Case Report

Coinfection of Pulmonary Paragonimiasis and Pulmonary Tuberculosis in Thailand

Pichaya Petborom MD*,
Patcharasarn Linasmita MD*, Manaphol Kulpraneet MD*

** Department of Medicine, Faculty of Medicine, Srinakharinwirot University, Nakhon Nayok, Thailand*

The authors report a case of coinfection of pulmonary paragonimiasis and pulmonary tuberculosis which is an uncommon coinfection. The patient presented with a one-week history of nonmassive hemoptysis about 1 month after completion of treatment for smear-negative pulmonary tuberculosis (sputum polymerase chain reaction positive for Mycobacterium tuberculosis). She lived in Nakhon Nayok province and reported taking raw crabs from time to time. The complete blood count revealed eosinophilia and her chest radiograph showed patchy infiltration at right lower lung field. Computed tomography scan of the chest revealed consolidation with internal air bubbles at anterobasal segment of right lower lobe. The diagnosis of pulmonary paragonimiasis was confirmed by detecting eggs of the genus Paragonimus in her wet-mount sputum. She was treated with oral praziquantel for 3 consecutive days with improvement. To our knowledge, although coinfection of pulmonary paragonimiasis and pulmonary tuberculosis is rare, it should be considered as the differential diagnosis in patients who live in the endemic area presenting with hemoptysis and eosinophilia.

Keywords: *Pulmonary paragonimiasis, Pulmonary tuberculosis, Hemoptysis, Eosinophilia*

J Med Assoc Thai 2016; 99 (Suppl. 8): S231-S236
Full text. e-Journal: *http://www.jmatonline.com*

Paragonimiasis is an important helminthic disease and the human gets infected accidentally[1,2]. Paragonimiasis has a worldwide distribution but is mainly encountered in Southeast Asia where *Paragonimus heterotremus* and *Paragonimus pseudoheterotremus* are proven causative pathogens[3]. The most common species causing human paragonimiasis in Thailand has been reported to be *Paragonimus heterotremus*[4,5]. Pulmonary paragonimiasis is the most common manifestation of this disease [1,2]. The infection is related to eating habits of people. It is acquired by consuming of raw, inadequately cooked crabs or crayfish containing encysted metacercariae which behave as second intermediate hosts in the life cycle of the parasite[6]. Diagnosis is often delayed owing to low index of suspicion and clinical presentation that can mimic TB, which is endemic in the population[7].

We report the coinfection of pulmonary paragonimiasis and pulmonary tuberculosis in a Thai woman who lived in Nakhon Nayok province presented with nonmassive hemoptysis and eosinophilia. She gave a history of eating raw crabs. Ova morphologically resembling *Paragonimus* species were detected in her sputum. Symptoms resolved with praziquantel treatment.

Correspondence to:
Petborom P, Department of Medicine, Faculty of Medicine, Srinakharinwirot University, 62 Moo 7, Ongkharak, Nakhon Nayok 26120, Thailand.
Phone: +66-37-395085 ext. 11001
E-mail: turn_turn@hotmail.com

Case Report

A 39-year-old Thai woman who lived in Nakhon Nayok province presented with nonmassive hemoptysis for 1 week in November 2014. Seven years earlier, she had a subacute cough and nonmassive hemoptysis, a chest radiograph showed increased opacity at right lower lobe (RLL) with cavity and smear negative pulmonary tuberculosis was diagnosed. She had been treated with antituberculosis drugs for 9 months (2 HRZE/7HR), she seldom had nonmassive hemoptysis after treatment. However, 7 months before this presentation, she had nonmassive hemoptysis everyday and weight loss and was diagnosed relapsed pulmonary tuberculosis. Her chest radiograph showed increased opacity at RLL (Fig. 1A). At that time, she had three negative sputum acid-fast smears. Culture for mycobacterium had no growth whereas polymerase chain reaction (PCR) for *Mycobacterium tuberculosis* was positive. She had been treated with antituberculosis drugs for 6 months (2HRZE/4HR) without completely improved (hemoptysis was gone

