Two Cases of *Paragonimus Westermani* Infection with Pulmonary and Brain Lesions

Rintaro Onoe¹, Yuko Komase¹, Ayano Usuba¹, Naoya Hida¹, and Masamichi Mineshita²

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Abstract

A Thai woman with lung lesions and her daughter with lung and brain lesions, both with a history of consuming raw freshwater crabs, were admitted to our institution. Based on the detection of worm eggs in the mothers' sputum by serum enzyme immunoassay/DNA sequence analysis, both mother and daughter were diagnosed as having *Paragonimus westermani* infection (triploids). Praziquantel treatment resulted in the normalization of blood eosinophil counts and eosinophil cationic proteins. Although the total IgE and various specific IgE antibodies were elevated in both the mother and daughter, no increases were detected in their urinary levels of leukotriene E4.

Key words

Paragonimus westermani infection, brain abscess, eosinophil cationic protein, leukotriene E4

Introduction

Paragonimus westermani infection is a typical form of food-borne parasitosis that is caused by consuming raw meat from mitten crabs, freshwater crabs, or wild boars that have been infected with metacercaria (the infective larva). Parasitosis is prevalent in various Asian countries, including Japan^{1–3)}. We report two patients diagnosed as having *Paragonimus westermani* infection after consuming raw freshwater crabs.

Case Reports

Case 1: A 36-year-old Thai woman, mother of Case 2

Chief complaint: Cough and bloody sputum.

Past history: Unremarkable.

Dietary history: Freshwater crabs.

Present condition: The patient, who currently re-

sides in Japan, developed a cough that gradually worsened to where she noticed blood in her sputum. She consulted our institution in May 20XX after visiting Thailand for 2 months. She had no history of fever after returning to Japan. Chest auscultation was normal, and percutaneous arterial oxygen saturation (SpO₂) was 98% (room air).

Laboratory examinations: Her white blood cell (WBC) count was 7.8×10^3 cells/ μ L (62.5% neutrophils, 4.5% lymphocytes, 5.5% monocytes, and 17.5% eosinophils), serum C-reactive protein level was 0.14 mg/dl, and erythrocyte sedimentation rate was 51 mm/h. Her IgE level was 17,000 IU/ml, and PR3-ANCA and MPO-ANCA were normal. Smears and cultures of gastric aspirates were negative for tuberculosis. However, sputum cytological examination revealed parasitic eggs with inflammatory cells, mainly eosinophils (**Fig. 1**).

Imaging findings: Chest X-ray and chest computed

¹ Department of Respiratory Internal Medicine, St. Marianna University School of Medicine, Yokohama-City Seibu Hospital, Yokohama, Kanagawa, Japan

² St. Marianna University School of Medicine, Division of Respiratory and Infectious Diseases, Department of Internal Medicine, Kawasaki, Japan

Figure 1. Parasitic eggs discharged in the sputum of patient. Light-brown, oval parasitic eggs accompanying inflammatory cells, mainly consisting of eosinophils, were detected in sputum. DNA sequence analysis of the parasitic eggs led to the diagnosis of *P. westermani* (triploids) infection.

Figure 2. Image findings for Case 1 at first examination
A multi-locular cyst is observed in the upper lobe of the right lung.
There are no disseminated shadows present.

tomography (CT) showed a cavitary shadow in the upper lobe of the right lung (**Fig. 2**).

Clinical course: Enzyme-linked immunoassay of the sputum conducted at the National Institute of Infectious Diseases was positive for *P. miyazaki* IgG and *P. westermani* IgG (**Fig. 3**).

DNA sequence analysis of the parasitic eggs detected in the sputum samples led to the diagnosis of *P. westermani* (triploids) infection. The patient showed improvements in subjective symptoms, laboratory test results, and imaging findings following treatment with praziquantel. As shown in **Figure 4**, the serum IgE levels and blood eosinophil counts decreased following drug treatment, and the serum lev-

els of eosinophil cationic protein (ECP) and urinary levels of leukotriene E4 (LTE4) also decreased, although these levels were within normal range prior to the administration of praziquantel. Urinary LTE4 levels were measured according to Mita *et al.*⁷⁾ at the Clinical Research Center for Allergy and Rheumatology of the Sagami National Hospital.

