Case Report: Paragonimiasis Presenting with Pericardial Tamponade

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Abstract. We report an unusual case of paragonimiasis in a Nepali patient presenting with massive pericardial effusion and pericardial tamponade. The patient reported neither the consumption of crabs or crayfish nor the consumption of wild animal meat, which are the usual sources of infection. It is suspected that the source of infection was instead the ingestion of raw live slugs as part of a traditional medicine treatment.

CASE REPORT

A 45-year-old Nepali woman living in Kathmandu presented to a chest physician, with a history of dyspnea (increasing with exercise), migratory chest pain, recurrent fever in the evenings, and night sweats for several weeks. She reported no relevant medical history besides having sustained a traumatic humerus fracture 2 months before, for which she had ingested raw live slugs (“chiple kira”). Ingestion of raw slugs is a traditional remedy to accelerate the bone healing process (in traditional medicine, these slugs are also ingested as remedy against jaundice and to increase sexual potency; see YouTube video: <https://www.youtube.com/watch?v=8LJ1dvDd4GU>). Besides a decreased breathing sound in the right lower lung field, lung and heart auscultation and other physical examinations were unremarkable. The chest X-ray revealed a right-sided pleural effusion, and laboratory investigations showed a total leukocyte count of 11,300/ μ L with marked eosinophilia (41%; absolute eosinophil count 4,633/ μ L), mild anemia (Hb 10.3 g%), a normal platelet count, and a raised erythrocyte sedimentation rate of 87 mm/hour. Because of the marked eosinophilia, the consulted physician suspected an underlying parasitic infection, and the patient received empirical antiparasitic treatment with ivermectin for 2 days and diethylcarbamazine for 21 days; judging from the choice of treatment, filariasis (“tropical pulmonary eosinophilia”) was apparently the primary suspected differential diagnosis. Although the treatment was followed by a mild symptomatic improvement and a temporary decrease in eosinophil count (27%; absolute count 2,673/ μ L), the eosinophilia level returned to the pretreatment level (42%; absolute count 4,970/ μ L) at the end of the 21 days of medical treatment.

Because the patient’s clinical situation slowly deteriorated, she was referred to Medanta The Medicity hospital in Gurgaon, India, for further diagnostic evaluation and exclusion of a possible underlying hematological condition. At admission, the patient reported that she recently noticed a palpable and increasingly painful migratory nodule on her anterior chest below the breast which now also became visible (Figure 1C). The chest X-ray showed bilateral pleural effusion and a heart silhouette suggestive of pericardial effusion (Figure 1A). A computed tomography (CT) scan confirmed these findings

(Figure 1B) and uncovered the presence of several hypodense areas (Figure 1D) and thin hypodense subcapsular tracks in several liver segments (Figure 1E). Because an additional echocardiography showed the presence of hemodynamic features of pericardial tamponade, therapeutic pericardiocentesis and thoracocentesis were performed, and the drained fluid was sent for analysis. To prevent hypereosinophilia-related cardiac tissue damage, treatment with prednisolone was started but changed to colchicine the next day.

The cell count of the pleural and pericardial fluid showed 70% and 5% eosinophils, respectively. A skin biopsy of the migratory lesion on the trunk was performed, and the sample was sent for histopathological and microbiological evaluation (Gram stain, Ziehl-Neelsen stain, GeneXpert, and culture). The histopathology report described nonspecific panniculitis, and the microbiological results came back negative. Additional microscopic stool examinations for parasite eggs and larvae as well as blood microscopy for microfilaria and testing for circulating filarial antigen were negative. In the absence of cough, no sputum samples could be investigated at that time.

Because the CT scan strongly suggested visceral larva migrans (VLM) syndrome due to a tissue-invasive parasite, a serum sample was sent to the Swiss Tropical and Public Health Institute in Basel, Switzerland, to perform serological testing for tissue-invasive parasites. The serum sample was tested in a standard in-house panel of serological assays consisting of highly sensitive enzyme-linked immunosorbent assays used for screening, followed, if positive, by highly specific immunofluorescence antibody test assays for confirmation, and enzyme-linked immunoelectrotransfer blots (Western blots) (Table 1).

Following the serological results, repeated microscopic investigations of induced sputum samples finally detected *Paragonimus* spp. eggs and confirmed the serological diagnosis (Figure 2).

Praziquantel treatment (75 mg/kg/day divided in three doses for 3 days) was administered, and the patient’s condition slowly improved. Fifteen days after treatment, the patient’s symptoms and eosinophilia had disappeared.

DISCUSSION

To date, six human paragonimiasis cases have been reported from Nepal.^{1,2} Because diagnostic options in Nepal are limited to very few reference centers and many physicians may not even be aware of paragonimiasis as a differential diagnosis, it cannot be excluded that significant underreporting or misdiagnosis of cases may currently occur.

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FIGURE 1. (A) X-ray showing pleural effusion and cardiac silhouette suggestive of pericardial effusion. (B) CT image showing pleural and pericardial effusions. (C) Migratory skin lesion on the trunk. (D and E) CT image showing multiple hypodense lesions and tracks suggestive of visceral larva migrans in the liver parenchyma. This figure appears in color at www.ajtmh.org.

