CASE REPORT

Pulmonary Paragonimiasis Diagnosed by Fine-Needle Aspiration Biopsy

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We report a case of paragonimiasis involving a 12-year-old Latin American boy. The diagnosis was made by fine-needle aspiration biopsy of a pulmonary nodule. Identification of the species by morphometric analysis of the eggs indicated that the infection was caused by Paragonimus mexicanus.

CASE REPORT

A 12-year-old boy with a 2-year history of seizures, headaches, and intermittent hemoptysis presented to the Ben Taub General Hospital emergency room after a cluster of five seizure attacks. The boy was from El Salvador, had been in the United States for 14 months, and had been treated with phenytoin for his seizures. On presentation, his head computed tomography (CT) scan showed a calcified cystic lesion in the left anterior frontal area. The electroencephalograph was abnormal, with recurrent slow wave spikes in the left temporal lobe and a frontal slow-wave spike. He was diagnosed with symptomatic localized epilepsy with secondary generalized tonic/clonic seizures. He was started on carbamazepine (Tegretol) and followed monthly by the Neurology Service. He had been seizure free for 9 months when he presented to the emergency room for a second time with two episodes of self-limited tonic/clonic seizure at school, each lasting less than 1 minute. There was no loss of bladder or bowel control. The patient reported a 1-year history of intermittent hemoptysis. His sputum was reported to be blood streaked with no gross blood. He had an occasional productive cough but no hematemesis, nasal congestion, chest pain, or shortness of breath. He occasionally had fever but no chills or night sweats. The patient’s mother reported that he had a 20-pound weight loss over the previous year. No diarrhea was reported. His physical activity was normal and he did not complain of fatigue. Headaches had been worse over the past few months; therefore, he had missed several days of school. The headaches were frontal, throbbing, and associated with photophobia. He was also complained of problems with visual acuity. He denied any syncope, vomiting, or persistent poor vision. His headaches were relieved with acetaminophen (Tylenol).

His physical examination was unremarkable. His laboratory investigation documented a normal complete blood count with no eosinophilia. His metabolic panel was also normal. His cerebrospinal fluid sample had four white cells and no red cells; cerebrospinal fluid culture was negative for bacteria, fungi, and viruses. Abdominal and pelvic CT scans were normal. His chest X-ray and CT scan showed multiple lung nodules measuring up to 2.2 cm but no lymphadenopathy (Fig. 1). Pulmonary angiography showed no evidence of hypervascular tumor or arteriovenous malformation. A head CT scan revealed a focus of encephalomalacia in the left superior frontal gyrus involving the underlying white matter and a 2- to 3-mm focal calcification. A CT-guided lung biopsy using fine-needle aspiration showed abundant necrotic cellular debris surrounding numerous thick-walled parasite eggs morphologically consistent with those of the trematode or lung fluke Paragonimus mexicanus (Fig. 2). The specimen was sent to the Centers for Disease Control and Prevention (CDC), where the species identification was confirmed. The patient was treated with six doses of 1,200 mg of praziquantel. He was discharged on carbamazepine.

The patient has been followed for 5 years. He was admitted recently because of an increased frequency of seizures. His head CT showed no change in the size of the cyst and no enhancing brain lesion.

Discussion. Paragonimiasis is a zoonotic disease caused by the trematode Paragonimus spp. Other names of this disease are oriental lung fluke, endemic hemoptysis, Mason hemoptysis, pulmonary diastomiasis, and parasitic hemoptysis (11). An estimated 20 million people are currently infected in Africa, Asia, and the Americas (18). About 48 species of Paragonimus have been described, but only 16 of these infect humans (2, 17), including Paragonimus westermani in the Far East and Southeast Asia, Paragonimus africanus in West Africa, Paragonimus mexicanus in Central and South America, and Paragonimus kellicotti in North America (3). Adult flukes reside mainly in the lung, but ectopic localizations such as lymph nodes, heart, mediastinum, adrenal glands, and kidneys have also been reported (11, 12). P. westermani is the most common species infecting humans, causing pulmonary, pleuropulmonary, and...
cerebral paragonimiasis (2, 16). *P. kellicotti* is the second most common cause of diagnosed human cases and is the species that is endemic in the United States.

