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Case Report

A Case of Severe Paragonimiasis Miyazakii with Lung and Skin Lesions Showing Massive Egg Production in Sputum and Faeces

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Since Yokogawa *et al.* (1974) first reported human cases of paragonimiasis miyazakii, over 100 cases, majority of which were found in Kanto District, were reported in Japan (Odagiri, 1985). Thus, *Paragonimus miyazakii* is considered as one of important pathogens of zoonoses, although this lung fluke is principally a parasite of wild animals (Hatsushika, 1967). Majority of human cases resulted from ingesting freshwater crabs, *Geothelphusa dehaani* (Miyazaki and Toh, 1988), and few cases from eating uncooked flesh of wild boars, *Sus scrofa leucomistax* (Norimatsu, 1991). Pneumothorax and/or massive pleural effusion with eosinophilia are the typical clinical manifestations of paragonimiasis miyazakii and pulmonary infiltration with nodular or cavitating lesions is rather rare (Hibiya *et al.*, 1984; Odagiri, 1985). In previously reported paragonimiasis miyazakii cases, the parasite eggs were rarely detected from the patients; two cases from pleural effusion (Shibasaki *et al.*, 1975; Chiba and Terada, 1976) and two cases from sputum (Nishida and Gyoten, 1976; Imai *et al.*, 1987) including one case also from stool (Imai *et al.*, 1987). Here we report a confirmed case of paragonimiasis miyazakii with lung and skin lesions showing massive egg production in sputum and faeces.

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Case Report

The patient is a 62 years-old female who was born and grew up in Fukushima Pref. and has been working in Osaka City for 40 years. Since 1981 she has been suffering from bronchial asthma due to air pollution. She has no experience of travelling overseas. She has never eaten flesh of wild boars, *S. scrofa leukomistax*, nor freshwater crabs, *Eriocheir japonicus*.

On June 1989, the patient was admitted to the Yodogawa Christian Hospital because of high fever, cough and sputum (reddish-brown in color). Pleural effusion was noted by chest roentgenography. After unsuccessful treatment with antibiotics, she was diagnosed as PIE (pulmonary infiltration with eosinophilia) syndrome because of elevation of peripheral blood eosinophil count (10–21%) and total IgE (580 IU/ml), and she was treated with steroids. Suddenly on July 1989 epileptic seizure developed and she was diagnosed as cerebral infarction. After an improvement of neurological findings she was discharged from the hospital, although moderate eosinophilia (around 10%) remained unchanged. On January 1990, a mobile nodular lesion developed on her right anterior chest wall, which disappeared spontaneously within a week. On July 1990 she became unconscious during working and admit-

ted to the hospital. She was diagnosed again as cerebral infarction. The presence of flocculating shadows was noted in both lungs by chest roentgenography. High fever developed shortly after admission and CRP was (+++). Absolute eosinophil count was 7,500/mm^3 and remained high level (30–50%). In addition to the neurological treatment, she was treated with steroids and antibiotics for PIE syndrome. After discharge from the hospital, mobile nodular lesions reappeared on the anterior chest wall repeatedly on July 1990 and November 1991. Biopsy of the skin lesion was performed on November 1991 and eosinophilic granuloma formation was noted. At this stage she was diagnosed as allergic granulomatous angitis and treated with steroids.

On April 1992 she had an asthma attack. Because abnormal shadows were noted in both lungs, she was admitted to the hospital on May 1992 and treated with steroids. Although asthma was improved by the treatment, chest pain, cough and bloody sputum developed and continued. Computed tomogram revealed the presence of multiple nodular lesions in both lungs (Fig. 1). On 19 July 1992, a nodular skin lesion (3×1.5 cm) developed on the right chest wall, which disappeared spontaneously by 23 July. A similar skin lesion reappeared on the same site on 1 August so that this lesion was biopsied. From the biopsied specimen, a small (6×3×2 mm) Rugby ball-shaped worm having oral and ventral suckers was dissected out. Unfortunately the parasite was immediately fixed in formalin, embedded in paraffin wax, and cut at 4 μm sections (Fig. 2), so that the detailed morphological and morphometric study was impossible. Within the cross sections, the parasite eggs were not detected and the reproductive organs seemed to be poorly developed so that the parasite was identified as immature *Paragonimus* spp. Since paragonimiasis was strongly suspected, her sputum was examined and numerous parasite eggs were detected. The eggs isolated from sputum, fresh stool, and the serum from the patient were sent to the Department of Parasitology, Miyazaki Medical College for confirmation of the diagnosis and identification of parasite species.

