Hydropneumothorax as an Rare Manifestation of Secondary Hypereosinophilic Syndrome - A Case Report

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Abstract :

We present a case of a young man who presented with cough and shortness of breath for two weeks with peripheral eosinophilia of unknown cause leading to left-sided pleural effusion. He was initially administered antiparasitic drugs (Ivermectin and Praziquantel). After one week the patient presented with an acute increase in SOB and was diagnosed with bilateral hydropneumothorax. A bilateral pigtail was inserted. Pleural fluid analysis was done which was purulent with lymphocyte predominance and high adenosine deaminase. The patient was treated with anti-tubercular therapy and steroids. After six months of therapy, the patient was asymptomatic. The hypereosinophilic syndrome can be presented in several ways and this study presented in a distinct way via hydropneumothorax.

Introduction

Hypereosinophilic syndrome (HES) is a rare group of disorders marked by sustained overproduction of eosinophils and eosinophil-mediated organ damage or dysfunction.[1] Based on the underlying etiologies, HES is classified as primary (clonal), reactive, and idiopathic HES.[2] The World Health Organization (WHO) has defined HES as a sustained increase in the absolute eosinophil count (AEC) above 1500/µL for longer than 6 months and tissue damage.[3] Though the underlying pathophysiology remains unclear, clonal eosinophilic expansion and overproduction of eosinophilopoietic cytokines and their enhanced activity-mediated rise in eosinophils are the most accepted theories.[2] Since the onset is usually insidious, the disease might remain obscured for a long period.[3] Thus, it is extremely important to identify the subtle clinical features along with performing routine blood investigations for early diagnosis and management.[3] Limited studies have presented the case details of the rare condition with eosinophil-mediated organ damage or dysfunction. The clinical and other features of the case presented in this study will contribute to expanding our understanding of this kind of rare health condition focusing on the resources-limited settings where tertiary care accessibility has several challenges. This case study aims to present an adult man, a case of secondary hyper eosinophilic syndrome in a tertiary care center in Nepal.

Keywords: Case Report, Hydropneumothorax, Peripheral eosinophilia, Secondary Hypereosinophilic Syndrome

Case History

A 38-year-old male, migrant worker, a returnee from Malaysia presented to the outpatient Department of Internal Medicine at Dhulikhel Hospital, Nepal with a history of dry cough and exertional shortness of breath for two weeks. In investigations, the laboratory findings suggested peripheral eosinophilia (AEC: 8000/μL) and his chest x-ray showed left-sided pleural effusion (Figure 1).

Suspecting a potential parasitic infestation, he was initially managed with oral antiparasitic medications that included tablet praziquantel 75mg/kg/day in three divided doses for 3 days and tablet Ivermectin 12 mg once daily for 3 days. As he was progressing gradually during hospital admission, he got discharged after three days of admission with the prescription of oral steroids (prednisolone 1mg/kg/day) for 14 days.

A week after, the patient revisited the emergency department with complaints of sudden onset shortness of breath for a few hours. A Chest X-ray was repeated, which revealed bilateral hydro-pneumothorax with collapsed lungs (Figure 2). A diagnostic and therapeutic tube thoracotomy was performed by inserting chest tubes on both sides. Purulent pleural fluid was present, whose analysis showed increased eosinophil and lymphocyte with adenosine deaminase (ADA) value of >100IU/L. (Table 2). Then, the case started receiving anti-tubercular therapy (ATT) and continued the prednisolone. This was based on the pleural fluid analysis reports keeping pleural tuberculosis as the differential diagnosis through his sputum gene xpert was negative for *Mycobacterium tuberculosis* . After this medication, his shortness of breath and other clinical status were improving. Despite the completion of the initiation phase of the ATT, his cough could not subside, and his AEC remained more than 25000/μL. These findings raised the suspicion of eosinophilic leukemia prompting a bone marrow aspiration and biopsy along with Fluorescent In-situ Hybridization (FISH) analysis–the results of which have been mentioned below in table 1.

