***Paragonimiasis Miyazakii* Associated with Bilateral Pseudochylothorax**

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Abstract

A 37-year-old man who suffered from bilateral pleural effusions, subcutaneous abdominal induration and blood eosinophilia, was admitted to our hospital. He had ingested raw crabs at a pub-restaurant before the onset of his symptoms. His pleural effusions were chyloform containing cholesterol crystals, and a high level of immunoglobulin E (36,580 IU/ml) and anti-*Paragonimus miyazakii* antibody were detected. He was effectively treated with praziquantel. This case suggests that paragonimiasis should be strongly suspected if blood eosinophilia, pseudochylothorax, and a high level of immunoglobulin E in pleural effusion are detected.

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Key words: eosinophilia, immunoglobulin E, cholesterol crystal, larva migrans, praziquantel.

Introduction

The prevalence of parasitic diseases has become low in Japan as the living environment has modernized. Because of this, it is difficult for the inexperienced physician, especially in urban areas, to detect these diseases. Patients with paragonimiasis suffer from pleural effusions, pneumothorax, intrapulmonary lesions, etc. The observation that pleural effusion is common (40–78%) in these diseases has not been emphasized in the literature (1, 2), and paragonimiasis can be mistreated as tuberculosis (3, 4). We report a case of *paragonimiasis miyazakii* with bilateral pseudochylothorax and blood eosinophilia. In our case, precise examinations of pleural effusions including immunoglobulin E (IgE) measurement were helpful to the diagnosis.

Case Report

A 37-year-old man, who was a current smoker and alcohol drinker, but had no family or past history of specific disorders, was referred to our hospital because of bilateral pleural effusions and blood eosinophilia in July 1998. During the summer of 1996, he was drunken and jestingly ate two raw freshwater crabs (*potamon dehaani*) in a pub-restaurant in Osaka, Japan. In February 1997, he suffered sudden left chest pain, and was admitted to a hospital because of left pleurisy and blood eosinophilia. Although a conclusive diagnosis was not made, his symptom spontaneously improved and he was discharged. However, he continued to suffer from general fatigue. In June 1998, he went on a picnic, and ingested a small raw crab with alcohol for fun at the seashore near an estuary, and in the following one month he suffered from severe general malaise and sweating at night. Bilateral pleural effusions were found by his doctor and he was referred to our hospital.

On admission, we found a subcutaneous induration (5×4 cm, elastic hard) at the right abdominal wall, which spontaneously disappeared 10 days later. The patient was obese (body weight=85 kg, height=178 cm); anemia, icterus, or surface lymph node swelling were not observed; respiratory and heart sound, and body temperature were normal. His chest radiographs revealed bilateral pleural effusions (Fig. 1) and chest CT scan detected no apparent abnormal shadow in his lungs or mediastinal lymph node swelling (Fig. 2). Blood laboratory test on admission revealed blood eosinophilia (white blood cells count; 9,100/ml, eosinophil 20.8%); elevated erythrocyte sedimentation rate (40 mm/1hour); C-reactive protein (0.7 mg/ml); α_1 -globulin (3.1%, total protein 7.5 g/dl); α_2 -globulin (9.9%); γ -globulin (21.7%); aspartate amino transferase (35 IU/l); alanine aminotransferase (55 IU/l); γ -glutamyl transpeptidase (76 IU/l); and triglyceride (351 mg/dl). Blood levels of total cholesterol (213 mg/dl) and immunoglobulin E (341 mg/dl) were within normal ranges. Results of urinalysis, sputum, stool examinations were normal. Parasitic egg in sputum or stool was not detected. A skin test of purified protein derivative of tuberculosis was positive (12×13/40×32 mm). Vital capacity was

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Figure 1. Chest radiograph on admission. Bilateral pleural effusions were found.

decreased to 62.6% of predicted. Abdominal CT scan detected only fatty liver. The subcutaneous induration in the right abdominal wall was not found, because the tumor was shrunk at the time of examination.

Thoracentesis and pleural biopsy were performed, but we could not detect a specific diagnostic finding from the biopsied pleura. Pleural effusions from both pleural cavities were turbid and milky yellow (Fig. 3, left). In order to distinguish chiliform from chylous effusion, we performed the following test. The effusion remained opaque after centrifugation but the turbidity cleared when ethyl ether was added. Microscopic finding revealed many large polyhedral crystals (Fig. 3; right), but no parasitic egg in the effusions. We concluded the effusion was chiliform (5). As shown in Table 1, the effusions were exudate with low glucose, low triglyceride, high lactate dehydrogenase, and high cholesterol level. IgE levels were extraordinarily high in both pleural effusions compared with serum IgE levels. When we performed thoracentesis again, appearance of right pleural effusion changed to bloody. In order to confirm the diagnosis, we measured serum anti-paragonimus antibody by enzyme immunoassay (SRL, Tokyo). The titer of antibody was borderline level (32×; normal level <32×). In order to obtain a specific diagnosis of paragonimiasis, we performed immunoelectrophoresis using his serum, pleural effusion, and antigens from *Paragonimus westermani* (*P. westermani*) or *P. miyazakii* (kindly performed and advised by Professor Moriyasu Tsuji, Department of Tropical Diseases and

Figure 2. Chest CT scan. Bilateral pleural effusions were found. No abnormal finding in the lungs, or no lymph node swelling in mediastinum was found.

