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Short Communication

Clinical, Laboratory and Radiological Features of Paragonimiasis Misdiagnosed as Pulmonary Tuberculosis

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Abstract

Background: Paragonimiasis presents with nonspecific symptoms and radiologic findings, allowing for the possibility of misdiagnosis. Diagnosis is generally delayed due to lack of suspicion and presentation similar to pulmonary tuberculosis.

Methods: A prospective observational study was carried out on 20 subjects at Civil Service Hospital of Nepal from March 2015 to June 2019 who presented with eosinophilia and pulmonary symptoms, and were treated empirically with Anti-tubercular therapy for suspicion of pulmonary tuberculosis.

Results: The median age of the patient was 34 years. Mean blood absolute eosinophil count was 16678/ul. Fever was present in 80% (n=16). Cough was present in 90% (n=18). Pleural effusion was noticed in 100% (n=20). Chest computed tomography showed ground-glass opacities in 65% (n=13) of patients. Pleural fluid eosinophilia (>10%) was evident in all patients. Pleural fluid LDH was elevated in 85% (n=17) of patients. Similarly, ADA was high (>40U) in 75% (n= 15) of patients, and pleural fluid sugar was low in 80% (n=16) of patients. All patients (100%) gave a history of crab or snail consumption. *Paragonimus* egg was detected in five (25%) patients. Twenty patients fulfilled definite or probable diagnostic criteria of paragonimiasis. Ninety-five (n=19) patients responded to praziquantel.

Conclusion: Unavailability of serologic tests or failure to demonstrate parasitic egg under the microscope should not discourage physicians to consider the diagnosis of paragonimiasis when marked eosinophilia, high LDH levels, and low glucose levels are identified in pleural fluid of a patient with a history of raw crab or snail consumption.

Introduction

"Paragonimiasis, or lung fluke disease, is caused by infection with several species of trematodes belonging to the genus *Paragonimus*. It is an important cause of pulmonary disease worldwide especially in Asia, West-Central Africa, and Central and South America" (1). The infection is related to the eating habits of the local public and is acquired by ingestion of raw, inadequately cooked crab or crayfish (2).

Establishing the diagnosis of paragonimiasis is a challenge if serologic tests are not available. Microscopic demonstration of parasite eggs in the stool, sputum, or BAL is possible only in some patients. Eosinophilia is a common laboratory finding in Paragonimiasis. The degree of eosinophilia is significantly higher in patients who have pulmonary symptoms (3). "Diagnosis is generally delayed due to lack of suspicion and presentation similar to tuberculosis which is endemic in the population" (4).

Here, we present a cohort of 20 patients who presented with eosinophilia and pulmonary symptoms and initially mimicked pulmonary tuberculosis.

Methods

An observational study was carried out on 20 subjects from March 2015 to June 2019 who presented at Civil Service Hospital of Nepal with eosinophilia and pulmonary symptoms. All 20 subjects enrolled in this study were initially treated empirically with anti-tubercular therapy (ATT) for suspicion of pulmonary tuberculosis in other centers after ruling out autoimmune disease, common parasitic infestations, bacterial infection, and malignancies with appropriate and relevant laboratory, serological and radiological tests. Subjects were referred to our center when their presenting signs and symptoms did not improve despite being treated with ATT for two months.

The study was approved by an institutional review board of the Civil Service Hospital of Nepal. Detail demographic data, clinical and travel history including prior use of any drugs, history suggestive of autoimmune disease, allergy, vasculitis, consumption of raw crab or snail, history of parasitic/helminth infestation, and family history of eosinophilia were sought. Physical examination was meticulously carried out to look for eosinophilia-related specific organ abnormalities in the skin, chest, heart, lymph nodes, liver, spleen, and nervous system. Complete blood count, peripheral blood smear study, chest computed tomography (CT), and echocardiogram were done. Pleural fluid was analyzed for total and differential count, adenosine deaminase (ADA), lactate dehydrogenase (LDH), sugar, Acid Fast Bacilli stain, and microscopic examination on those presenting with pleural effusion. Eggs/ova of parasites and helminths were also examined in stool and sputum. Diagnosis of paragonimiasis was confirmed if eggs were detected in pleural fluid, stool sample, or sputum. If eggs were not detected and there was a history of crab or snail consumption along with pleural fluid findings of high LDH (>1000 IU/dl) or low glucose (<10mg/dl) and high eosinophil counts, patients were presumed to have probable paragonimiasis infestation.

Confirmed and probable subjects were treated with Praziquantel (75 mg/kg/day in three divided doses, for three days). Response to treatment was defined as resolution of blood eosinophilia (<10%), improvement in radiological findings, and clinical symptoms. The clinical and hematological response was evaluated on day 21 of the medication. CT scan of the chest was done after 6 weeks of praziquantel.

Statistics

The mean, median, standard deviation, ranges and frequency, and percentage were calculated for variables. Statistical Package for the Social Sciences Version 20 (IBM Corp., Armonk, NY, USA) was used for analysis.

Results

The median age of the patient was 34 years. Mean blood absolute eosinophil count was 16678/ml (Range).

Fever was present in 80% (n=16) and 70% (n=14) presented with pleurisy. Cough was present in 90% (n=18). Overall, 25% (n=5) presented with hemoptysis. Pleural effusion was noticed in 100% (n=20). Paragonimus egg was detected in five (25%) patients (Three in sputum and 2 in pleural fluid). (Table 1). All (100%) patients gave a history of ingestion of raw or inadequately cooked crab or snail. Based on microscopic findings of egg in sputum and pleural fluid, and the diagnostic criteria set for presumed paragonimiasis, all 20 patients were diagnosed with paragonimiasis.