The life cycle of *Paragonimus* spp. is complex, involving two intermediate hosts and one definitive host (11). The early developmental stages are carried through the snails of Pleuroceridae and Thiaridae families. Over a period of 10 to 12 weeks, they transform through sporocyst and redia stages and eventually become cercariae. The cercariae leave the snail and through water reach the second intermediate host, a crustacean like a freshwater crab or crayfish (2, 17). Here they develop into encysted forms (metacercariae), and human infection occurs where these contaminated crustacea are eaten poorly cooked or raw (19). Metacercariae excyst in the duodenum and within 1 h pass through the intestinal wall into the peritoneal cavity (16). After 3 to 6 h, they migrate into the abdominal wall and then through the diaphragm into the pleura and lung tissue (16, 19), where they become encapsulated, usually in pairs or triplets. It takes 65 to 90 days for the flukes to develop fully, although the symptoms may begin earlier. Eggs are shed around the worm and with rupture of the contents of the encapsulated cyst into bronchioles; the eggs are excreted in the sputum or swallowed and excreted in the feces.

Disease is caused by inflammation and fibrosis elicited by worms in the lung or ectopic locations. Manifestations depend on the duration of infection and probably the intensity of infection. Flukes and eggs initially elicit an acute inflammatory response, consisting predominantly of eosinophils, which is followed by formation of a fibrous capsule (16). The cysts are 1.5 cm in diameter, and these may rupture into the bronchioles, extruding blood, eggs, and inflammatory exudate. Several excretory-secretory and somatic products from tissue-invading helminths have been related to the modulation of the host’s immune response, e.g., through the induction/inhibition of different host immune mediators such as nitric oxide (NO) (7). NO plays an important role in many infectious diseases due to both its direct effector function and its potent immunoregulatory properties (6). It has been shown that excretory-secretory products from *P. mexicanus* adult worms trigger NO production from alveolar macrophages (1). Further studies are needed to reveal the exact effect of NO production on the host immune system. Histologically, a fibrous and granulomatous reaction may be seen in association with the eggs. Secondary bronchopneumonia is common. Pleural involvement is common (16) and can cause an eosinophilic empyema that can be confused clinically with tuberculosis. Long-standing lesions exhibit fibrosis and decreased inflammatory response, which may eventually calcify. Common ectopic locations of flukes are the pleura, abdominal wall, viscera, and brain. Brain involvement in particular is a serious complication (16). The adult fluke is thick, ovoid, and red-brown and with a rounded anterior aspect and a tapered posterior. It measures 7.5 to 12 mm in length and 4 to 6 mm in thickness. It may live for 20 years (19).

The initial illness is characterized by diarrhea, abdominal pain, urticaria, fever, malaise, and eosinophilia that last from days to weeks, when the immature flukes are migrating. As
larvae penetrate the diaphragm and migrate within the pleural cavity, pleuritic chest pain may develop, occasionally associated with pleural effusion and pneumothorax. Pulmonary manifestations include dyspnea, cough, and hemoptysis. Leukocytosis with prominent eosinophilia and transient pulmonary infiltrate occurs during this time. Signs and symptoms due to the involvement of ectopic locations can also be seen at this stage.