but she still had a productive cough). Her chest radiograph after complete treatment was slightly improved but still revealed increased opacity at RLL (Fig. 1B). One month after completion of treatment she had nonmassive hemoptysis with white sputum for 1 week. She did not have fever, shortness of breath, chest pain and weight loss. Regarding her eating habits, it was disclosed that she had consumed raw crabs twice a week for more than 10 years. She had never smoked. She worked as a housekeeper. No family members had similar symptoms, and her family history was negative for tuberculosis. Physical examination revealed a normosthenic-built woman, fully conscious. She did not have fever or respiratory distress and had normal vital signs (temperature 37.3°C, blood pressure of 144/78 mmHg, pulse rate of 84/min, respiratory rate of 16/min). Respiratory system showed trachea in midline, equal chest expansion, resonance on percussion both lungs, normal breath sound, no adventitious sound. The rest of physical examinations were within normal limits. The complete blood count (CBC) showed a hematocrit of 36.3%, and a WBC count of 10,410 cells/mm^3 with 41% neutrophils, 31.7% lymphocytes and 10.4% eosinophils (absolute eosinophil count = 1,083 cells/mm^3), platelet count was 376,000 cells/mm^3. Sputum acid-fast smears were negative for 3 consecutive days. A chest radiograph (Fig. 1C) showed patchy infiltration at RLL. Computed tomography scan of the chest (Fig. 2A and 2B) revealed consolidation 1.3x1.3 cm with internal air bubbles at anterobasal segment of right lower lobe, favoring lung abscess or necrotizing pneumonia, no pleural effusion. Her first wet-mount sputum examination revealed eggs which were yellow-brown, ovoidal and operculated in outline with a thick shell 70-100 μm x 40-60 μm (Fig. 3). These eggs were compatible with eggs of the genus *Paragonimus*. *Paragonimus* eggs were not obtained by stool concentration technique. The definite diagnosis was pulmonary paragonimiasis. She was treated with praziquantel 25 mg/kg of body weight 3 times/day for 3 consecutive days. No side effects were noted. Her symptom was improved and hemoptysis disappeared after treatment. Sputum wet-mount examination at 1 week and 1 month after treatment did not find *Paragonimus* eggs. One month after treatment the absolute eosinophil count in CBC decreased to 681 cells/mm^3.

Discussion

Human infections with the *Paragonimus* species have been identified in many parts of the world, but they most commonly in eastern Asia[7]. The first case report of human paragonimiasis in Thailand was quoted by Prommas in 1928, a patient from Lom Sak District, Phetchabun Province[8]. From the epidemiological surveys showed that there were at least six species of *Paragonimus* in Thailand[3,9,10]. Only three species have been found to be infective to man in Southeast Asia including Thailand: *P. westermani*, *P. heterotremus* and *P. pseudoheterotremus*[3]. Saraburi, Nakhon Nayok and Loei Province disclose the endemic areas, because people living in these areas usually eat raw, inadequately cooked crabs, shrimps or fish[4]. Our case report is from Nakhon Nayok Province often takes raw crabs which may harbor metacercariae of *Paragonimus* species. She presented with nonmassive hemoptysis which can be seen in 79-92% of those with pulmonary paragonimiasis[11,12]. She also had

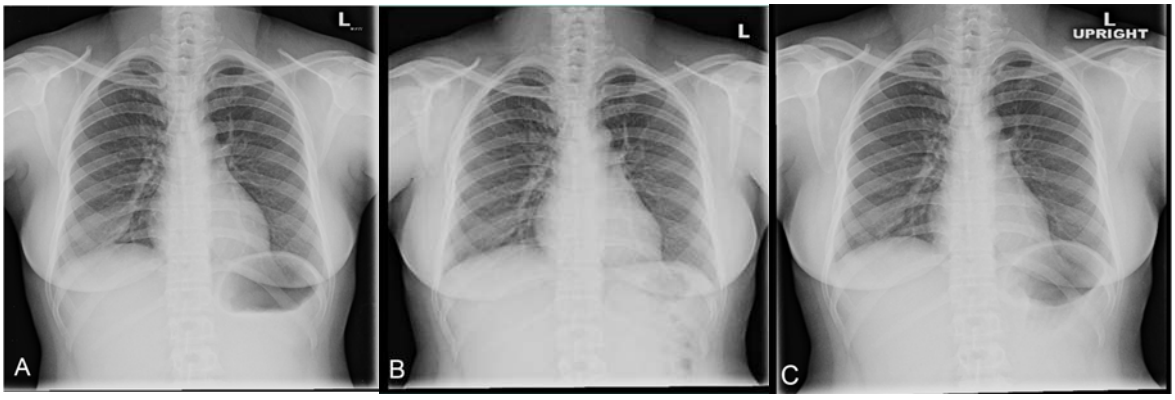

Fig. 1 Chest radiograph of patient. (A), patchy infiltration at right lower lobe at 7-month before this presentation; (B), improvement of infiltration at right lower lobe at 6-month of anti-tuberculosis treatment; (C), progression of patchy infiltration at right lower lobe at this presentation.

