Pulmonary Paragonimiasis Misdiagnosed as Tuberculosis: With Special References on Paragonimiasis

Kouichi NAGAKURA, Motofumi OOUCHI [*], Keiko ABE [**], and Kunioki ARAKI [***]

Department of Infectious Diseases, Tokai University School of Medicine;
Departments of [*]Surgery and [**]Clinical Laboratories,
National Sanatorium Minami-Yokohama Hospital;
[***]Department of Environmental Parasitology,
Graduated School of Medicine,
Tokyo Medical and Dental University

(Received September 13, 2002; Accepted November 2, 2002)

The diagnosis of tuberculosis by X-ray radiogram is often confused with pulmonary carcinoma, bacillary and parasitic infections, and chronic mycosis. A case of pulmonary paragonimiasis misdiagnosed as tuberculosis by X-ray radiogram is reported. With this case, the smears of sputum were rechecked by an inspection technician's discernment, and *Paragonimus* eggs along with numerous eosinophils and Charcot-Leyden crystals were detected. In suspected cases of tuberculosis, a history of crab-eating plus sputum examinations, image findings, and serodiagnosis are necessary to rule out paragonimiasis.

Key words : *Paragonimus westermani*, lung flukes, paragonimiasis, Tuberculosis, diagnosis

INTRODUCTION

Tuberculosis has reemerged as a major public health problem worldwide. New cases of tuberculosis in Japan are on the rise, and the prevalence rate is presently at 34.8 per 100,000 individuals. Frequent outbreaks are occurring in schools and hospitals, and multidrug resistant *Mycobacterium tuberculosis* poses a serious problem [1]. In the other hand, paragonimiasis caused by the infection of *Paragonimus* Trematoda is also on the rise in Asian countries including Japan, especially in China where it is estimated to occur in 1 million patients [2]. Tuberculosis and paragonimiasis are two diseases, which overlap in many countries in the Asia [3].

The diagnosis of tuberculosis by X-ray radiogram is often confused with pulmonary carcinoma and bronchial cancer, bacillary and amebic lung abscesses, pulmonary hydatidosis, filarial or paragonomid parasitic infections, and chronic mycosis [4]. Here a case of paragonimiasis misdiagnosed as tuberculosis is reported and discussed on paragonimiasis by *Paragonimus pulmonalis* (= *P. westermani*).

A CASE REPORT

The patient was a 31-year-old Thai woman who was worked in bars and nightclubs, no back to her home country since 1995. She had a history of two bouts of pneumothorax (December, 1998 and April, 1999), complained of chest-pain at coughing, and hemoptysis in May 1999. At local clinic, diffuse nodular lesions in both lung fields (right center field and left front field) were detected by chest X-ray radiogram and a positive PPD reaction (27 × 12 mm) was obtained. She was admitted to our sanatorium for a tuberculosis checkup on June 18, 1999.

At admission, a thoracic CT scan revealed diffuse multiple lesions at right S_4, S_6 and S_{10} and left S_{1+2} regions, as well detected by chest X-ray. A nodular lesion in right center field was attached to the thoracic cavity by MRI imaging. Laboratory findings were as follows; WBC 15,300 /mm^3, with 50 %

Koichi NAGAKURA, Department of Infectious Diseases, Tokai University School of Medicine, Isehara, Kanagawa 259-1193, Japan
TEL: 081-463-93-1121 ext 2602 FAX: 081-463-95-5450 E-mail: nagakura@is.icc.u-tokai.ac.jp

eosinophils, C-reactive protein: 10.3 mg/ml, erythrocyte sedimentation rate: 60 mm/hr, IgE: 4,530 IU/ml, *M. tuberculosis* bacteria: not detected in sputum smear, and sputum culture: only normal flora and class I malignant cells. Her sputum was reddish-brown in color. The stool was not examined. Other laboratory tests were within normal limits. Although the patient was then treated with anti-tuberculosis antibiotics, chest-pain at coughing, and hemoptysis continued, and the lung lesions in CT scan remained unchanged.

A laboratory technician had doubt about the symptoms accompanied with leucocytosis, especially eosinophilia, and reexamined the sputum smear stained by Papanicolaou's methods. And she found the *Paragonimus* eggs along with numerous eosinophils and Charcot-Leyden crystals in the specimen. The maximum width of the eggs (mean, 90 × 52 μm), plus an operculum at one end, led to the identification of *P. pulmonalis* [(Bealz, 1880) Miyazaki, 1978] (= *P. westermani* [Kerbert, 1880]) (Fig. 1).