Parasitological observations

Parasite eggs isolated from the sputum were examined directly under a microscope. Those in the stool were collected by AMS-III method and then examined. Both sputum and stool contained numerous eggs of similar size and shape (Figs. 3a, b). The eggs were pale yellow in color, thin-shelled, having a flattened operculum at one end, and rarely had knobs on the non-opercular end. From each sample 50 eggs were measured microscopically. The average and the range of the size of eggs were 74.5 (67.2–84.0) × 47.0 (42.0–52.5) μm for those in the sputum and 75.3 (65.1–84.0) × 46.3 (42.0–52.5) μm for those in the stool.

By a multiple dot-enzyme-linked immunosorbent assay (ELISA) test (Fig. 4) and an Ouchterlony's double diffusion test (Fig. 5), her serum gave stronger reaction against *P. miyazakii* than *P. westermani* antigen. Immuno-serodiagnosis for paragonimiasis miyazakii was further confirmed by an ELISA inhibition test (Fig. 6).

After diagnosis, the patient stated that, according to her relative's recommendation, she had taken the homogenate of freshwater crabs, *G. dehaani*, a famous intermediate host of *P. miyazakii*, as a traditional medicine to relieve cough on 1988. She was successfully treated with two sets of prazyquantel administration at a dose of 75 mg/kg for 2 days. The lung lesions almost disappeared and the serum antibody titer significantly decreased within 4 months after the second set of treatment; IgG-ELISA values

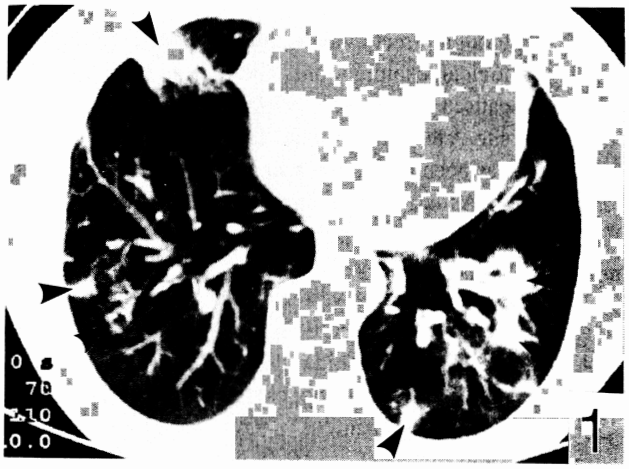
Fig. 1 A computed tomogram showing multiple cavitating lesions (arrow heads) in the lungs of the patient.

Fig. 2 Cross section of the worm dissected out from the biopsied skin. Scale bar = 1 mm

Fig. 3 Eggs isolated from sputum (a) and stool (b). Scale bar in the inset = 20μm

Fig. 4 The multiple dot-ELISA showing positive reaction against *P. miyazakii* antigen.
HS: Normal human serum, Di: *Dirofilaria immitis*, Pw: *Paragonimus westermani*, Tc: *Toxocara canis*, Pm: *Paragonimus miyazakii*, Al: *Ascaris lumbricoides*, Fh: *Fasciola hepatica*, As: *Anisakis simplex*, Se: *Spirometra erinacei*, Ad: *Ancylostoma duodenale*, Gd: *Gnathostoma doloresi*, Sr: *Strongyloides ratti*, Ts: *Trichinella spiralis*

