[Jpn. J. Parasitol., Vol. 45, No. 3, 242–246, June, 1996]

Case Report

A Case of Chronic Pleural Empyema by *Paragonimus westermanii* Infection Resistant to Chemotherapy and Cured by Surgical Decortication

MASAKI TOMITA[1)], HIDEKI ICHINARI[1)], YASUNORI MATSUZAKI[1)], KOICHIRO SHIBATA[1)], YASUNORI KOGA[1)], RYOKO YAMAGUCHI[2)], HIROSHI MUKAI[2)], HIDEO MASUMOTO[2)], SHIGERU MATSUKURA[2)], HARUHIKO MARUYAMA[3)] AND YUKIFUMI NAWA[3)]

[1)]*2nd Department of Surgery,* [2)]*3rd Department of Internal Medicine, and* [3)]*Department of Parasitology, Miyazaki Medical College, Kiyotake, Miyazaki 889-16, Japan.*

(Accepted April 9, 1996)

Key words: *Paragonimus westermanii*; paragonimiasis; pleural effusion; chronic empyema.

Paragonimiasis is an important food-borne parasitic zoonosis. Miyazaki Prefecture, being located in the south-eastern part of Kyushu District, Japan, used to be an endemic area of paragonimiasis (Hayashi, 1978). Even nowadays a few new cases have been found sporadically in this area every year (Nawa, 1991). As far as we have dealt with, almost all these newly discovered cases were cured effectively with either bithionol (Bithin®, Tanabe Pharmaceutical Co., Osaka: no longer available) or praziquantel (Biltricide®, Beyer, Germany). Here we report a case of chronic pleural empyema due to paragonimiasis which was resistant to the repeated chemotherapy with these anthelminthics. The pleural lesion of the patient was eventually removed by surgical decortication.

Case Report

The patient is a 57 year-old male who was born and grown up in Tano-Cho, near Miyazaki City, Japan. He has never been abroad. He often eats flesh of wild boars and freshwater crabs. He visited a regional hospital on March 19, 1994, because of high fever, cough and sputum for 4 days. A plain chest radiogram showed diffuse infiltration in the left lower lung field and right pleural effusion. Although his symptoms as well as the infiltration in the left lung field were improved by treatment with antibiotics, pleural effusion was not decreased. Because an immediate type skin test with *Paragonimus westermanii* antigen was positive, he was given praziquantel (PZQ: 25 mg/kg/day) for 2 days. In spite of PZQ treatment, pleural effusion remained unchanged on radiological examinations 6 weeks later (Figs. 1 and 2), so that he was admitted to the 3rd Department of Internal Medicine, Miyazaki Medical College, for further work-up. Laboratory data on admission were as follows; total white blood cell: 7200/mm^3 (57% neutrophils, 33% lymphocytes, 5.5% monocytes, 4.0% eosinophils, 0.4% basophils), total serum IgE: 192.1 IU/ml, LDH 255 IU/dl. Pleural effusion was turbid, pale yellow in color, and contained 4.71 g/dl protein, 73 mg/dl glucose, 434 IU/ml LDH, 27.8 U/l adenosine deaminase, and 1.5 ng/ml carcinoembryonic antigen. Cytological examination of the pleural effusion showed 25% neutrophils, 39% lymphocytes and 36% macrophages but no eosinophils. Ultrasonography showed that the pleural lesion was compartmentalized by septal formation with fibrous tissues (Fig. 3). The biopsied pleura showed chronic inflammatory changes but no signs of bacterial infec-

Correspondence: Yukifumi Nawa, paras@macqm.miyazaki-med.ac.jp

富田雅樹[1]，市成秀樹[1]，松崎泰憲[1]，柴田紘一郎[1]，古賀保範[1]，山口涼子[2]，迎　寛[2]，増本英雄[2]，松倉茂[2]，丸山治彦[3]，名和行文[3]，([1]宮崎医科大学第2外科，[2]宮崎医科大学第3内科，[3]宮崎医科大学寄生虫学教室)

tion or malignancy.

By a multiple dot-ELISA test, the patient's serum, but not pleural effusion, specifically bound to *P. westermanii* antigen (Fig. 4). After in-