The patient's serum had a positive titer by ELISA against *P. westermani*, but not by EIA (< × 32). In diffusion-in-gel, a single band formed only with *P. westermani* antigen. There were no cross-reactions with other antigens, including *P. miyazakii.*

Praziquntel (Biltricide, Bayer, 2,400 mg, 2d) was orally administrated. After chemotherapy, symptoms such as chest-pain at coughing and hemoptysis improved. Eosinophil counts returned to normal limits, and the patient was discharged on 2 July 1999. There has been no recrudescence to date. The Thai patient described how she and her friends often ate a vegetable salad dressed with mayonnaise and a crabmeat.

DISCUSSION

Many species of *Paragonimus* are widespread throughout the world, with *P. westermani* being the most important in Asia including Japan. Humans become infected by eating raw or poorly cooked freshwater crabs contaminating *Paragonimus* metacercariae. Many cases were occurred not only by ingestion of metacercariae in the eating meals but also by orally taking of metacercariae through hands and utensils, such as chopping blocks and knives [5]. In the 1950s, it was estimated that 3-5 hundred thousand cases of paragonimiasis existed in Japan [6]. Because the diagnosis for tuberculosis was unsatisfactory, the PPD-negative patients with paragonimiasis often have been compelled to recuperate in the sanatorium. However, due to rapid progress in diagnosis, development of effective chemotherapy for both diseases,

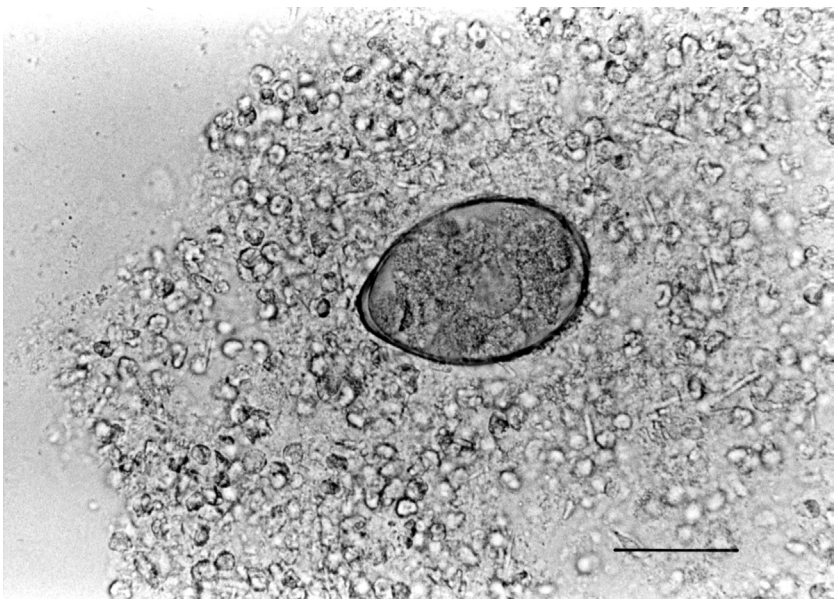

Fig. 1 Paragonimus egg in the sputum of a 31-year-old Thai woman initially diagnosed as pulmonary tuberculosis. Scar bar = 50 μm

and improved public health procedures, the numbers of patients have greatly decreased [4]. Recently, the rise of infection ingested *Paragonimus* larvae in wild boar meat is reported [6]. Now the two diseases, tuberculosis and paragonimiasis, are reemerging.

An adult of *P. westermani* was first found in the lung of Indian tiger in the Netherlands, and the ova of the parasite were found in the sputum of a patient diagnosed as pulmonary tuberculosis by Baelz, in 1878 [7]. For more than 100 years, it was thought that *P. westermani* is a single species. However, Terasaki reported that the species of *P. westermani* can be divided into diploid-type (2n = 2x = 22) and triploid-type flukes (2n = 3x = 33), according to chromosome analysis [8]. Adult diploid-type flukes, which reproduce bisexually, are distributed in tropical Asian countries such as India, Sri Lanka, Malaysia, Indonesia, the Philippines, in the northern part of China and Southern Russia, as well as only an island of Korea (Jeju), Aichi and Akita Prefectures in Japan. On the other hand, triploid-type flukes, which reproduce parthenogenically because of aspermatic testes, are limited to Japan except Aichi and Akita Prefectures, an island of Korea (Jeju), and Taiwan Island. In Jeju island of Korea, both types of flukes were distributed. Therefore, Miyazaki named the diploid-type flukes *P. westermani* [Miyazaki, 1983] and the triploid-type flukes *P. pulmonalis* [(Bealz, 1880) Miyazaki, 1978] [9].