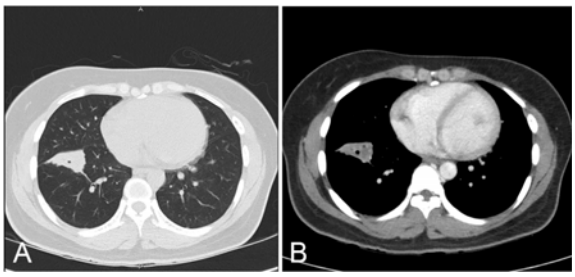

Fig. 2 Computed tomography scan of the chest revealed consolidation with internal air bubbles at anterobasal segment of right lower lobe; lung window (A), and mediastinal window (B).

Fig. 3 Wet-mount sputum revealed egg of the genus *Paragonimus*. The egg was yellow-brown, ovoidal and operculated in outline with a thick shell.

eosinophilia which could be found in 62-80% of patients[13-15]. Radiographic abnormalities in Asian patients usually show air-space consolidation (52%) and pleural effusions (37%)[16]. Our patient developed consolidation with internal air bubbles at anterobasal segment of RLL. In term of definitive diagnosis, detection of paragonimiasis egg in wet-mount sputum is specific but its sensitivity is low (28-38%)[7]. Repeat sputum examinations may increase the sensitivity of this test to 50%[14]. Fortunately, in our patient we could detect *Paragonimus* eggs in the first sputum wet-mount specimen. Stool examination is also insensitive in adult[17]. In our patient, *Paragonimus* eggs were not obtained by stool concentration technique. Serological testing is useful for establishing the diagnosis of paragonimiasis because of the relatively low percentage of egg detection. Serologic tests aid in diagnosing extrapulmonary disease where eggs are not shed in sputum or stool. Both antigen capture enzyme-linked immunosorbent assay (antigen capture-ELISA) and DNA hybridization were found to have 100% specificity, with sensitivity of 73.7% and 100%, respectively[18]. This patient already had the definite diagnosis by detection of *Paragonimus* eggs in sputum therefore the serology testing was not done. The current recommended treatment for paragonimiasis is praziquantel. The recommended dose is 25 mg/kg, three times a day, for 3 consecutive days, resulting in a 100% cure rate[19,20]. Our patients had excellent clinical responses to praziquantel, with improved symptoms and resolution of eosinophilia. In developing countries, co-infection of tuberculosis and parasitic diseases in humans is an important public problem in co-endemic areas. The systemic review of co-infection of tuberculosis and parasitic diseases in humans from 1984 to 2012 did not find the co-infection of tuberculosis and paragonimiasis[21]. The previous study from two hospitals in Korea conducted in tuberculosis patients found that skin tests had positive reactions to *Paragonimus* antigen 15.2% and 22%[22]. In 2014, the integrated surveillance of pulmonary tuberculosis and paragonimiasis in Zamboanga del Norte, the Philippines revealed that co-infection rate was 0.3%, with two identified cases among 836 patients[23]. Lee et al reported a case of pulmonary paragonimiasis diagnosed after initial improvement with anti-TB therapy (this patient had positive results in both tuberculin skin test and interferon γ release assay)[24]. In our patient PCR for *Mycobacterium tuberculosis* (MTB) was positive in her sputum 7 months ago so she has already been diagnosed with pulmonary tuberculosis. Although a definite diagnosis of pulmonary tuberculosis could not be done because she had negative sputum acid-fast smears and culture negative for MTB. The sensitivity and specificity of PCR were 93 and 84%, respectively and PCR detected *M. tuberculosis* in 11.7% of the culture-negative suspects[25]. The risk of a false-positive PCR result in a TB assay includes contamination of the sample with TB organisms or DNA in laboratories and situation involves potential amplification of DNA from nonviable organisms present in samples during or after antimycobacterial treatment[26]. Although PCR TB could be falsely positive due to nonviable organism even treatment is complete, such the longest duration reported in literature is 2.5 years[26]. The positive PCR TB in this patient which treatment completion was

7 years ago infer that this should be an active infection, not a nonviable organism. In our patient, the coinfection of pulmonary paragonimiasis and pulmonary tuberculosis should be occur 7 months before the diagnosis of pulmonary paragonimiasis was done because her symptom and her chest radiograph were not much improved after anti-tuberculosis treatment. Furthermore, The absolute eosinophil count at that time was 1,488 cells/mm^3, so she may already have been infected with *Paragonimus* species. To the best of our knowledge this patient is the first case report of coinfection of pulmonary paragonimiasis and pulmonary tuberculosis in Thailand.

