Abstract. A 66-year-old man visited our hospital with primary complaint of cough. Chest roentgenogram showed slight pleural effusion and pneumothorax in the left lung. Eosinophilia (22.8%) was also found in his peripheral blood. Multiple-dot enzyme-linked immunosorbent assay (dot-ELISA) for the detection of parasite-specific immunoglobulin (Ig) G antibody was used to screen his serum against various parasitic diseases, but no significant binding was observed with any of the 12 parasite antigens examined, including those of Paragonimus westermani and P. miyazakii. Although he seemed to have been spontaneously cured without treatment, a nodular shadow appeared in the right upper medial lung field on the chest roentgenogram 6 months later. This time, his serum was positive for anti-P. westermani IgG antibody by the same method. A reexamination of the first and second admission serum samples for parasite-specific IgM and IgG antibodies revealed significant level of IgM antibody in the serum of the first admission, which had decreased at the time of the second admission. Conversely, the level of IgG antibody, which was low at the first admission, became dominant in the second admission serum 6 months later. These results clearly show that although the dot-ELISA to detect IgG antibody is generally useful for screening and detecting paragonimiasis, detection of IgM antibody seems to be a useful aid and should also be included in immuno-serological diagnosis, especially if the patient is considered to be in the early stage of infection.

INTRODUCTION

Paragonimiasis is an important food-borne parasitic zoonosis. Miyazaki Prefecture, located in southern Kyushu, Japan, had been known as one of the endemic areas of Paragonimiasis westermani. The prevalence of this disease peaked around 1956 and then drastically decreased after successful eradication programs. Paragonimiasis was considered a disease of the past in the 1970s. Recently, however, sporadic cases of paragonimiasis have occurred in Miyazaki and adjacent areas every year, and the number of patients per year has increased gradually over time. Immunoserological examination is critically important for parasitic zoonoses, including paragonimiasis, because direct demonstration of parasite eggs or worm bodies is possible only in rare instances. In this respect, multiple-dot enzyme-linked immunosorbent assay (dot-ELISA) was developed and is currently successfully applied routinely for rapid diagnosis of parasitic diseases by the detection of parasite-specific immunoglobulin (Ig) G antibody in serum, tissue fluid, or both. In fact, between 1986 and 1997, we have recorded > 100 cases of paragonimiasis mainly by this method.

We report here an exceptional case of P. westermani infection in a patient whose serum was initially negative for the specific IgG antibody by multiple-dot ELISA but who had a high titer of specific IgM antibody. To our knowledge, this is the first case showing the possible diagnostic value of detecting IgM antibody in paragonimiasis.

CASE REPORT

A 66-year-old man visited a regional hospital because of persistent left chest pain and cough that had persisted for 2 weeks, and left pleural effusion was found by chest roentgenogram in mid-February 1997. Although his symptoms improved without treatment, he was referred to our hospital on March 26, 1997. His general medical history and his family’s medical histories were unremarkable, although he was an ex-smoker and had a history of eating the flesh of wild boars. His height was 165 cm, body weight 75 kg, and body temperature 36.2°C. The initial laboratory findings in this patient included C-reactive protein of 0.0 mg/dL, red blood cell count of 4.98 × 10^12 cells/mm^3, and total white blood cell count of 5,800 cells/mm^3 (36.2% neutrophils, 36.7% lymphocytes, 3.7% monocytes, 22.8% eosinophils, and 0.6% basophils). Biochemical tests revealed elevated levels of serum lactate dehydrogenase (418 IU/L). The levels of total serum IgE (318 IU/mL) and carcinoembryonic antigen (CEA) (3.3 ng/mL) were within normal ranges.

Chest roentgenogram and computed tomogram demonstrated left slight pleural effusion and pneumothorax (Figure 1A). Cytological examination of the sputum showed no malignant cells, parasite eggs, or eosinophils, and sputum cultures were also negative for bacterial or fungal growth. Because parasitic diseases were strongly suspected on the basis of eosinophilia and radiological findings of the lung, his serum was examined by dot-ELISA for the diagnosis of various parasitic diseases. However, his serum was negative for all 12 parasite antigens examined, including P. westermani and P. miyazakii. Bronchososcopic examination showed normal findings. His symptoms and roentgenographic abnormalities spontaneously disappeared without treatment, and so he was discharged.

