RE-EMERGENCE OF PARAGONIMIASIS IN KYUSHU, JAPAN

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Abstract. During 1986-1998 we found 104 paragonimiasis cases, which were referred to our laboratory for immunodiagnosis or identification of parasite eggs in sputum or bronchoscopic aspirate smears, or in histopathological sections. A majority of patients were middle-aged males. Except for 2 cases of chronic occult infection in an unexpected site, 102 cases were assumed as having active infection. Abnormal findings in chest radiograms were noted over 80% of the patients, though about 20% of them were asymptomatic. Parasite egg detection rates in sputum or bronchoscopic aspirate smears were about 50%. About 80% of patients have eosinophilia and/or elevated serum IgE level. Paragonimiasis is a re-emerging public health issue in Kyushu, Japan.

INTRODUCTION

Paragonimiasis is a common food-borne parasitic disease in Asia. In Japan two species, *Paragonimus westermani* and *P. miyazakii*, are the causative pathogens of human paragonimiasis. Infection occurs by ingesting freshwater crabs, *Eriocheir japonicus* or *Geothelphusa dehaani*, the second intermediate host for *P. westermani* (Yokogawa, 1952) and *P. miyazakii* (Kamo *et al*, 1961), respectively, or by eating raw meat of wild boar, *Sus scrofa leucomistax*, a paratenic host for both species (Miyazaki and Hirose, 1976). Southern part of Kyushu district has been known as a major endemic area in Japan (Yokogawa, 1964). For instance, Miyazaki Prefecture has been an representative endemic nidus in Kyushu where over 300 cases were reported in the 1950s (Hayashi, 1978). After mass screening and prevention campaigns by the local government during the 1950-1960s, the prevalence of paragonimiasis drastically decreased, to the extent that in the 1970s paragonimiasis was considered a disease of the past in this area (Hayashi, 1978). However, from the late 1980s, new cases have emerged sporadically (Nawa, 1991). Subsequently the number of paragonimiasis patients has been gradually increasing in southern Kyushu (Uchiyama *et al*, 1998b) and the disease is now considered a major parasitic zoonosis in the area (Maruyama *et al*, 1996). Here we summarize 104 paragonimiasis cases diagnosed in our laboratory during 1986 and 1998.

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MATERIALS AND METHODS

Subjects and samples

A total of 104 of about 1,000 cases referred to our laboratory were diagnosed as paragonimiasis cases during 1986-1998. Except for 2 occult infection cases diagnosed by detecting calcified *P. westermani* eggs in histopathological sections (Nabeshima *et al*, 1991; Shimao *et al*, 1994), 102 cases were considered as having active infections. Specific antibody against *P. westermani* or *P. miyazakii* in sera and/or pleural effusion was examined by immunoserological tests. In some cases, stool, sputum or biopsied tissue sections were also examined. Clinical data of the patients were gathered from the consultation sheets from attending physicians.

Immunodiagnostic methods

For the immunodiagnosis of parasitic diseases, only an Ouchterlony's double diffusion test in agarose gel had been used in our laboratory until 1991. Thereafter, multiple-dot ELISA test has been employed for a routine primary screening and Ouchterlony's method and/or binding inhibition ELISA for the identification of the causative parasite species. Details of the immunodiagnostic methods were described previously (Maruyama *et al*, 1996).

RESULTS

A total of 104 paragonimiasis cases were found among about 1,000 cases referred to us during 1986-1998. Except for 2 cases of chronic occult infections, 102 cases were considered as having active infections and were subjected to further analysis.

The incidence of paragonimiasis cases gradually increased during the period examined (Fig 1). A majority of these cases were infection due to *P. westermani*, with only 6 cases being due to *P. miyazakii*. The cases diagnosed in our laboratory were from patients resident in Kyushu District except for 1 case from Kochi and 2 cases from Osaka (Fig 2). About 70% of the patients (70/102) had a history of eating raw materials predominantly raw wild boar meat (Table 1).

Analyses of individual records also revealed that most patients were over 30 years old and that 69.6% were males (Fig 3). Clinical manifestations of patients are summarized in Table 2. Of 102 patients considered as having active infection, 62 cases (60.8%) had respiratory symptoms such as cough, sputum and dyspnea, and most of them (60/62: 96.8%) had abnormal findings in the chest X-ray. However, it should be noted that 22 (21.6%) patients were asymptomatic and that the presence of lung lesions was discovered during routine regular health checks. In one of these cases, the patient received an open lung biopsy under a suspicion of having a malignant disease but was diagnosed histopathologically as having paragonimiasis (Yoshino *et al*, 1998).