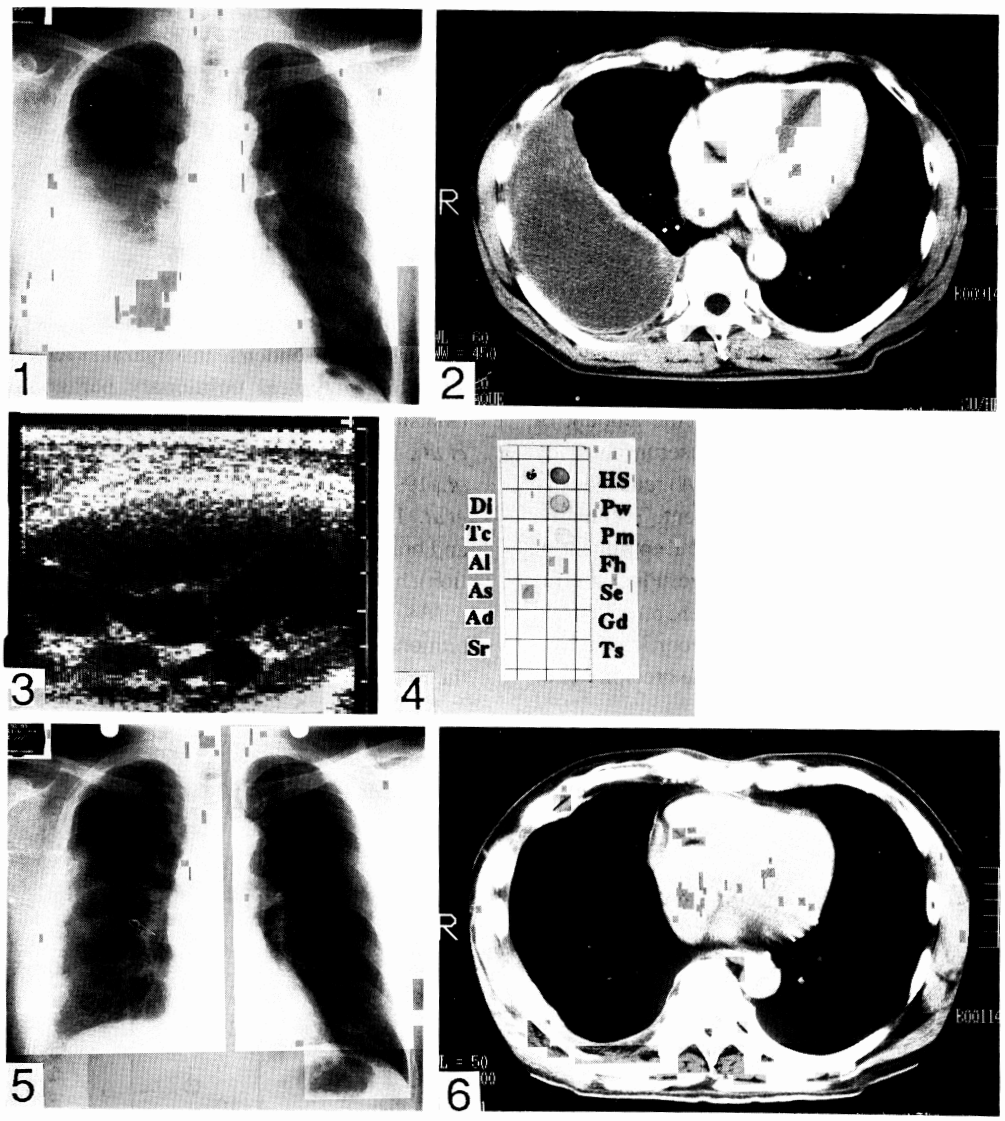

Fig. 1 Chest radiogram showing right pleural effusion.

Fig. 2 Computed tomogram showing right pleural effusion and thickening of pleura.

Fig. 3 Ultrasonogram of the pleural lesion showing extensive compartmentalization by fibrous septa.

Fig. 4 Multiple-dot ELISA showing positive reaction of the patient's serum (×200 dilution) against *P. westermanii* antigen.

HS: Normal human serum, Di: *Dirofilaria immitis*, Pw: *Paragonimus westermanii*, 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 Chest radiogram after surgical decortication of the pleural lesion.

Fig. 6 Computed tomogram taken at the same time as Fig. 5.

complete aspiration of pleural effusion, he was treated again with PZQ (75 mg/kg/day) for 2 days. Although the amount of pleural effusion was not decreased for over a month, he had become asymptomatic so that he was discharged and followed up as an out-patient. One month after the discharge pleural effusion still remained at the same degree, so that he had received the third set of PZQ (75 mg/kg/day) treatment for 2 days. By laboratory examinations, the pleural effusion did not contain bacteria or malignant cells. Two months after the third set of PZQ treatment, specific antibody to *P. westermanii* in the serum was still positive, and pleural effusion did not reduce in amount and became bloody. Since PZQ seemed to be ineffective, he had received a set of bithionol treatment (30 mg/kg/day: every alternate days for 20 days). However, the amount of pleural effusion did not reduced and serum antibody titer (measured by microplate ELISA) reduced only slightly one month after the treatment. Eventually, the patient was admitted to the 2nd Department of Surgery, Miyazaki Medical College. Pleural effusion and the inner fibrous tissues were removed and the thickened pleura was entirely decorticated. Neither worms or eggs were found in the precipitates of the pleural effusion. By histopathological examinations, the thickened pleura composed of homogenous fibrous tissue almost free from inflammatory cell infiltration. Neither worms nor eggs were found in the pleural tissues examined. After surgical treatment, pleural effusion never reappeared (Figs. 5 and 6) and the serum antibody titer measured by microplate ELISA slowly but gradually decreased except for transient rise shortly after surgical operation (Fig. 7).