Case 2: An 8-year-old girl, daughter of Case 1

Chief complaints: Headache, vomiting, ophthalmalgia, and afebrile convulsions.

Past history: Low birth weight.

Dietary history: Freshwater crabs.

Present condition: She had a generalized chronic

Figure 3. Results of serum enzyme immunoassay for Case 1. Detection of IgG antibody specific to three parasitic egg antigens was conducted by enzyme-linked immunosorbent assay (ELISA). The test was positive for *Paragonimus* antigen (Rightmost column).

Figure 4. Clinical course for Case 1.

After treatment with praziquantel, the blood eosinophil counts, serum IgE and ECP, and urinary LTE₄ levels decreased.

convulsion in March, 20XX, with frequent vomiting. After a second convulsion in April, she was transported to our hospital by ambulance. On admission, she was alert and conscious, with a height of 116.5 cm and body weight of 19.1 kg. Her blood pressure was 90/60 mmHg with a body temperature of 36.6°C.

Her pulse was 90 beats/min, and respirations were 22 breaths/min with a SpO₂ of 98% (room air). No superficial lymph nodes were palpable. She had audible respiratory sounds and there were no heart murmurs. Her abdomen was soft with no tenderness and no finger clubbing or pedal edema was noted.

Neurological findings: Examination revealed no evidence of facial paralysis or upper or lower extremity paralysis. No sensory disturbances or apraxia was present.

Laboratory examinations: Her WBC count was 7.7×10^3 cells/ μ L (31.5% neutrophils, 38.5% lymphocytes, 5.5% monocytes, and 22.0% eosinophils), serum C-reactive protein level was 0.03 mg/dl, and IgE level was 870 IU/ml. PR3-ANCA and MPO-ANCA were normal.

Imaging findings: Brain CT revealed a ring-shaped, enhanced space-occupying lesion in the right parietal lobe (Figure 5). A plain preoperative chest X-ray revealed a suspicious left-sided pleural effusion, which was diagnosed as being without pathological importance.

Clinical course: Because the brain lesion was partially calcified, a diagnosis of cavernous hemangioma was made, and a craniotomy was performed to remove the hematoma in April. The postoperative diagnosis was arteriovenous malformation. Several months later, the patient's mother was diagnosed as having *P. westermani* infection, based on which the patient herself was also suspected of the same infection, and the pathological diagnosis was reconsidered. A repeat histopathological examination revealed marked infiltration by eosinophils, indicating erratic parasitism in the brain, although the presence of *P. westermani* could not be confirmed. The serum enzyme immunoassay revealed positive results for both

P. miyazaki IgG and *P. westermani* IgG. After the lesion was surgically removed, the patient had been followed up without additional treatment. However, as the chest X-ray and CT obtained in June showed cystic lesions (Fig. 6), she was also treated with praziquantel. As shown in Figure 7, her serum IgE levels and blood eosinophil counts decreased following surgery and drug treatment. The serum levels of ECP and LTE-4 urinary levels also decreased, although these levels were within their normal ranges prior to the administration of praziquantel.

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Discussion

Paragonimiasis is a subacute-to-chronic parasitic infection caused by one of the species belonging to the genus *Paragonimus*. Most cases of paragonimiasis diagnosed in Japan are caused by infection with *P. westermani*, although there have been some reports of the infection being caused by *P. miyazaki*. In addition to infections transmitted through native Japanese dietary habits, such as eating boar meat or raw Japanese mitten crabs (*Eriocheir japonica*), an increasing number of cases of paragonimiasis have been reported among long-term residents in Japan from other Asian countries. These individuals often eat their own traditional meals made from uncooked freshwater and brackish water crabs¹⁻³. In our present

Figure 5. Chest X-ray and brain CT findings for Case 2 at first examination.

Left-sided pleural effusion was suspected. Brain abscess with edema is observed in the right occipital lobe.

Figure 6. Chest findings for Case 2 during follow-up
Multi-lobular cysts are observed in the right middle lung field.

Figure 7. Clinical course for Case 2.