There were 7 cases of subcutaneous paragonimiasis. Two of them had lung lesions as well. In 2 cases, a parasite was found in the biopsied skin

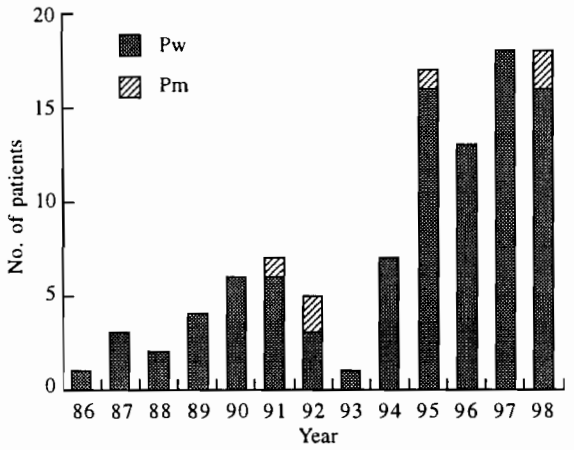

Fig 1–Annual number of paragonimiasis westermani and miyazakii patients diagnosed in our laboratory.

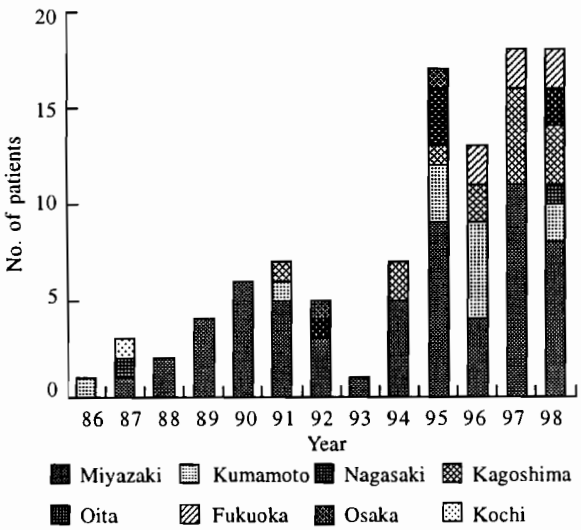

Fig 2–Geographical distribution of the patients.

Table 1
History of eating raw materials.

	Pw	Pm
Wild boar meat	53	3
Freshwater crabs		
Eriocheir japonicus	13	2
Geothelphusa dehaani	6	4
Others	8	2
Venison	3	2
Horse	1	0
Snail	2	0
Freshwater fish	2	0

Pw: Paragonimiasis westermani
Pm: Paragonimiasis miyazakii
*70 cases had history of eating raw materials.

Table 2
Clinical symptoms of patients.

Respiratory symptoms	62 (60.8%)
Sputum	40
Cough	38
Chest pain	8
Dyspnea	3
Dysphoria	1
Others	12 (11.8%)
Fever	8
Subcutaneous nodule	7
Abdominal pain	2
Convulsion	1
Arm tenderness	1
General fatigue	1
Back pain	1
No symptoms	22 (21.6%)
Unknown	6 (5.8%)

Table 3
Chest X-p findings.

	Pw (n=80)	Pm (n=6)
Pleural lesion	30 (37.5%)	1 (16.7%)
Pleural effusion (PE)	26	1
Pneumothorax (PT)	1	0
PE + PT	3	0
Parenchymatous lesion	40 (50.0%)	1 (16.7%)
Nodular lesion (PN)	27 (7)*	1
Infiltration shadow (PI)	13	0
Pleuro-parenchymatous lesion	10 (12.5%)	4 (66.6%)
PE + PN	4 (1)*	2 (1)*
PE + PI	2	2
PE + PT + PI	2	0
PE + PN + PI	2	0

Pw: Paragonimiasis westermani.
Pm: Paragonimiasis miyazakii.
* Numbers in parenthesis showed cavitating lesion.