Discussion

Hypereosinophilic Syndrome (HES) is defined by an abnormal overproduction and deposition of eosinophils in the blood or peripheral organs leading eosinophil - mediated organ damage or dysfunction.[4] HES has been further divided based on etiology into primary (stem cell, myeloid or eosinophilic malignancy), secondary (parasitic infections, solid tumors, T cell lymphoma), or idiopathic.[3] According to various sources idiopathic HES is an extremely rare disease and its incidence ranges from 0.04 to 0.17 per 100,000 persons and the prevalence ranges from 0.15 to 0.89 cases per 100,000 persons.[5] Due to advances in diagnostic techniques, causes of eosinophilia can be identified in a proportion of cases that in the past would have been classified as idiopathic. However, due to the unavailability of services in Nepal, some of the investigations of the indexed case were sent to India for further evaluation. The hypereosinophilic syndrome reports male predominance, with a male-to-female ratio of 9:1.[5] HES is commonly diagnosed in patients aged 20-50 years, with a peak incidence in the fourth decade. This study also exemplified that 38 years-old male case presented with rare clinical manifestations of hypereosinophilic syndrome.

The most common cause of eosinophilia in the United States is an allergic reaction or allergic disease.[6] Worldwide, the most common cause of eosinophilia is parasitosis.[7]Several mechanisms have been proposed for the pathogenesis of hypereosinophilic syndrome, including the overproduction of eosinophilopoietic cytokines, their enhanced activity, and defects in the normal suppressive regulation of eosinophilopoiesis.[8] Eosinophils amplify the inflammatory cascade by secreting chemoattractants that recruit more eosinophils.[9] Organ damage-induced HES is due to the eosinophilic infiltration of the tissues accompanied by the mediator (major basic protein, eosinophil peroxidase, eosinophil-derived neurotoxin, and eosinophil cationic protein) release from the eosinophil granules.[9] The case presented in this study was suspected of the parasitic infestation and later further investigations reported that the cause could be eosinophilic leukemia. A similar case of hypereosinophilic syndrome case was presented with features of dilated cardiomyopathy as a dilemma to approach and treatment, as our case with the presentation of bilateral hydro pneumothorax as presentation.[10]

HES is a heterogeneous disease process with multiple manifestations that may occur simultaneously or individually.[4] The presentation can be sudden and dramatic, with cardiac, neurologic, or thrombotic complications, but, more often, the onset is insidious. HES can involve any organ system but commonly involves

the respiratory tract, skin, central nervous system, and cardiac.[4]Many patients experience fever and night sweats. Some sources identify anorexia and weight loss as common presenting manifestations. Cardiac involvement is the leading cause of mortality and common symptoms of cardiac involvement include chest pain, dyspnea, or orthopnea. A chronic, persistent cough, usually nonproductive, is the most common respiratory symptom reported in hypereosinophilic syndrome. Rhinitis or angioedema is sometimes a presenting feature. Dyspnea may occur in cardiac or respiratory involvement. Embolic or thrombotic strokes or transient ischemic episodes may occur and are often the initial manifestations. Some patients with HES experience encephalopathy caused by CNS dysfunction. Peripheral neuropathies account for about 50% of all neurologic symptoms in HES.

Arthralgia, myalgia, pruritus, diarrhea, and fatigue are relatively common manifestations of HES but are non-specific. However, the case in this study demonstrated some of the abovementioned clinical such as shortness of breath, dry cough, and chest pain.

The decision to use a drug for the treatment of HES depends partly on the presence or absence of organ involvement.[4] So, the initial evaluation of the patient with eosinophilia should include tests that facilitate the assessment of target organ damage. In asymptomatic patients' treatment is postponed till a diagnostic workup is completed and a specific diagnosis is made. Early initiation of therapy is reasonable in clonal eosinophilia associated with imatinib mesylate—sensitive molecular markers (eg, *FIP1L1-PDGFRA, PDGFRB* rearrangement, *BCR-ABL*). In idiopathic HES no evidence to support early drug treatment. Periodic follow-up with monitoring of complications is reasonable (no evidence to support this).[2] Symptomatic patients with clonal HES imatinib mesylate are the first drug to be considered in the presence of*FIP1L1-PDGFRA* or *PDGFRA/PDGFRB* translocations. For induction of remission and maintenance 100mg/d of Imatinib mesylate is recommended. In the case of rare mutant *FIP1L1-PDGFRA, imatinib-resistant, other tyrosine kinase inhibitors or interferon-alpha is sensitive for induction of remission.* In refractory cases, allogeneic hematopoietic cell transplant needs to be considered.[8] The case in this study firstly was treated with oral antiparasitic medications and steroids, later he underwent anti-tubercular therapy.

