

CASE REPORT

PARAGONIMIASIS IN NAN PROVINCE, NORTHERN THAILAND

Dorn Watthanakulpanich¹, Jitra Waikagul¹, Paron Dekumyoy¹, Panida Muangkhum², Rangson Praevanit³ and Srisuchart Mongkhonmu³

¹Department of Helminthology, Faculty of Tropical Medicine, Mahidol University, Bangkok; ²Thung Chang Hospital, Thung Chang District, Nan Province; ³Bangkok School of Tropical Medicine, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand

Abstract. Two cases of paragonimiasis were identified within the hill-tribe population living on the Thai-Laotian border of Nan Province, northern Thailand, where information on *Paragonimus* was then still limited. The patients were in the habit of eating improperly cooked crabs and freshwater prawns. A survey for natural intermediate hosts to complete the life cycle was in progress at that time, and the detection of paragonimiasis cases indicated that there was persistence of paragonimiasis in the endemic area of Nan Province.

INTRODUCTION

Paragonimiasis is an important cause of pulmonary disease worldwide. It is a food-borne parasitic disease caused by the *Paragonimus* fluke that lives in cavities in the lungs or other viscera of mammals. Only two species have been found that parasitize humans in Southeast Asia: *P. heterotremus* and *P. westermani*. In Thailand, the former is known as the pathogen of human paragonimiasis (Miyasaki and Harinasuta, 1966; Vanijanonta *et al*, 1981; Cheunsuchon *et al*, 1998) while infection by the latter has not been reported (Dekumyoy *et al*, 1998). The signs and symptoms are chronic cough and bloody sputum, which are similar to those for tuberculosis. Transmission of paragonimiasis in Thailand is related to the habit of eating raw or improperly cooked mountain or waterfall crabs, which are the second intermediate hosts.

In Thailand, there have been some occasional cases or paragonimiasis reported in the remote, hilly areas of the northern region, which includes Nan Province, along the border with Lao PDR. The first human case of paragonimiasis was reported in 1928 from a male inhabitant of

Lom Sak District, Phetchabun Province, northern Thailand (Prommas, 1928). Other areas in the north from which cases were reported include Chiang Rai (Sutthipunthu *et al*, 1978), Chiang Mai (Ratdilokpanich, 1980); Nan (Bunnag *et al*, 1981); Mae Hong Son (Ekarohit *et al*, 1990); Lamphun (Thamprasert, 1993), and Phitsanulok (Pariyanonda *et al*, 1997).

The first aim of this report is to remind clinicians of paragonimiasis and, if a patient has a history of chronic cough with bloody sputum, this condition should be considered in differential diagnosis along with tuberculosis, fungal infections and lung cancer. The second aim is to stimulate further research to determine what are the reservoir hosts for the purposes of prevention and control. In this regard, it would be quite interesting to identify what intermediate hosts are involved in the life cycle of the *Paragonimus* trematode.

CASE 1

A 13-year-old Thai-Hmong girl, who resided in Pang Kae, Thung Chang District, had about 5-10 *Paragonimus* eggs/HD in her stool examination by Kato Katz thick smear and direct smear methods in a deworming program project. The eggs were oval and operculated in outline and measured about 80-100 x 40-50 μ (Fig 1). She had a 3-year history of chronic productive cough,

Correspondence: Dr Dorn Watthanakulpanich, Department of Helminthology, Faculty of Tropical Medicine, Mahidol University, Bangkok 10400, Thailand.
Tel: 66 (0) 2643-5600; Fax: 66 (0) 2643-5600
E-mail: tmdwl@mahidol.ac.th

particularly in the early morning and sometimes with old bloody sputum, but no history of chest pain, anorexia, weight loss, or malaise. She was the eldest daughter of her family with two younger sisters and one younger brother. No other family member had similar symptoms, and her family history was negative for tuberculosis. She had a history of eating improperly cooked mountain crabs from the stream flowing near her parents' lychee gardens, as her mother used those crabs for cooking crab sauce.