The case reported here is special because of the unusual clinical presentation with massive pericardial effusion and tamponade. Unlike the typical presentation of paragonimiasis as an eosinophilic pulmonary syndrome with pleural effusions, pneumothoraces, and pulmonary infiltrates/migratory tracks/cavities, pericardial involvement remains rather rare³⁻⁸ and may even confuse the differential diagnosis.⁹

In patients presenting with eosinophilia and pericardial involvement, the primary and most obvious parasitic differential diagnosis is toxocariasis because this parasite is widely prevalent and responsible for most cases of VLM in humans.¹⁰ Toxocara cases similar to the here reported *Paragonimus* case have been reported.¹¹ Of note, one case of toxocariasis presenting with severe neurologic, ocular, and pulmonary

involvement has been reported following the ingestion of slugs (interestingly also as a traditional remedy).¹² Because slugs do not play a role as an intermediate host in toxocariasis, the authors of this case report suggest that slugs may be contaminated by the parasite's eggs in the environment and serve as a vehicle for human infection.

Regarding the patient's history of ingesting raw live slugs, another tissue-invasive parasite would come to mind: *Angiostrongylus cantonensis*, the most common parasite causing eosinophilic meningitis worldwide.¹³ Although the parasite is highly tissue invasive, the invasiveness is largely limited to the central nervous system (the brain and eye), and overt pulmonary or cardiac involvement in angiostrongyliasis has, to our knowledge, never been reported.

TABLE 1
Results of serological testing

Parasite-specific serology	Type of assay	Reference range/cutoff values		Test result	Interpretation of test result
		Negative	Positive		
<i>Angiostrongylus cantonensis</i>	EITB	n.a.	n.a.	Negative	Negative
<i>Fasciola hepatica</i>	ELISA	< 0.3	≥ 0.5	0.72	False positive*
	IFAT	< 1/160	≥ 1/320	1/320	False positive*
<i>Filaria</i> spp.	ELISA	< 0.5	≥ 0.7	0.46	Negative
<i>Gnathostoma spinigerum</i>	EITB	n.a.	n.a.	Negative	Negative
<i>Paragonimus westermani</i>	EITB	n.a.	n.a.	Positive	Positive
<i>Schistosoma</i> spp.					
AWA	ELISA	< 0.15	≥ 0.3	0.06	Negative
SEA	ELISA	< 0.3	≥ 0.6	1.29	False positive*
	IFAT	< 1/80	≥ 1/160	< 1/40	Negative
<i>Strongyloides stercoralis</i>	ELISA	< 0.5	≥ 0.7	0.42	Negative
<i>Toxocara</i> spp.	ELISA	< 0.5	≥ 0.7	0.00	Negative
<i>Trichinella</i> spp.	ELISA	< 0.5	≥ 0.7	0.64	Equivocal†
	IFAT	< 1/160	≥ 1/320	1/160	Equivocal†

AWA = adult whole antigen; EITB = enzyme-linked immunoelectrotransfer blot; ELISA = enzyme-linked immunosorbent assay (values: optical density); IFAT = immunofluorescence antibody test (values: titer); n.a. = not applicable; SEA = soluble egg antigen. Bold values indicate important and significant findings.

* Cross-reaction with *Paragonimus* antibodies.

† Equivocal range between negative and positive cutoff values of ELISA and IFAT.

FIGURE 2. (A) Microscopy of the sputum sample: *Paragonimus* egg (~100 × 50 µm). (B) Life cycle of *Paragonimus* spp. This figure appears in color at www.ajtmh.org.

A widely prevalent parasite infecting humans and typically presenting with VLM syndrome is *Fasciola hepatica*. Although primarily involving the liver, aberrant migration may occur and extrahepatic manifestations (including the skin, heart, and brain) have been reported.^{14,15} Although snails are the first intermediate host of *F. hepatica*, neither their ingestion nor the ingestion of slugs is reported to cause human infection. In our patient, the positive *Fasciola* serology is interesting: considering the rather severe clinical picture, the weak positive serological results are conspicuously disproportional and suggest cross-reactivity (Table 1). Because *Fasciola* and *Paragonimus* are both trematodes (flukes), and cross-reactivity in serological assays is primarily a problem with phylogenetically related parasites, these results highlight the necessity to ideally cross-evaluate serologies in panels and interpret the results with caution. This is especially important in cases where direct methods fail to detect the parasite (or its eggs) and the diagnosis is solely based on serological results.

Although snails are the first intermediate host of *Paragonimus* spp., until recently, only the second intermediate hosts, crustaceans such as crabs or crayfish, were considered to be infective for humans (Figure 2). Recently, another source of infection, the consumption of meat from wild boar and deer (paratenic hosts) was identified as a potential source of human infection in Japan.¹⁶ Nevertheless, because the patient neither reported the consumption of crabs or crayfish nor the consumption of wild animal meat, ingestion of the slugs remains highly suggestive as the source of infection.

Received January 8, 2019. Accepted for publication March 5, 2019.

Published online May 13, 2019.

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