Discussion

As a food-borne zoonotic parasitosis, paragonimiasis is still endemic in Miyazaki Prefecture. In addition to typical pulmonary paragonimiasis (Matsuoka *et al.*, 1986; Ichiki *et al.*, 1989; Taniguchi *et al.*, 1995), cases of a cutaneous lesion (Ogata *et al.*, 1990), or of old lesions in the liver (Nabeshima *et al.*, 1991), peritoneal cavity (Shimao *et al.*, 1994) and brain (Marutsuka *et al.*, manuscript in preparation), have also been accidentally found in this area.

As for the chemotherapy of paragonimiasis, bithionol, which was initially developed as an anthelminthic drug for veterinary use, was proven to

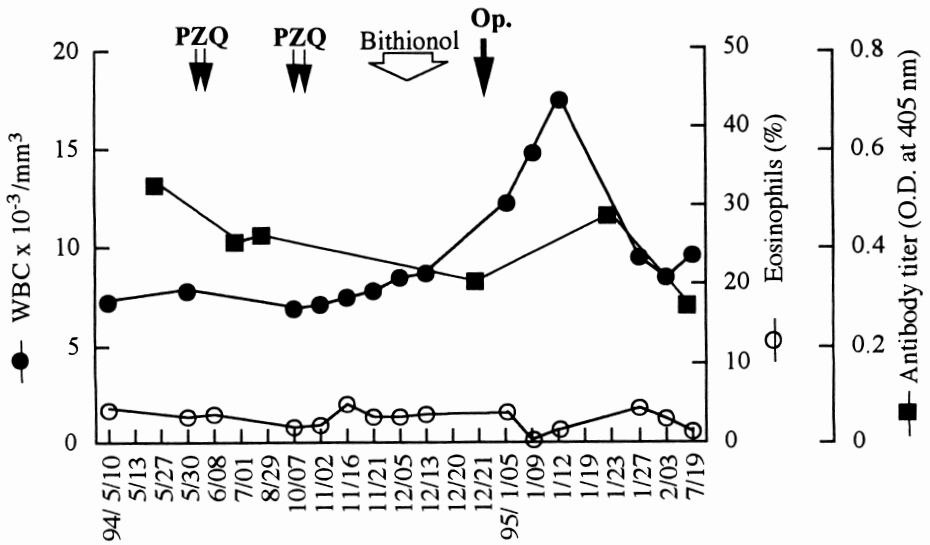

Fig. 7 Clinical course of the patient.
Clinical course of the patient during the first admission to the regional hospital during March to May 1994 was not included in this figure.
PZQ: praziquantel (75 mg/kg/day), Op: surgical decortication of thickened pleura.

be effective for paragonimiasis (Yokogawa *et al.*, 1963). Unfortunately, however, the pharmaceutical company has recently quitted to produce this effective drug. As an alternative of bithionol, PZQ, which was developed for the treatment of schistosomiasis (reviewed by Davis, 1982), was proven to be effective for paragonimiasis (Rim and Chang, 1980), and also other trematode (Wegner, 1984) and cestode (Thomas and Gönnert, 1977) infections. Although the manufacturer's recommended dose of PZQ is 40 mg/kg/day for 2 days, a higher dose (75 mg/kg/day for 2–3 days) was preferred to obtain complete cure of paragonimiasis (Rim and Chang, 1980). In the present study, in spite of extensive chemotherapy with three sets of PZQ and an additional set of bithionol, the amount of pleural effusion was not reduced though other symptoms were markedly improved. Although the precise reason for ineffective chemotherapy is unclear, one possible explanation is that *Paragonimus* worm(s) invaded into pleural cavity only transiently to trigger nonspecific, aseptic chronic exsudative inflammations. In fact, neither worms or eggs was detected in the pleural effusion or thickened pleural tissues. Furthermore, eosinophil infiltration was not observed in the pleural effusion and specific antibody was detected only in the serum but not in the pleural effusion. If this were the case, parasite should be located ectopically somewhere else such as in the peritoneal cavity, since no lesion was found in the lung parenchyma and serum antibody remained positive long after the treatments. Alternatively, inefficacy of chemotherapy might be due to dilution of the drug by massively retained pleural effusion.