In 2018 RN Das et al reported the first case in Nepal of idiopathic HES presented with fatal eosinophilic cardiomyopathy and dysphagia.[11] They reported the case of a farmer presenting with symptoms of persistent fever, cough, dyspnea, and refractory heart failure for 7 months with peripheral eosinophilia. They found no cause for eosinophilia despite a thorough evaluation.[12] In 1971, similarly Rickles et al reviewed 16 cases of hypereosinophilic syndrome, most of which were doubtful eosinophilic leukemia.[13] In 2009, a multicenter study conducted by Princess U Ogbogu in 161 patients with eosinophilia found FIP1L1-PDGFRA test positive in 18 patients. [11]

The strength of this case study is that this has reported a rare case, and this has been reported in a tertiary care hospital in Nepal. This case report has been presented with several limitations. This case report reported only one case; thus, several such case studies would help to provide us with comprehensive information. Due to the limitations in the equipment and other resources, timely diagnosis has been one of the major challenges. Many investigations were sent to India due to unavailability in Nepal. So, the studies highlighting the challenges might contribute to disseminating the information and filling up the gap.

Conclusion

The hypereosinophilic syndrome can be presented in several ways and this study presented in a distinct way via hydropneumothorax. The unavailability of sufficient equipment and the materials to test and diagnose the hypereosinophilic led to a delay in the diagnosis. The case underwent several investigations and therapy to get it diagnosed. Thus, further studies and future researchers should emphasize the requirement of early and prompt diagnostic studies to contribute to minimizing this challenge.

Conflict of Interest All authors declare that they have no conflicts of interest in the context of this work.

Consent Statement:

Written informed consent was obtained from the patient to publish this report in accordance with the journal's patient consent policy.

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Table 1: Findings of ANCA, FISH, and bone marrow aspiration

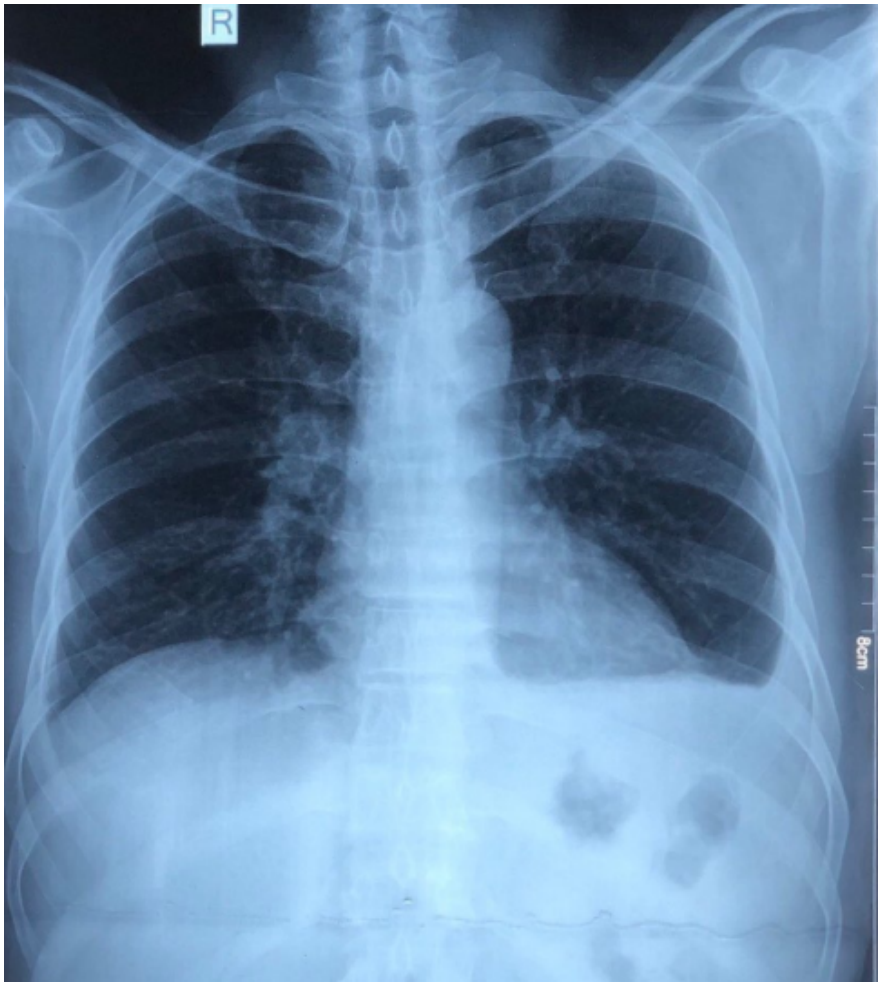
Parameters	**Findings**
Anti Neutrophil Cytoplasmic Antibodies (IFA)	**Anti Neutrophil Cytoplasmic Anti**
c-ANCA	c-ANCA
p-ANCA	p-ANCA
Fluorescent In situ hybridization (FISH)- Eosinophilic Leukemia Panel	**Fluorescent In situ hybridization (**
PDGFRA rearrangement (4q12)	PDGFRA rearrangement (4q12)
PDGFRB rearrangement (5q33)	PDGFRB rearrangement (5q33)
FGFR1 rearrangement (8p11.22-11.23)	FGFR1 rearrangement (8p11.22-11.23)
CBFB rearrangement (Inv 16)	CBFB rearrangement (Inv 16)
Bone marrow examination	**Bone marrow examination**
Cellularity	Cellularity