Physical examination revealed a thin girl, fully conscious, having no obvious clinical signs. She also had no fever or respiratory distress and had normal vital signs. She was adequately nourished and weighed 49 kg. The abnormal physical findings were dullness to percussion and absent breath sounds in the lower two-thirds of the left chest, with secretory bronchi, and decreased breath sounds over the left hemithorax with no crepitation. There was no lymphadenopathy and no subcutaneous nodules presented on her body. The other physical examinations were within normal limits, except that there were many warts on the fingers of both hands and the toes of both feet. The complete blood count (CBC) showed a hematocrit of 36%, and a WBC count of 7,900 cells/mm³ with 63% neutrophils, 31% lymphocytes and 6% eosinophils. Acid-fast stained sputum was negative, and no *Paragonimus* eggs were obtained by sputum examination. Chest radiograph showed patchy infiltration in the middle lobe of the left lung that displayed a cluster of well-defined densities in the left mid-zone, in which translucent or cystic areas had developed. The general impression was of bubbles developing with a shadow of eccentric wall thickening with an enlarged right hilum (Fig 2). Diagnosis was made (Fig 3) and treatment with praziquantel was initiated. Praziquantel 25 mg/kg/day in three divided doses was administered as a 3-day course. No side effects were noted.

CASE 2

A 10-year-old Thai-Karen girl, who resided in Huai Nam-ree Phatthana, Chaloe Phra Kiat District, had one operculated egg in her stool as examined by Kato Katz thick smear method, showing a uniformly thickened birefringent shell,

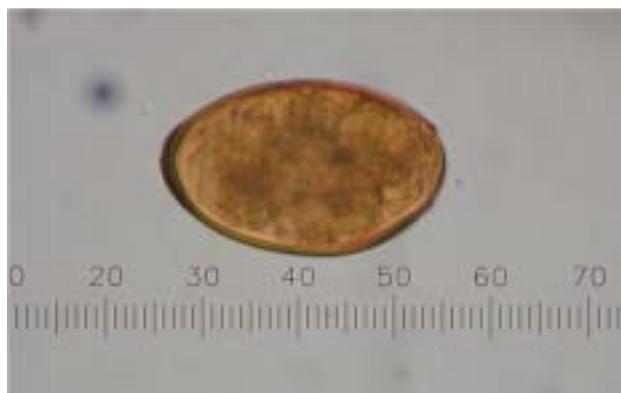


Fig 1—Morphology of *Paragonimus* egg found in the stool examination.

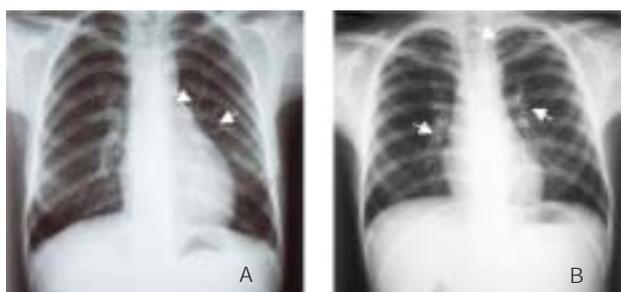


Fig 2—Chest radiographs of two patients: case A (Lt lung) shows ring-like cysts (arrows) with eccentric wall thickening (A, case 1) while case B (Lt lung) shows oval ring shadow with speckled calcification (arrows)(B, case 2).

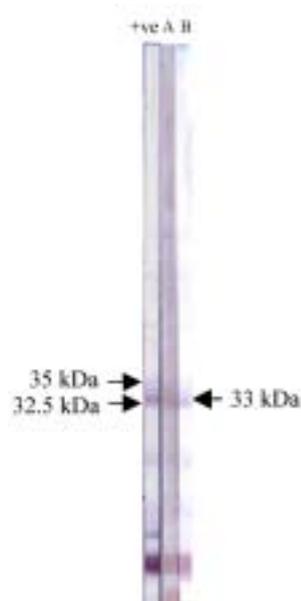


Fig 3—Immunoblot patterns of patients' infected sera (A, case 1 and B, case 2) comparison with one positive control pooled serum (+ve).

which is a feature of the *Paragonimus* species (Radomyos, personal communication, May, 2003). Her primary complaint was of chronic cough for 3 years, particularly in the morning, with no old bloody sputum. She was the third child of her family, with one elder brother, one elder sister, and one younger brother. Nobody had similar symptoms, and her family history was negative for tuberculosis. Improperly cooked mountain crab, obtained from a nearby flowing stream, was part of her diet.