Later in the chronic stage, when the adult worms reside in the lungs and produce eggs, the patient may develop chronic cough, expectoration of rusty or pigmented sputum, and hemoptysis, as in our case. Dyspnea, chest pain, fever, and constitutional symptoms are found less frequently. Chest X-ray findings are variable and nondiagnostic. Localized or multisegmental infiltrates, usually poorly defined, are most common, but nodular (as in our case), cystic, cavitary, and ring shadow patterns are also found. Pleural effusion, empyema, pleural thickening, and calcification of lesion can also be seen. In contrast to what is seen for tuberculosis, apical lesions are not predominant, cavities are smooth and regular, and infiltrates are less well defined. Although lung involvement alone appears to cause little mortality, morbidity and mortality are significant with ectopic lesions. Acute involvement of the brain is associated with the sudden onset of neurologic symptoms, usually in the presence of pulmonary disease, as in our case. Chronic brain involvement occurs in up to 10% of patients and is associated with seizure and long-term deficits (16, 19). Most lesions of cerebral paragonimiasis are located in the posterior loci of the cerebral hemispheres (parietal, occipital, and/or posterior temporal area), but frontal lobe involvement, as it presented in this case, is not uncommon. The brain stem, the cerebellum, and the spinal cord are rarely involved. The radiological findings of cerebral paragonimiasis are variable, depending on the evolutional stage of the cerebral infection. Diagnosis of cerebral paragonimiasis in the early stage is important, because curative therapy with praziquantel is possible. Today, CT and magnetic resonance imaging are the imaging methods of choice in the evaluation of the nature and extent of cerebral infection as well as for virtually all other intracranial abnormalities (4, 5). In the chronic stage of cerebral paragonimiasis, the granulomas may become calcified. The classical pattern of calcification is seen as congregated multiple round nodular or cystic lesions (so-called soap bubble or egg shell appearance) on plain skull radiographs (10, 14).

The pulmonary lesions are most commonly mistaken for tuberculosis (in some series in about half of the patients). Indeed, tuberculosis is common in countries where paragonimiasis is endemic. The lesions of paragonimiasis are more peripheral located and much more common in the mid- and lower lung zones, as opposed to the predominantly apical location of tuberculous cavities. In the chronic inactive stage of cerebral paragonimiasis, the calcified lesions may be mistaken for cystercerosis, tuberculosis, or other chronic inflammations unless the characteristic conglomerate and soap bubble appearances are identified by plain-film radiography, CT, or magnetic resonance imaging (5, 9).

The eggs of Paragonimus spp. may be mistaken for those of other operculate trematodes, including Clonorchis sinensis, which are much smaller (26 to 35 μm), and those of Fasciola hepatica and Fasciolopsis buski, which are considerably larger (130 to 140 μm). The eggs of Schistosoma japonicum are about the same size and shape, but schistosome eggs lack an operculum, have thinner shells, and are not birefringent (2, 15).

Diagnosis is established by the detection of the characteristic ova in stool or sputum. The eggs of Paragonimus spp. are yellow to brown with a flattened operculum at one end. In addition, as a result of their thick shell, the eggs are birefringent with polarized light (Fig. 2). Over time, the eggs may undergo calcification (19). The eggs of P. mexicanus measure on average 80 by 40 μm. The intact eggs from our patient measured on average 79 by 48 μm. Egg size and the geographic location of our index case were helpful in establishing the Paragonimus species involved in our patient’s infection (Table 1) (12).

Concentration techniques may be needed for the detection of eggs in lightly infected patients or in those with suspected ectopic lesions. In acute disease, eggs may not be detected until 2 to 3 months after exposure (16). Serological testing for antiparagonimus immunoglobulin G by enzyme-linked immunosorbent assay has a sensitivity of 100% and a specificity of 91% to 100% (13). This test is available mainly at CDC.

The intradermal test has been widely used, mainly for screening patients in areas of endemicity. A positive reaction does not always mean active infection, and a test can remain positive as long as 20 years after complete recovery. Praziquantel is the treatment of choice at 25 mg/kg of body weight/day for 2 days, and it is usually given three times a day. The overall cure rate is more than 90% (8, 15). In cases of cerebral lesions, higher doses must be given but only in combination with steroids to prevent epilepsy secondary to perilesional edema. Older drugs like bithionol and niclofolan are also effective but more toxic (15).

In summary, P. mexicanus is an uncommon cause of paragonimiasis in North America. Infected patients are usually from South American countries or have histories of travel to South America. The most common presentation is pulmonary involvement. Brain involvement usually occurs in the presence of pulmonary lesions and can cause a hemorrhagic lesion and even death. The recognition of brain involvement in early stages is critical, since it can be treated with medication. In the late stages, brain lesions calcify and can cause seizures and long-term deficit. Our patient displayed both pulmonary and cerebral lesions, and we were able to establish the diagnosis via biopsy of one of the pulmonary nodules by fine-needle aspiration.

### REFERENCES