Chest computed tomography showed pulmonary involvement in 100% patients (Table 2).

Table 1: Pleural fluid findings of 20 patients with confirmatory or presumed Paragonimiasis

Variables	*Mean+/- Std dev****	*Range of values*	*Proportion (%) of total number of tested*
Eosinophil	35.00±13.32	<10%	0 (0)
		>10%	20 (100)
LDH*	2025.00±1195.11	>1000	16 (80)
		<1000	4 (20)
Glucose	12.44±13.05	<10	16 (80)
		>10	4 (20)
ADA**	40.15±13.25	<40	14 (70)
		>40	6 (30)

*Lactate dehydrogenase /** Adenosine deaminase /*** Standard deviation

Table 2: Computed tomography of 20 patients with confirmed or presumed paragonimiasis

Computed Tomography Findings	*Proportion (%) of total number of patients*
Ground glass opacities	65
Consolidation	55
Cavitation	20
Nodular opacities	30
Linear opacities	5
Pleural effusion	100
Hydropneumothorax	5

Totally, 95% (n=19) patients responded to Praziquantel. All 19 patients had resolution of blood eosinophilia on follow-up. The decrease in blood eosinophilia was associated with the improvement of clinical symptoms. Significant improvement of radiological findings in CT scan was noted in all 19 patients after 6 weeks of treatment. Three patients

required an additional 1 dose of praziquantel and responded after two weeks. One patient did not respond to praziquantel. He was subsequently diagnosed with hypereosinophilic syndrome (HES). Praziquantel was well tolerated and all the patients completed the planned treatment. Twenty percent experienced nausea with praziquantel, which resolved without medical intervention.

As all patients were treated with ATT before presenting to our center, ATT-induced adverse effect (AE) was also evaluated. ATT-induced AE was noted in 5 (20%) patients in the form of hepatitis (16%), severe nausea and vomiting (8%), and sensory neuropathy (4%).

Discussion

Pulmonary paragonimiasis resembles chronic bacterial infection, mycobacterial infection, or carcinoma of the lung (5). Laboratory diagnosis of paragonimiasis is made by demonstration of ova in sputum/feces/pleural fluid or by serology (6). However, it is not possible to detect ova in all suspected cases. In addition, diagnosis of paragonimiasis can be made presumably based on clinical presentation, pleural fluid analysis, and exposure history (7). Most patients with pleuro- pulmonary paragonimiasis have pleural fluid with eosinophilia (>10%), high LDH level (>1000IU/L), high ADA, and a low glucose level (<10mg/L) (7). We used the same parameters to suspect paragonimiasis if eggs/ova could not be detected in sputum, stool, or pleural fluid and there is a history of crab or snail consumption. Based on our diagnostic criteria 15 (75%) patients were presumed to have paragonimiasis, as eggs were detected only in 5 (25%) patients.

We were interested in this study because of our prior experience with five subjects who had consumed freshwater crab or snail and presented with eosinophilia and pulmonary symptoms. All those five patients were empirically treated with ATT in other centers and later diagnosed with paragonimiasis in our center. This interesting encounter boosted by a depth literature review provoked us to enquire about the consumption of raw crab and snail to the subsequent patients who were referred to us for evaluation of eosinophilia with chest symptoms. This urged us to design this prospective study. To our surprise, in our study, all patients gave the history of consumption of crab or snail although crab and fresh snail are not considered a preferred delicacy in Nepal.

Fever, cough, and hemoptysis, which are cardinal features of pulmonary tuberculosis, are also the common presentations of Paragonimiasis (8). In our cohort, the majority of patients presented with fever, cough, and hemoptysis.

Radiographic findings associated with lung paragonimiasis consist of transient, migratory pulmonary infiltrates, patchy pulmonary infiltrates, nodule and/or calcifications, pleural effusion, and cavitation (9, 10). In our cohort pleural effusion, GGO and consolidation were the most common radiological findings.

Praziquantel (75 mg/kg/day in three divided doses, for three days) is generally considered the treatment of choice for all species of paragonimiasis (11). All 5 patients, who were diagnosed based on detection of egg or ova (confirmed diagnosed) responded. For those patients with presumed paragonimiasis based on our diagnostic criteria, 14 patients responded (3 required an additional dose of praziquantel). There are reports of patients requiring an additional dose of praziquantel in paragonimiasis in the published literature (12).

Diagnosing paragonimiasis on 19 patients out of 20, who were treated with ATT challenges the old school notion to start ATT for fever with chest symptoms if the cause is unknown.

In Nepal, we have a dearth of data about the incidence and nature of helmin-

thic/parasitic infestations. Our study underscores the need for well-conducted epidemiological studies. Such studies would then potentially promote the rational use of medications like ATT and would broaden the spectrum of differential diagnoses that the clinicians would consider during their practice.

Conclusion

We believe the results of our study will prompt clinicians to maintain a high index of suspicion for paragonimiasis infestation in a patient presenting with eosinophilia and pulmonary symptoms. Although tuberculosis remains the public health concern in Nepal, clinicians should consider the diagnosis of paragonimiasis when marked eosinophilia, high LDH levels, and low glucose levels are identified in pleural fluid of a patient with a history of raw crab or snail consumption.

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Conflict of interest

The authors declare that there is no conflict of interests.

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