Fig. 5 The Ouchterlony's double diffusion test in agar showing precipitin bands against *P. miyazakii* (Pm) and *P. westermani* (Pw) antigens.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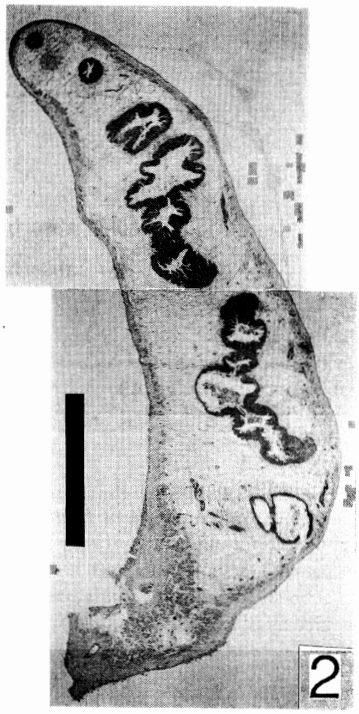
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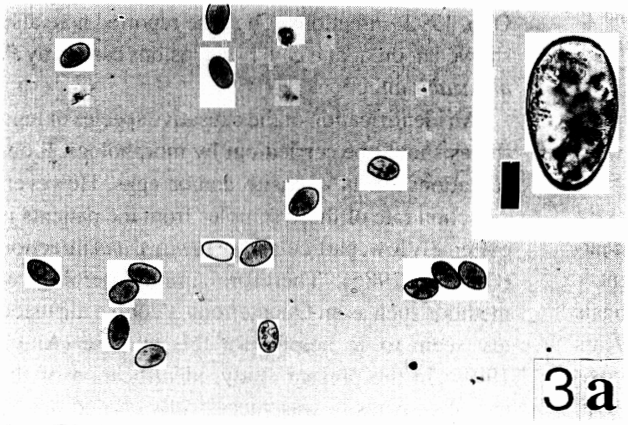
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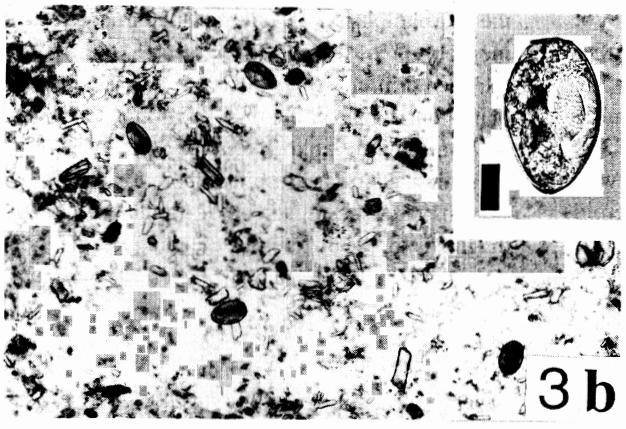
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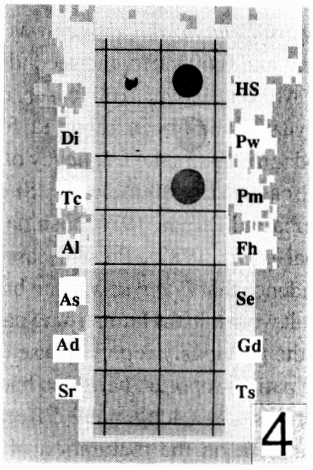
HS
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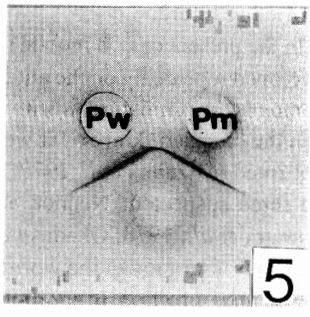
Pw
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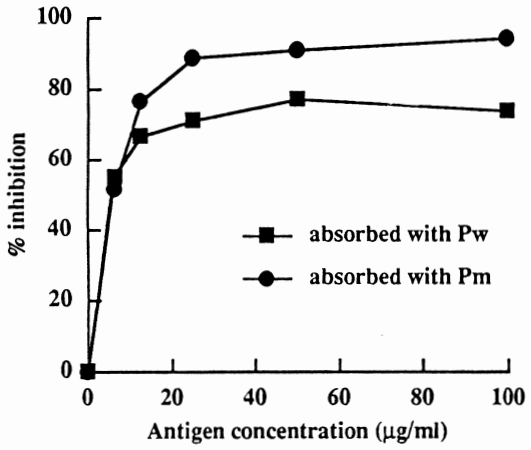