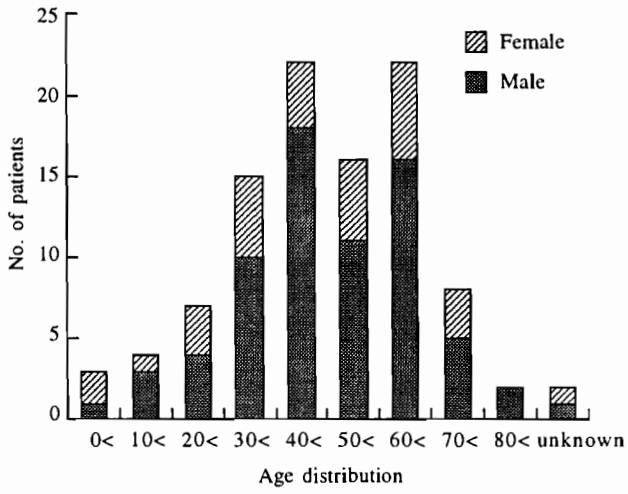

Fig 3–Age and sex distribution of the patients.

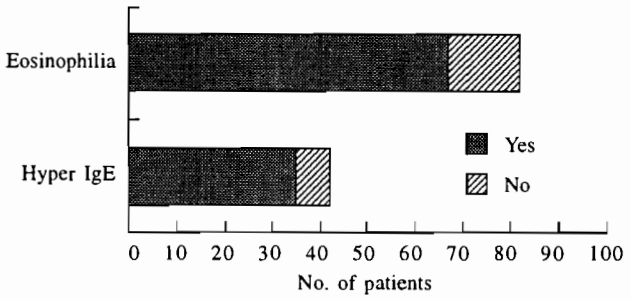

Fig 4–Association of eosinophilia and elevation of total IgE in the patients.

specimen (Ogata *et al*, 1990; Okamoto *et al*, 1993). There was only 1 case of cerebral paragonimiasis diagnosed by a combination of past history, radiological findings and immunoserological test.

Analysis of the chest X-ray showed that 86 patients (84.3%) had abnormal findings in the lungs which were classified into three types: (1) pleural lesion: pleural effusion or pneumothorax, (2) parenchymatous lesion: nodular, cavitating or infiltrating shadows, and (3) combination of pleural and parenchymatous lesions (Table 3). Regardless of either paragonimiasis westermani or miyazakii, all types of pleuro-parenchymatous lesions were observed with varying proportions. Detection rate of *Paragonimus* eggs in sputum or bronchoscopic aspirate smear was about 50% (Table 4). The eggs were detected in stool in only one case (Okamoto *et al*, 1993).

Peripheral blood eosinophil count was available in 82 cases, and 67 of them (81.7%) had eosinophilia (Fig 4). Most of patients (58/82) had mild to moderate (7~40%) eosinophilia (Fig 5). The most striking eosinophilia was observed in a 7-year-old boy infected with *P. westermani* whose total white blood cell was 84,000/mm^3 with 91% eosinophils (Kan *et al*, 1995). Total IgE level in serum was available in 42 cases, and 35 of them (83.3%) showed elevated serum IgE level (Fig 4).

DISCUSSION

In spite of the successful eradication of filariasis and schistosomiasis, as well as the successful control of soil-transmitted parasitic diseases, food-

Table 4
Egg detection rate in sputum or bronchoscopic aspirate smears.

	Positive	Negative
Sputum (n=27)	14 (51.2%)	13 (48.8%)
Bronchoscopic aspirates (n=13)	7 (53.8%)	6 (46.2%)

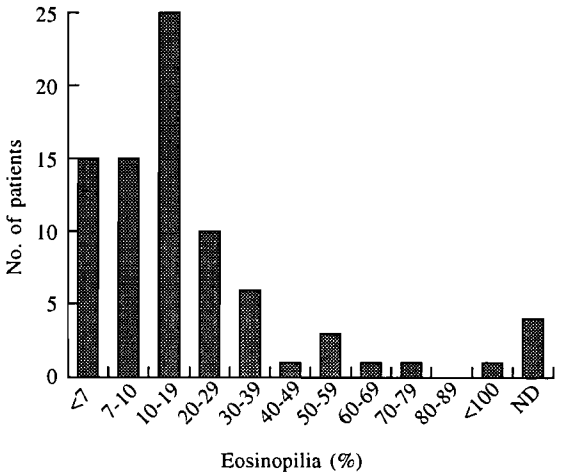

Fig 5–Degree of eosinophilia of the patients.

borne parasitic diseases of zoonotic nature are still endemic in Kyushu, Japan, and paragonimiasis accounted for about a third of such parasitic diseases diagnosed in our laboratory (Maruyama *et al*, 1996). The present results show that the number of paragonimiasis patients has rather increased with time in Kyushu. In addition, a total of 101 paragonimiasis patients in Japan (80 *P. westermani* and 21 *P. miyazakii* infections) in 75 papers were analysed during 1990-1997 by literal survey on the database (Uchiyama *et al*, unpublished data). Similar to the results in Kyushu, this annual national incidence of paragonimiasis gathered by case report papers gradually increased with time. Almost all these patients were from previously endemic areas in Japan. Among 104 cases we reported here, only 23 cases were appeared in 11 case report papers. Therefore, it is possible that a substantial number of unreported paragonimiasis cases could exist in Japan.