On August 29, however, he consulted our hospital again because of cough and hemoptysis. His chest roentgenogram and computed tomogram this time showed a nodular shadow in the right upper medial lung field (Figure 1B). Bronchosopic examination showed a stenosis of right B2, together with reddish and edematous mucosa. A sample of bronchoalveolar lavage showed an increased percentage of neutrophils and eosinophils (5% macrophages, 3% lymphocytes, 77% neutrophils, and 15% eosinophils) but was negative for parasite eggs or malignant cells. Because we still strongly suspected paragonimiasis, his serum was retested by dot-ELISA. This time, his serum generated a weak but positive reaction against P. westermani antigen.
Comparative study of the pair of sera obtained at the first and second admissions was carried out for parasite-specific IgG and IgM antibodies by microplate ELISA. The results clearly showed that the IgM antibody titer was high at the first admission and decreased at the second admission (Figure 2). Conversely, his IgG antibody titer showed a massive increase at the second admission compared with that at the first admission. He was successfully treated with praziquantel therapy (75 mg/kg per day) for 3 days from October 1, 1997. The lung lesion completely disappeared, and the IgG antibody titer in the serum (measured at ×1,000 dilution) significantly decreased 4 months after chemotherapy.

DISCUSSION

A typical route of migration of *P. westermani* in human or other natural final hosts is as follows. When metacercariae, an infective stage of the parasite, are ingested by the final hosts, they excyst in the intestine and penetrate the abdominal cavity. The immature worms migrate into abdominal muscles, lodging there for a while, then reappearing in the abdominal cavity. They then migrate through the diaphragm and the pleural cavity and finally reach the lung where they become mature worms.\(^{10}\) The patient reported here showed typical clinical features of paragonimiasis with eosinophilia, pleural effusion, and pneumothorax, then a nodular shadow in the right upper medial lung 6 months later, which was consistent with the migratory route of *Paragonimus* worms.

In this patient, his serum at first admission was negative to *Paragonimus* or other parasite antigens by dot-ELISA, although eosinophilia, pleural effusion, and pneumothorax were present. Instead, his serum at the time had a high titer of IgM antibody against *P. westermani*. The patient’s serum was IgG antibody positive to *P. westermani* antigen at re-admission, with a nodular lesion in the right lung appearing 6 months later. The class switch from IgM to IgG antibody is a well-known immunological phenomenon after primary exposure to various protein antigens. However, most patients with paragonimiasis have a high titer of specific IgG antibody against worm antigens. In fact, as mentioned earlier, >100 cases of paragonimiasis, most of which were considered to be primary infections, were diagnosed in our laboratory, mainly by dot-ELISA, which detected IgG antibody, between 1986 and 1998; we found that the dot-ELISA method for detecting IgG antibody is generally useful for the diagnosis of paragonimiasis.\(^{7,8}\) This is probably because of the requirement of one to several months for ingested metacer-
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cariae to become mature adults in the lung, thus causing the host to manifest lung lesions.10

Because many patients with paragonimiasis with pleural effusion are IgG-antibody positive,7–8 the reason why the present patient had dominant IgM response at the pleural migration stage followed by class switch to IgG antibody as the disease progressed remains unclear. One possibility is that the patient had a low degree of infection, so the antigenic stimuli was not sufficient to induce rapid class switch of antibody response. Alternatively, because the majority of patients with paragonimiasis live in endemic areas with a history of repeated ingestion of infected freshwater crabs or wild boar, they were already exposed to and sensitized by Paragonimus antigens before the onset of the disease, a situation in which class switch would have occurred before admission.

Whatever the explanation, the present case indicates that although the dot-ELISA method to detect IgG antibody is generally useful, IgM antibody measurement would appear to be necessary and should also be considered, especially for the diagnosis of paragonimiasis at the earlier stages, when IgG antibody would normally be negative in serum, pleural effusions, or both of patients with lung lesions with eosinophilia.

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Authors’ addresses: Hiroshi Mukae, Haruko Taniguchi, Jun-ichi Ashitani, and Shigeru Matsukura, Third Department of Internal Medicine, Miyazaki Medical College, Miyazaki, 889-1692, Japan. Fukumi Uchiyama and Yukifumi Nawa, Department of Parasitology, Miyazaki Medical College, Miyazaki, 889-1692, Japan.

Reprint requests: Hiroshi Mukae, Third Department of Internal Medicine, Miyazaki Medical College, Kiyotake, Miyazaki, Japan 889-1692, Telephone: 985-85-2965, Fax: 985-85-8305 (e-mail: hmukae@post.miyazaki-med.ac.jp).

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