On physical examination, the patient looked thin, fully conscious, well-nourished with no anemia, and weighed 47 kg. She was afebrile, had no dyspnea, and had normal vital signs. No subcutaneous mass was found. The remainder of her physical examination was normal, including the respiratory system. Laboratory investigations showed a hematocrit of 34%, and a WBC count of 11,800 cells/mm³ with the differential measured as 61% neutrophils, 38% lymphocytes, and 1% basophils. Sputum specimen was not performed for acid-fast bacilli as her sputum could not be collected, and no *Paragonimus* eggs were found. Her chest radiograph (Fig 2) revealed a smooth oval shadow that was hazy, with ill-defined margins in the upper left zone, possibly resulting from encysted pleural fluid, which gave it a cotton wool appearance. This case also showed speckled calcification, in one hilum each, with an associated shadow in the lung parenchyma. The patient received treatment with praziquantel, 25 mg/kg/three times for 3 days. No side effects were noted. Follow-up was to be scheduled to assess her response to therapy.

DISCUSSION

Two cases of pulmonary paragonimiasis have been reported; both were children who lived in districts near the Thai-Laotian border. These districts were in hilly areas where streams flowed down from the mountains to join the Nan river. Wild animals, such as tigers, bears and wild pigs inhabit the area, and they have been reported to be reservoir hosts of the *Paragonimus* worm (Liat and BeHerton, 1977; Kong *et al*, 1994). It was likely that these children became parasitized by the consumption of the infective metacercaria larval stage of the *Paragonimus* worm that had contaminated uncooked or inadequately cooked

freshwater crab (Sharma, 1989). Samples of crabs that live in or near streams in these areas should be collected and screened for metacercariae. However, contamination could also have occurred during food preparation as the hemolymph of the crabs could carry the metacercariae of *Paragonimus* worm (Komalamisra *et al*, 1988; Sachs and Cumberland, 1990). People in these areas have the habit of eating uncooked crab, shrimp and fish, and thus might have acquired infection in this way. The incidence of paragonimiasis in these two patients had been mainly associated with consumption of improperly cooked crabs harboring metacercariae.

These patients looked healthy as they were young and still in an uncomplicated status. They both developed a chronic productive cough, particularly in the early morning, with blood-tinged sputum for Case 1. The duration of symptoms was equally three years; however, few signs were observed on physical examination. The diagnosis of paragonimiasis was not suspected because the patients were healthy, except for the clinical manifestation of chronic cough and hemoptysis. Clinical diagnosis had to differentiate between bronchitis, pneumonia, and tuberculosis due to the similar symptoms. Unfortunately, acid-fast staining of a sputum examination for Case 2 could not be performed due to a difficulty in acquiring an adequate specimen sample. Although the patients' symptoms could be similar to those of tuberculosis, the clinical symptoms did not seem to be as severe as it would have been considering the duration of the condition, and the family history was negative for TB. The infection may have been unrecognized as these affected patients had limited access to medical services, because they were of low economic status and the patients did not visit the hospital until the condition became chronic. No subcutaneous nodules were found in our patients, which was consistent with a previous study indicating that extrapulmonary paragonimiasis had rarely been reported in Thailand (Thamprasert, 1993). Neither of these patients had any evidence of malignancy. Diagnosis was done by identifying the characteristic operculated egg in the sputum, stool or pleural fluid (Vajrasthira, 1969; Ogakwu and Nwokolo, 1973). Direct microscopic examination of the patients' sputum and stool samples was per-

formed; however, eggs were not found in the sputum, which agrees with a previous study where sputum examination for eggs may yield negative results (Panarunothai *et al*, 1988). Microscopic examination of the stool samples revealed the oval-shaped characteristics of *Paragonimus* eggs (Fig 1). The eggs might be released in the stool after the sputum has been swallowed. Such means of infection was suspected, therefore, the diagnosis was confirmed serologically by immunoblot technique, which was quite reliable for the accurate diagnosis of paragonimiasis as indicated by the parasite-specific IgG antibody. This test would be particularly valuable with patients who are unable to produce sputum at the time of collection, as was the case with one of our patients, or for apparently healthy persons with chronic cough and hemoptysis.

These two patients were finally diagnosed with paragonimiasis based on a history of chronic cough and consumption of improperly cooked crabs, the presence of *Paragonimus* eggs in the stool, and positive results by immunoblotting. Both cases were infected with *P. heterotremus* because of the antibody reaction against 32.5, 33 and 35 kDa of *P. heterotremus* adult worm extract (Dekumyoy *et al*, 1995). It was also found that the infection caused by *P. heterotremus* was the same as previously reported, confirming that *P. heterotremus* is the primary cause of paragonimiasis in Thailand (Miyazaki and Harinasuta, 1966).