In the 1950-1960s, paragonimiasis was mainly a disease of schoolchildren and the major source of infection was freshwater crabs (Komaki, 1959). At that time, pulmonary tuberculosis was the most important disease to be considered in differential diagnosis. In the present study, a majority of patients are over 30-year-old males and wild boar meat is the major source of infection. Such transitions of the disease status may be, in part, due to reduced out-door activities of schoolchildren and excessive food supply. Those who keep traditional eating habits have a chance of infection.

Although respiratory symptoms with chest X-ray abnormality are the typical findings of paragonimiasis, the worms sometimes migrate into ectopic sites and cause unexpected clinical manifestations. Based on the sites affected, Musgrave (1907) classified paragonimiasis into 4 types: (1) pulmonary paragonimiasis, (2) abdominal paragonimiasis, (3) cerebral paragonimiasis and (4) generalized paragonimiasis. All four types were observed in the present study. It should, therefore, be noted that a paragonimiasis patient does not always present with respiratory symptoms.

It is said that in chest radiogram intrapulmonary lesions such as nodular or cavitating lesions or infiltrating shadows are typical of paragonimiasis westermani, whereas pleural lesions such as pleural effusion or pneumothorax are typical of paragonimiasis miyazakii (Yokogawa, 1964). However, paragonimiasis westermani cases having pleural lesion (Ichiki *et al*, 1989), or paragonimiasis miyazakii cases with intrapulmonary lesion (Ono *et al*, 1992; Okamoto *et al*, 1993) were reported. Chest radiographic analysis of paragonimiasis miyazakii cases revealed that about 70% of patients had pleural lesion and about 30% had intrapulmonary lesion (Hibiya, *et al*, 1984; Odagiri, 1985; Matsumine and Araki, 1985). In the present study, 5/6 of paragonimiasis miyazakii patients had pleural effusion and 4 of them had pleuro-parenchymatous lesions (Table 3). Moreover, 40 of 80 paragonimiasis westermani patients had pleural effusion and 30 of them had no parenchymatous lesions. These results show that it is almost impossible to distinguish causative *Paragonimus* species by chest radiographic findings alone. Variance in chest radiographic appearances might merely reflect the stage of worm migration and/or the magnitude of infection (Im *et al*, 1993).

Because majority of recent paragonimiasis cases occur in middle-aged people, detection of chest X-ray abnormality often leads attending physicians to suspect the presence of malignant lung diseases. When malignancy is suspected, patients are subjected to

expensive and invasive examinations in admission. In the present study, eosinophilia and elevated total IgE level in serum were noted in over 80% of the patients. Therefore, lung abnormalities associated with eosinophilia and/or hyper IgE is sufficient to suspect possible paragonimiasis or other parasitic diseases. Although egg detection in stool or sputum specimen is the definite way of diagnosis for paragonimiasis, egg detection rate was only about 50% probably due to low worm burden in the patients. Instead, rapid, reliable, and inexpensive immunodiagnostic methods are now available for paragonimiasis. Once a patient is diagnosed as having paragonimiasis, he/she can be effectively treated with praziquantel with the dose of 75 mg/kg/day for 3 days (Rim and Chang, 1980, Uchiyama *et al*, 1998a).

In conclusion, paragonimiasis is a serious re-emerging public health parasitosis in Japan. An earlier consultation is highly recommended for differential diagnosis of patients having lung lesions associated with eosinophilia and/or elevated IgE, in order to avoid the expensive and invasive examinations for nonexistent malignancies in such patients.

ACKNOWLEDGEMENTS

The authors wish to thank Dr DN Onah for his critical reading the manuscript. We also thank Ms Ayumi Tanaka for her excellent technical assistance in immunodiagnosis, and Shigefumi Ueno and Shuichi Yatsuga, students of Miyazaki Medical College, for their help in database search. This study was supported in part by a grant from the Kurozumi Medical Foundation.

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