Fig. 6 ELISA inhibition test.
Various concentrations of *P. miyazakii* (●) and *P. westermani* (■) antigens were added to ×100 diluted patient's serum. After incubation at 4°C overnight, antibody titers against *P. miyazakii* antigen were measured by ELISA.

(O.D. at 405 nm) of 200-fold diluted patient's sera against *P. miyazakii* antigen was 1.815 before treatment and 0.695 after the second set of treatment.

Although over 100 cases of paragonimiasis miyazakii has been reported for about 20 years (Odagiri, 1985), the frequency of parasite egg-positive cases was extremely low (Shibasaki *et al.*, 1975; Chiba and Terada, 1976; Nishida and Gyoten, 1976; Imai *et al.*, 1987). Present case provide a further evidence that *P. miyazakii* can become fully mature adult worms in the human lung parenchyma. Similar to the previously reported case (Imai *et al.*, 1987), the patient reported here also had been treated with steroids for a long time. Effects of such steroid treatment on the maturation of worms should be clarified in future.

In the present case, a mobile nodular skin lesion developed repeatedly on the anterior chest wall and eventually an immature worm was dissected out from the biopsied skin. So far we could gather, two confirmed (Mizuno *et al.*, 1977; Akao *et al.*, 1988) and three suspected (Nishida and Gyoten, 1976; Ichimura *et al.*, 1978; Okada *et al.*, 1981) cases of cutaneous migration of the worms were reported in *P. miyazakii* infection. In addition to the skin lesion, the patient showed neurological symptoms twice which were diagnosed as cerebral infarction. Although direct evidence was not obtained by radiological examinations, these symptoms might be caused by transient ectopic migration of the parasite. A few cases of cerebral migration of *P. miyazakii* has been reported (Odagiri, 1985).

As has been pointed out by Norimatsu (1991), the concept that pulmonary infiltration with nodular or cavitating lesions is characteristic for paragonimiasis westermani and pneumothorax and pleural effusion is typical for paragonimiasis miyazakii (Yoshida, 1991) is no longer tenable because the cases opposing to this have been accumulated both in *P. westermani* (Matsuoka *et al.*, 1986; Ichiki *et al.*, 1989; Norimatsu, 1991) and *P. miyazakii* (Takahashi *et al.*, 1975; Imai *et al.*, 1987; Ono, 1992) infections. The case reported here also showed nodular and cavitating lesions caused by *P. miyazakii* infection.

An identification of the causative species of lung flukes should be carried out by morphological observations of the parasite and/or eggs. However, detection rate of these samples from the patients is extremely low, particularly in *P. miyazakii* infection (Odagiri, 1985). Therefore, immunoserological methods such as an Ouchterlony's double diffusion test seem to be helpful for this purpose (Araki, 1991). In the present study, identification of the causative parasite was successfully carried out by the morphology of eggs in the sputum and faeces, morphology of the parasite dissected out from the biopsied skin, and also by using three different ways of immunodiagnostic methods, multiple dot-ELISA, Ouchterlony's double diffusion in agar and ELISA-inhibition test. The results reported here clearly demonstrates the reliability of immunoserological diagnosis for the differential diagnosis of infections caused by two *Paragonimus* species, *P. westermani* and *P. miyazakii*.

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