Conclusion

This case highlights the importance of recognizing unusual coinfection of pulmonary paragonimiasis and pulmonary tuberculosis in the patient who had a history of eating raw crabs and presented with hemoptysis and eosinophilia. This coinfection can occur especially in the endemic area of tuberculosis and paragonimiasis. In pulmonary tuberculosis patients who do not have the definite diagnosis and do not response to anti-tuberculosis drugs, pulmonary paragonimiasis should be considered.

What is already known on this topic?

Nakhon Nayok province is the endemic area of pulmonary paragonimiasis. People in this area, including our patient, have the habit of eating uncooked crab thus might have acquired infection in this way. Hemoptysis and eosinophilia are the common presentations of pulmonary paragonimiasis. Radiographic abnormalities are common among patients with paragonimiasis in Asia, with half of patients (including our patient) having air-space consolidation. A definite diagnosis of pulmonary paragonimiasis is the detection of paragonimus egg on sputum wet-mount. The current recommended treatment for paragonimiasis is praziquantel 25 mg/kg given orally 3 times daily for 3 days.

What this study adds?

This patient was the first case report that had coinfection of pulmonary paragonimiasis and pulmonary tuberculosis in Thailand. To our knowledge, although coinfection of pulmonary paragonimiasis and pulmonary tuberculosis is rare, it should be considered as the differential diagnosis in patients who present with hemoptysis and eosinophilia. This coinfection can occur especially in the endemic area of tuberculosis and paragonimiasis and doctors should ask the patients about the history of eating raw crabs. Finally, in pulmonary tuberculosis patients who do not have the definite diagnosis and do not response to anti-tuberculosis drugs, pulmonary paragonimiasis should be considered.

Potential conflicts of interest

None.

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การติดเชื้อร่วมกันของพยาธิใบไม้ในปอดชนิดพาราโกนิมัส (Paragonimus) และวัณโรคปอดในประเทศไทย

พิชญา เพชรบรม, พัชรสาร ลีนะสมิต, มนะพล กุลปราณีต

คณะผู้เขียนรายงานผู้ป่วยที่มีการติดเชื้อร่วมกันของพยาธิใบไม้ในปอดชนิดพาราโกนิมัส (Paragonimus) และวัณโรคปอด ซึ่งเป็นการติดเชื้อร่วมกันที่พบไม่บ่อย ผู้ป่วยมีอาการไอเป็นเลือดไม่รุนแรงมา 1 สัปดาห์ โดยเริ่มมีอาการ 1 เดือนหลังจากได้รับการรักษาวัณโรคเสมหะลบ (แต่ผล polymerase chain reaction ในเสมหะเป็นผลบวกต่อเชื้อ Mycobacterium tuberculosis) ด้วยยาต้านวัณโรคครบ ผู้ป่วยอาศัยอยู่ที่จังหวัดนครนายกและมีประวัติรับประทานปูดิบเป็นประจำ ผลการตรวจนับความสมบูรณ์ของเม็ดเลือดพบว่ามีเม็ดเลือดขาวชนิดอีโอซิโนฟิลสูง และภาพถ่ายรังสีทรวงอกพบฝ้าขาวที่ปอดขวาส่วนล่าง เอกซเรย์คอมพิวเตอร์ทรวงอกพบฝ้าขาวที่มีโพรงอยู่ด้านในที่ส่วนฐานด้านหน้าของปอดกลีบขวาล่าง การวินิจฉัยโรคพยาธิใบไม้ในปอดชนิดพาราโกนิมัสถูกยืนยันได้จากการพบไข่ของพยาธิ Paragominus ในการตรวจเสมหะแบบสด (wet-mount) ผู้ป่วยได้รับการรักษาด้วยยากิน praziquantel นาน 3 วันติดต่อกันและมีอาการดีขึ้นหลังจากการรักษา ถึงแม้ว่าการติดเชื้อร่วมกันของพยาธิใบไม้ในปอดชนิดพาราโกนิมัสและวัณโรคปอดพบได้ไม่บ่อย แต่ควรต้องคิดถึงการติดเชื้อร่วมดังกล่าว ในผู้ป่วยที่อาศัยอยู่ในถิ่นระบาดที่มีอาการไอเป็นเลือด และมีอีโอซิโนฟิลในเลือดสูง