The metacercaria of diploid-type (*P. westermani*) are found mainly in the smaller crab, *Potamon dehaani*, whereas triploid-type (*P. pulmonalis*) metacercariae are found in the giant crab, *Eriocheir japonicus*. The clinical symptoms caused by the two flukes differ [6]. Most of the young adult *P. westermani* larvae develop into mature adult flukes in the lung, and are found inside the bronchial lumen where they cause 'worm cyst' or 'burrows' (abscess cavities). In contrast, *P. pulmonalis* flukes are unable to develop further in the lung, giving rise to a pneumothorax or a pleurisy with an eosinophilic pleural effusion, i.e., a 'visceral larva migran's. Because *P. pulmonalis* ova (85-90 × 46-45 μm) are significantly greater than that of *P. westermani* (70-77 × 40-45 μm) where the maximum width of the egg is in the center [6], eggs in the sputum and/or stool of the patient can be easily distinguished on basis of the size and morphology. The ova found in the sputum from the present patient seem to be that of *P. pulmonalis*. In fact, the Thai patient is cooked the giant crab from Japan.

Pulmonary tuberculosis may be classed into primary and postprimary forms, and radiographic findings in both types are well recognized. However, the utility of X-ray in the diagnosis of tuberculosis is not enough to distinguish the parasitic infections although granuloma surround parasitic larvae (*Dilofilaria immitis*) or adult worms (*P. westermani*) [2, 4]. Lee *et al*. was able to differentiated 4 cases of Korean paragonimiasis from tuberculosis with CT scan [4]. And Milanez de Campos *et al*. reported thoracic CT scan helped to better characterize the multiple nodules and/or bilateral lesions in *D. immitis* [10]. The observations suggest that parasitic lesions in the lung can be differentiated from tuberculosis with CT scan.

Paragonimiasis may be increase by the rise of imported foods accompanying internatinalization of Japan, of a visit-to-Japan foreigner and an overseas traveler, and by the change of eating habits according to gourmet boom. However, Iiyama *et al*. reported a case of domestic paragonimiasis in Thai people, as well as the present case [11]. Thai people usually have the freshwater crab-eating habits. Therefore, in suspected cases of tuberculosis in area endemic for human paragonimiasis, a history of crab-eating plus sputum examinations, CT findings, and serodiagnosis are necessary to rule out paragonimiasis.

REFERENCES

1) The National Institute of Infectious Diseases and Infectious Diseases Control Division, Ministry of Health and Welfare: Tuberculosis, as of 1998, Japan. Infectious Agents Surveillance Report. 1999; 20: 238-239.
2) Hotez PJ, Zheng F, Long-qi X, *et al*. Emerging and reemerging helminthiases and the public health of China. Emerg Infect Dis 1997; 3: 303-310.
3) Belizario V, Guan M, Borja L, *et al*. Pulmonary paragonimiasis and tuberculosis in Sorsogon, Philippines. Southeast Asian J Trop Med Publ Health. 1997; 28; 37-45.
4) Lee KS, Hwung JW, Chung MP, *et al*. Utility of CT in the evaluation of pulmonary tuberculosis in patients without AIDS. Chest 1998; 110: 977-984.
5) Gyoten J. Changes of life stile and risk factors from epidemiological data of paragonimiasis. Jpn J Parasitol 1994; 43: 462-470. (In Japanese)
6) Nishida H. paragonimiasis in Japan, with special

reference to species and their symptoms. Saishin-Igaku 1989; 44: 843-850. (In Japanese with English summary)
7) Baelz E. Über eine neue Parasiten des Menshen. Berlin Klic Wschr. 1883; 20: 234-236.
8) Terasaki K. Studies on chromosomes of the lung flukes in Japan. J Parasitol 1977; 26: 222-236.
9) Miyazaki I. On the newly proposed lung fluke, *Paragonimus pulmonalis* (Baelz, 1880) Bull Fukuoka Med 1979; 6: 267-276. (In Japanese with English summary)
10) Milanez de Campos JR, Valente Barbas CS, Brito Filometo LT, *et al*. Human pulmonary dirofilariasis. Analysis of 24 cases from Sao Paulo, Barazil. Chest 1997; 112: 729-33.
11) Iiyama T, Sekiya Y, Itou I, Kawana B, *et al*. A human case infected with *Paragonimus westermani* from Ibaraki prefecture, Japan. Jpn J Med Technology 49: 80-83. (In Japanese)