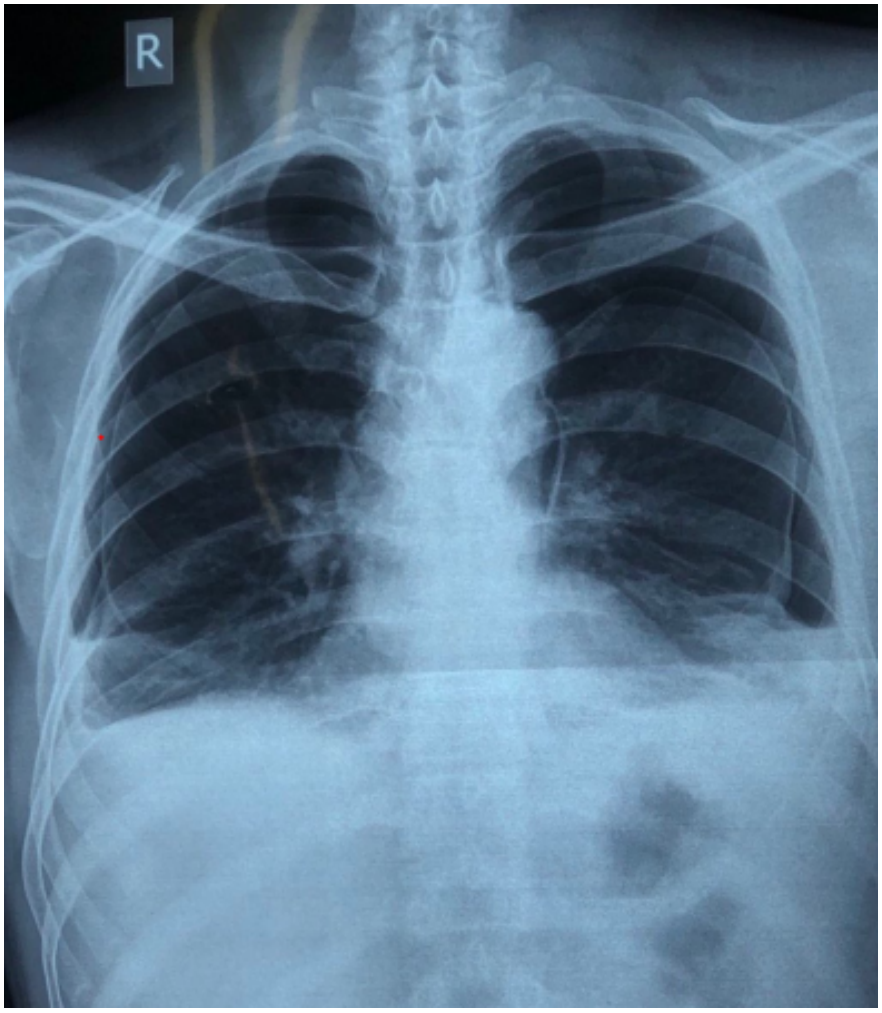
Erythroid series
Myeloid series

We referred the patient to another hospital for consultation. However, the hospital restarted the treatment with Praziquantel and Ivermectin. This made us doubtful of the judgment to continue ATT.

Table 2: Report on laboratory findings of the indexed case

Parameters	**Value**
Glucose	0.8 mg/dL (Low)
Albumin	2.9 g/dL
Protein	6.2 g/dL
Adenosine deaminase (ADA)	34 U/L
Total Leukocyte count (TLC)	21.9x10ˆ3/uL
Differential Leukocyte count (DLC)	(2 months later)
Neutrophil	22%
Lymphocyte	18
Monocyte	3
Eosinophils	57
Basophils	0
Hemoglobin	13.5 g/dl
Platelet count	333x10ˆ3/uL





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