Figure 3. Turbid and milky yellow appearance of pleural effusions (left figure) and cholesterol crystals on microscopy ($\times 20$ objective; right figure).

Table 1. Analysis of Pleural Effusions

	Pleural effusion			Serum
	Right (Aug. 4)	Right (Aug. 18)	Left (Aug. 18)	
Appearance	turbid milky yellow	bloody	turbid milky yellow	
Rivalta test	+	+	+	
Lymphocyte (%)	80	72	67	
Neutrophil (%)	3	19	21	
Eosinophil (%)	7	0	3	
Mesothelium/Macrophage (%)	10	7	9	
Total protein (g/dl)	6.9	5.7	7.9	3.7
Glucose (mg/dl)	14	38	0	76
Lactate dehydrogenase (IU/l)	1,698	3,002	4,360	286
Cholesterol crystals	+	—	+	
Egg	—	—	—	
Triglyceride (mg/dl)		25	32	448
Total cholesterol (mg/dl)		150	329	165
Immunoglobulin E (IU/ml)		3,730	36,580	378
CEA (ng/ml)	1.6			1.9
Adenosine deaminase (IU/l)	NA	24.1	NA	17
Hyaluronic acid (mg/ml)			0.055	

CEA: Carcinoembryonic antigen, NA: not analyzed because the effusion was too turbid.

Parasitology, Kyorin University School of Medicine, Tokyo). We detected specific immunoprecipitant against *P. miyazakii* using pleural effusion but not serum. From these data, we concluded *P. miyazakii* caused his disease, and we treated the patient with praziquantel (3.3 g $\times$ 2 days). We also treated his hyperlipidemia with bezafibrate. After the treatments, his symp-

toms and blood eosinophilia improved, and pleural effusions disappeared about two months later. The treatment using a regular dose of praziquantel was successful without adverse side effect, though slight dyspnea remained due to pleural adhesion.

Discussion

Humans can acquire paragonimiasis by eating raw, undercooked, or pickled freshwater crustacean (crabs, crayfishes) which contain infective parasite forms (metacercariae). These forms enter the peritoneal cavity through the intestinal wall and migrate to the abdominal wall, diaphragm, and finally pleural cavity to the lungs, where they mature into adult worms and produce eggs (6).

In Japan, *P. westermani*, and *P. miyazakii* are important flukes. Compared with *paragonimiasis westermani*, *paragonimiasis miyazakii* does not cause cystic lesions in the lungs and, migrating between the pleural cavity and lungs, causes pleural diseases such as pneumothorax and pleural effusions. It is hard to detect eggs in sputum or stool. Humans are not comfortable hosts for *P. miyazakii* (2). A typical finding of pleural fluid from patients with paragonimiasis is exudate, containing low glucose levels, low pH, high lactate dehydrogenase levels, and significant eosinophilia (5).

Yokogawa et al have reported that IgE levels in pleural fluid are higher than the simultaneous serum IgE levels in patients with pleural paragonimiasis (7). Ikeda et al demonstrated that paragonimiasis-specific IgE and IgG antibodies were much higher in pleural effusions than in sera (8). Whether the high pleural fluid IgE levels are specifically diagnostic of pleural Paragonimiasis remains to be determined (5). However, a high IgE level in pleural effusion and eosinophilia is strongly suggestive of this disease (9).

In long-standing pleural effusion, large amounts of cholesterol or lectin-globulin complexes can accumulate in the pleural fluid to produce a chyliform (not chylous) pleural effusion, pseudochylothorax (10). The turbulent pleural effusion from our patient was chyliform effusion containing many cholesterol crystals. Tuberculosis is by far the most frequent cause of pseudochylothorax (11). Though our patient had a positive skin test of tuberculosis, his chyliform effusion was not due to tuberculosis. Adenosine deaminase level in his pleural effusion was not high, and he was diagnosed by immunoelectrophoresis. Johnson and Johnson described 12 cases of chyliform pleural effusions secondary to paragonimiasis (1). Cholesterol crystals are found in many pleural effusions from patients with paragonimiasis (10). The mechanism of chyliform formation in paragonimiasis is not well understood.

The subcutaneous induration in the patient's abdominal wall disappeared spontaneously, and pleural effusion became bloody.

These findings might indicate larva migrans, although bloody pleural effusion could be a traumatic change after thoracentesis. Matumine et al reported only 3% of the patients with *paragonimiasis miyazakii* had subcutaneous lesions (2).

In conclusion, as indicated by this case, typical findings of pleural effusions including high levels of IgE and the appearance of chyliform are very diagnostic for paragonimiasis, as well as eosinophilia and eating history. Precise analysis of pleural effusion is essential before immunoelectrophoresis.

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