into the lungs. Therefore these pulmonary infiltrates may be histopathologically consistent with eosinophilic pneumonia. This has been, however little proven in the literature. In the present case, transbronchial lung biopsy demonstrated that its pulmonary infiltrates were an eosinophilic pneumonia. It appears that the TBLB-proven eosinophilic pneumonia of our case indicates that pulmonary infiltrates due to VLM are histopathologically compatible with eosinophilic pneumonia.

In 1932, Löffler clinically described “Löffler’s syndrome” in which pulmonary infiltrates were transient and cleared within 6 to 12 days (4). Nowadays, most cases of Löffler’s syndrome are thought to be due to parasitic etiology, especially VLM. In

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<th>Table 1. Hematologic Laboratory Values</th>
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<td>First treatment day</td>
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<td>WBC (×10&lt;sup&gt;3&lt;/sup&gt;)</td>
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<td>Eosinophils (%)</td>
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<td>IgE* (mg/dl)</td>
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WBC: white blood cells. *The normal range for IgE is 15 to 400 mg per deciliter.
On the other hand, her pulmonary infiltrates cleared 3 weeks after treatment with albendazole (600 mg per day for 8 weeks). Moreover, her cough lasting 7 months dissipated 2 weeks after the treatment. In addition, her elevated white blood cells, blood eosinophils and IgE values were normalized immediately after the treatment. In the present study, antibody titer in the sera of the patient remained unchanged even after the successful treatment. We speculate that this might be due to a gradual release of antigenic components from the destroyed larvae. During the treatment, skin eruptions were occasionally recognized and thought to be a side effect. They were, however not disabling in our patient at all. Hepatic and renal function tests remained normal throughout the course of treatment and afterwards. In a series of three children with VLM, they demonstrated rapid clinical and laboratory improvement after the use of the anthelmintic drug, thiabendazole (15). We believe that anthelmintic treatment is effective with the view towards relieving symptoms and decreasing convalescent time. Nevertheless, it should be determined in a trial whether or not the use of anthelmintic agents is efficacious.

The case reported here seems to be the first case of CEP due to VLM. The presence of such a case strongly suggests that some cases of idiopathic CEP might include CEP due to VLM. Since immunodiagnosis for VLM can be made without difficulty, CEP due to VLM should be excluded before diagnosed as idiopathic CEP.

References