Chest radiograph showed worm cyst formations in the left lungs of both patients, with chronic lung lesions of surrounding patchy infiltration. The left lung is more commonly involved than the right. Previous reports also indicated that cystic changes were the main manifestation of paragonimiasis on chest radiograph (Ogakwu and Nwokolo, 1973; Johnson and Johnson, 1983; Im *et al*, 1992). A cyst containing 1-7 worms was seen as a swollen mass, 0.5-2.0 cm, in the pleura. Plasma cells, lymphocytes, macrophages, epithelioid cells, multinucleated giant cells, eosinophils, and polymorphonuclear leukocytes were found with worms and eggs inside the cyst. The cyst was connected to bronchioles permitting eggs to escape into the respiratory tree. Nodular shadows (2 to 3 cm in di-

ameter) were seen in both patients. Although no radiographic appearance from the present series can be said to be pathognomonic of pulmonary paragonimiasis, a combination of appearances may be highly suggestive in a patient with typical blood-stained sputum in an endemic area.

Praziquantel has proven effective for paragonimiasis, both in adults and children (Bunnag *et al*, 1981; Ekarohit *et al*, 1990) and could be the drug of choice to treat the infection, due to the short treatment duration. The recommended dose was 25 mg/kg, three times a day, for 3 consecutive days, resulting in a 100 % cure rate (Srisont, 1983; Yaemput *et al*, 1988).

In conclusion, human infection with *Paragonimus* is generally located in the respiratory tract. Similar to our cases, and in most reports, the initial characteristic clinical manifestation was related to a history of chronic cough, and the imaging studies were similar. Although we did not recover any *Paragonimus* egg from sputum samples, the positive results of stool examinations and immunoblotting tests were sufficient to confirm the diagnosis of paragonimiasis. Changes in pulmonary lesions were seen in chest radiographs of both patients and this suggested paragonimiasis. Pulmonary findings include significant cyst worms with infiltrative lung lesions. Praziquantel treatment was very effective and had minimal side effects. Early diagnosis and treatment with praziquantel is therefore necessary for paragonimiasis.

ACKNOWLEDGEMENTS

This work was supported in part by a grant from the Ministry of Public Health and Mahidol University. The authors wish to thank Prof Prayong Radomyos and Assoc Prof Mario Riganti, for their assistance in confirming *Paragonimus* eggs in the patients' stool examinations and critically reading the chest radiographs, respectively; Assoc Prof Wanna Maipanich, Mr Chatree Muennoo, Mr Surapol Sanguankiat, Mrs Supaporn Nuamtanong and Mrs Somchit Pubampen of the Department of Helminthology for their assistance in stool examination. We are also grateful to Mrs Natiya Panyadet, staff of Thung Chang Hospital, for her assistance in

laboratory facilities; Mr Wallop Pakdee for his assistance in immunoblot analysis; and Mrs Tippayarat Yoonuan (PhD student) for information on paragonimiasis in northern Thailand.