In the present study, pleural thickening was already observed when the patient first visited a regional hospital, and the drainage of pleural effusion was unsuccessful because of compartmentarization of the lesion by septal formation with fibrous tissues, suggesting that the disease was already in chronic stage. Dietrick *et al.* (1981) reported 58 cases of chronic pleural empyema managed successfully by decortication, and 16 out of 58 cases were of a complication of *P. westermanii* infestation. Similarly, Norimatsu (1986) reported 4 cases of surgically treated paragonimiasis with pleural effusion and recommended the extensive drainage of pleural effusion before starting chemotherapy for the patients with pleural effusion. Since delayed diagnosis of the disease and/or insufficient drainage often causes complicated conditions such as chronic pleural empyema or insufficient inflation of lungs (Norimatsu, 1991), physicians practicing in the endemic area should be aware of such complications.

Acknowledgments

The authors are grateful to Dr. M. Niimura, Associate Professor, Department of Parasitology, Chiba University School of Medicine, for providing us with bithionol. Special thanks goes to Ms. Ayumi Tanaka for her excellent technical assistance for immunodiagnosis.

References

1) Davis, A. (1982): Management of the patient with schistosomiasis. In; Schistosomiasis, Epidemiology, Treatment and Control. P. Jordan and G. Webbe eds. William Heinemann Medical Books, London, pp. 184–226.
2) Dietrick, R. B., Sade, R. M. and Pak, J.-S. (1981): Results of decortication in chronic empyema with special reference to paragonimiasis. J. Thor. Cardiovasc. Surg., 82, 58–62.
3) Hayashi, E. (1978): A study on paragonimiasis. In; Medical History of Miyazaki Prefecture, pp. 1627–1680, I Tashiro ed., Miyazaki Prefectural Doctors Association (in Japanese).
4) Ichiki, M., Suzumiya, H., Hayakawa, K., Imai, J. and Nawa, Y. (1989): Two cases of paragonimiasis westermani with pleural effusion in young girls living in the southern part of Miyazaki Prefecture, Japan. Jpn. J. Parasitol., 38, 392–395.
5) Matsuoka, H., Shioiri, S., Nakashima, T., Tachibana, N. and Tsuda, K. (1986): A case of paragonimiasis westermani accompanying pleural effusion. Jpn. J. Chest Dis., 45, 418–433 (in Japanese with English abstract).
6) Nabeshima, K., Inoue, T., Sekiya, R., Tanigawa, M., Koga, Y., Imai, J. and Nawa, Y. (1991): Intrahepatic paragonimiasis – A case report –. Jpn. J. Parasitol., 296–300.
7) Nawa, Y. (1991): Recent trends of paragonimiasis westermani in Miyazaki Prefecture, Japan. South-east Asian J. Trop. Med. Publ. Hlth., 22 (Suppl.), 342–344.
8) Norimatsu, Y. (1986): Paragonimiasis. Respiration (Kokyu), 5, 144–151 (in Japanese).
9) Norimatsu, Y. (1991): Paragonimiasis. J. Therapy (Chiryo), 73, 2435–2438 (in Japanese).
10) Ogata, K., Miyagi, T., Inoue, S., Imai, J. and Nawa, Y. (1990): Cutaneous paragonimiasis – A case report –. Jpn. J. Parasitol., 39, 63–66.
11) Rim, H.-J. and Chang, Y.-S. (1980): Chemotherapeutic effect of niclofolan and praziquantel in the treatment of paragonimiasis. Korea Univ. Med. J., 17, 113–126.

12) Shimao, Y., Koono, M., Ochiai, A., Fujino, A., Ide, H., Kobayashi, T., Maruyama, H., Itoh, H. and Nawa, Y. (1994): A case report of intraperitoneal granuloma due to occult infection with Paragonimus sp. Jpn. J. Parasitol., 43, 315–317.
13) Taniguchi, H., Mukai, H., Ashitani, J., Ii, T., Masumoto, H., Matsukura, S., Matsuzaki, Y., Shibata, K. and Koga, Y. (1995): Four cases of paragonimiasis westermani with a nodular lesion indistinguishable from lung cancer. Miyazaki Med. J., 19, 229–233 (in Japanese).
14) Thomas, H. and Gönnert, R. (1977): The efficacy of praziquantel against cestodes in animals. Z. Parasitenkd., 52, 117–127.
15) Wegner, D. H. G. (1984): The profile of the trematodicidal compound praziquantel. Drug Res., 34, 1132–1136.
16) Yokogawa, M., Iwasaki, M., Shigeyasu, M., Hirose, H., Okura, T. and Tsuji, M. (1963): Chemotherapy of paragonimiasis with bithionol. V. Studies on the minimum effective dose and changes in abnormal X-ray shadows in the chest after treatment. Amer. J. Trop. Med. Hyg., 12, 859–869.