After operation, the blood eosinophil count, serum IgE and ECP, and urinary LTE₄ decreased; however, all of these parameters increased again prior to treatment, and subsequently, decreased after treatment with praziquantel.

cases, *P. westermani* infection occurred in a mother and daughter with the same familial eating habits. As both patients developed symptoms of the infection several months after visiting Thailand, it was considered that they might have acquired the infection there. The main causative pathogenic species of paragonimiasis found in the Indochina region, including Thailand, Vietnam and Laos, is *P. heterotremus*⁸⁾.

However, the results of the serological examinations in these patients genetically demonstrated that the infection was not caused by *P. heterotremus* in either patient. Therefore, it might be reasonable to assume that the infection was caused by eating raw crabs in Japan.

Eosinophilia and elevated IgE levels in the peripheral blood are important indicators of suspected

parasitosis. Although interleukin (IL)-5 is a cytokine that is known to be associated with eosinophils, it is also produced locally in lesions that are associated with eosinophilia in paragonimiasis. In the early phase of paragonimiasis, nodular or mass-like shadows are thought to appear due to the formation of parasitic capsules, followed by the appearance of infiltrative shadows that are caused by gradual eosinophilic infiltration (due to IL-5 production)⁹⁾¹⁰⁾. The chemotactic activity of eosinophils in parasitosis is also thought to be enhanced by an eosinophil chemotactic factor derived from the infectious parasite.

Although activated eosinophils at the inflamed sites of infection release specific granule proteins (e.g., ECP) in an attempt to kill the helminth or other parasites, this activation simultaneously damages the tissues of the host¹¹⁾. In our cases, the ECP levels were originally high, although they decreased as treatment progressed. Therefore, it appears that the number of activated eosinophils in the inflamed sites of infection was reduced because of decreased IL-5 production.

It has been reported that leukotrienes (LTs) increase and can be measured during parasitic infection⁴⁻⁶⁾. The involvement of LTs, particularly cysteinyl leukotrienes (CysLTs), in the pathology of bronchial asthma, has been emphasized due to their potent bronchoconstrictive effects and abilities to promote vascular permeability, and drive chemotaxis of various inflammatory cells. In addition, LTs act as an important biological factor that inhibits inflammation in various pathological states of infection. When the host is infected, leukocytes immediately begin migrating to the site of infection to eliminate the pathogenic microorganisms. CysLTs promote the migration of inflammatory leukocytes from the blood vessel to the site of infection by increasing the permeability of the vascular endothelial cells. In addition, LTs are associated with phagocytosis of the pathogenic microorganisms and other bactericidal mechanisms, which indicate that LTs play an important role in the immune response to infection¹²⁾. The half-life of LTC4 in blood is short, as LTC4 is rapidly metabolized to LTD4 and LTE4, and this metabolism complicates the measurement of LTC4 concentrations in the blood. However, as LTC4 and LTD4 are both converted to LTE4 in the renal tubules, urinary LTE4 levels are thought to accurately reflect the levels of LT released in the body¹³⁾. In this report, we describe the first measurement of urinary LTE4 levels in patients with paragonimiasis. In these cases, the urinary

LTE4 levels were slightly elevated compared to the increase in eosinophil counts, although this difference was not statistically significant. In addition, we assume that the possibility of CysLT involvement in paragonimiasis is low. However, there are reports of LTB4 involvement in cases of *Strongyloides venezuelensis* and *Toxoplasma gondii* infection⁴⁾⁵⁾ and LTC4 involvement in *Schistosoma mansoni* infection⁶⁾. Therefore, the defense mechanisms used by the host may vary depending on the parasites involved, and the mechanisms that the parasites use to avoid these defense mechanisms may also vary. However, the extent of LT involvement is not commonly understood. In the present cases, we measured only LTE4, not LTB4. It might be possible that in cases of paragonimiasis, the normal level of LTE4 may not be related to asthmatic symptoms.

In conclusion, we report two cases of paragonimiasis occurring in a mother and daughter, both of whom had similar dietary habits. Because of traditional dietary habits, the incidence of paragonimiasis in family members is expected to increase as the number of non-Japanese Asian residents living in Japan increases. The standard methods for diagnosing parasitic infection are the detection of parasitic eggs, measurement of serum antibody titers, and other similar techniques. However, measurement of LT levels may also be helpful for diagnosing parasitic infections that involve eosinophilic inflammation or for elucidating the mechanism of eosinophilic inflammation caused by parasites.

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