REFERENCES

- Bunnag D, Harinasuta T, Viravan C, Garcia DP. Paragonimiasis: endemic foci along the Riparian areas of Mekong River. *Southeast Asian J Trop Med Public Health* 1981; 12: 127-8.
- Cheunsuchon B, Mahakittikun V, Junnoo V. Paragonimiasis: a case report from Kanchanaburi Province, Thailand. *Siriraj Hosp Gaz* 1998; 50: 115-8.
- Dekumyoy P, Setasuban P, Waikagul J, Yaemput S, Saguankiat S. Human lung flukes *Paragonimus heterotremus*: differentiation of antigenic proteins of adult worms by enzyme-linked immunoelectrotransfer blot technique. *Southeast Asian J Trop Med Public Health* 1995; 26: 434-8.
- Dekumyoy P, Waikagul J, Eom KS. Human lung fluke *Paragonimus heterotremus*: differential diagnosis between *Paragonimus heterotremus* and *Paragonimus westernmani* infections by EITB. *Trop Med Int Health* 1998; 3: 52-6.
- Ekarohit D, Chesdapan C, Thitasut P, Sukonthason K, Choochote W. Paragonimiasis in Mae Hong Son Province, Northern Thailand: Case report. Proceedings of the 33rd SEAMEO TROPMED Regional Seminar, Chiang Mai, Thailand 1990: 340-1.
- Im JG, Whang HY, Kim WS, Han MC, Shim YS, Cho SY. Pleuropulmonary paragonimiasis: radiologic findings in 71 patients. *AJR Am J Roentgenol* 1992; 159: 39-43.
- Johnson RJ, Johnson JR. Paragonimiasis in Indochinese refugees: roentgenographic findings with clinical correlations. *Am Rev Respir Dis* 1983; 128: 534-8.
- Komalamisra C, Asavisanu R, Setasuban P. Distribution of *Paragonimus heterotremus* metacercariae in fresh water crab, *Tiwaripotamon beusekoma*-Bott 1970. *Southeast Asian J Trop Med Public Health* 1988; 19: 337-9.
- Kong Y, Yong HJ, Cho SY. Infectivity of *Paragonimus westernmani* developing in a final host to another final host. *Korean J Parasitol* 1994; 32: 277-80.
- Liat LB, BeHerson C. *Paragonimus westernmani* in Malaysian Felidae and Viverridae: probable modes of transmission in relation to host feeding habits. *J Helminthol* 1977; 295-9.
- Miyazaki I, Harinasuta T. The first case of human paragonimiasis caused by *Paragonimus heterotremus* Chen & Hsia, 1964. *Ann Trop Med Parasitol* 1966; 60: 509-14.
- Ogakwu M, Nwokolo C. Radiological findings in pulmonary paragonimiasis as seen in Nigeria: a review based on one hundred cases. *Br J Radiol* 1973; 46: 699-705.
- Panarunothai S, Sukmuang U, Dhiloklerd M, et al. Endemic area of *Paragonimus heterotremus*, Amphoe Nonemaprang, Phisanulok Province. *Reg 6 Med J* 1988; 2: 1-8 (In Thai).
- Pariyanonda S, Naiyanetr P, Maleewong W, Theraborn B. The edible crabs intermediate host of lung flukes *Paragonimus* spp in Loei and Phisanulok provinces [Abstract]. The Annual Meeting of the Thailand Association for Parasitology and Tropical Medicine, 14 March 1997.
- Prommas C. Paragonimiasis, opisthorchiasis and madura foot. *J Med Assoc Thai* 1928; 11: 67-77.
- Ratdilkopanch K. Pulmonary paragonimiasis: a case report. *Chiang Mai Med Bull* 1980; 19: 147-51.
- Sachs R, Cumberlidge N. Distribution of metacercariae in freshwater crabs in relation to *Paragonimus* infection of children in Liberia, West Africa. *Ann Trop Med Parasitol* 1990; 84: 277-80.
- Sharma P. The man who love drunken crabs. A case of pulmonary paragonimiasis. *Chest* 1989; 95: 670-2.
- Srisont D. Paragonimiasis in Nakorn Nayok Hospital. *Bull Med Serv* 1983; 8: 573-8.
- Sutthipunthu P, Songthanasak T, Kamboonruang C, Silprasert W, Menakarit W. Paragonimiasis: a case report from Chiang Rai Province, Northern Thailand. *J Med Assoc Thai* 1978; 61: 427-33.
- Thamprasert K. Subcutaneous abscess of neck, a granulomatous reaction to eggs of *Paragonimus*: a case report from northern Thailand. *Southeast Asian J Trop Med Public Health* 1993; 24: 609-11.
- Vajrasthira S. Paragonimiasis in Thailand. In: Harinasuta C, ed. Proceedings of the Fourth Southeast Asian Seminar on Parasitology and Tropical Medicine, Schistosomiasis and other Snail-transmitted Helminthiasis. Bangkok: Thai Watana Panich Press, 1969: 299-304.
- Vanijanonta S, Radomyos P, Bunnag D, Harinasuta T. Pulmonary paragonimiasis with expectoration of worms: a case report. *Southeast Asian J Trop Med Public Health* 1981; 12: 104-6.
- Yaemput S, Waikagul J, Visiassuk K, Maipanich W. Susceptibility of *Tricula aperta* (β race) to *Paragonimus heterotremus*. *Southeast Asian J Trop Med Public Health* 1988; 19: 337.