

TUBERCULOSIS MANIFESTING WITH SIGNIFICANT PERIPHERAL EOSINOPHILIA: A CASE REPORT AND REVIEW OF LITERATURE

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INTRODUCTION:

Tuberculosis (TB) is still one of the most prevalent infections, especially in the developing world. The World Health Organisation (WHO) estimates that there are 8 million new cases annually [1,2]. Cough, sputum with or without haemoptysis, fever, and constitutional symptoms are the hallmark manifestations of an active tuberculosis infection. In patients with pulmonary TB, an increase in haemoglobin levels is regarded as an indicator of a positive response to treatment. Furthermore, Omar et al. found that a fall in platelet count, white blood cell (WBC) count, and erythrocyte sedimentation rate (ESR) were strong indications of clinical response [3]. Despite the possibility of an increase in white blood cells (WBC), which results in lymphocyte predominance, in clinical practice, eosinophilia is a usual finding that is self-limiting in moderate cases, but it is exceedingly infrequent in TB [4,5].

Many allergic, viral, and neoplastic conditions may produce peripheral blood eosinophilia, necessitating a variety of examinations and subsequent therapy. Common causes of eosinophilia in children include infections with helminthic parasites, allergic diseases, malignancies, and adverse drug reactions [1,6]. One of the primary goals of the early evaluation is to identify an underlying cause that needs specific therapy. Even though difficulties linked with eosinophilia are more prevalent in individuals with higher eosinophil counts (>1500 eosinophils/uL), the peripheral blood eosinophil count does not accurately assess the risk of organ damage in each patient. A patient with modest peripheral blood eosinophilia may also have significant eosinophil organ involvement. Normal eosinophil counts in the human blood range between 0-350/mm³. This quantity accounts for between 1 and 3% of the differential leukocyte count [7]. Most reports of eosinophilia in tuberculosis describe local eosinophilia as opposed to peripheral eosinophilia [8]. To the best of our knowledge, reported cases are very rare. As a consequence, we describe one case of TB with considerable peripheral eosinophilia and the treatment outcome.

CASE PRESENTATION:

A 9-year-old male child was presented to the paediatrics department with his mother, reporting symptoms of fever and persistent cough of one month duration, associated with acute respiratory distress. The fever

was sudden in onset, low grade, and associated with chills. There were no aggravating factors, and it was alleviated through the use of medication. The child was active during the period between febrile episodes. The cough was productive, not associated with aggravating factors, and not relieved by medications. A history of weight loss and loss of appetite were present. There were no similar complaints among his family members.

The patient had a past medical history of fever and myalgia, which was diagnosed as typhoid fever. He had been given all the scheduled immunisations, including BCG, without experiencing any significant adverse effects.

On examination, the patient was thin-built, not active, and oriented to time, place, and person. The patient was tachypnoeic (38/min), afebrile, and hemodynamically stable. Cervical lymph nodes were palpable, nontender, firm, and 2-3 in number on both sides. A chest examination revealed bilateral crepitations in the mammary, infra-mammary, axillary, and infra-axillary regions. Other systems revealed no abnormalities.

Initial blood investigations (**Table 1**) revealed a total leucocyte count (TLC) of 36,000 cells per cubic mm, a differential count of neutrophils of 11%, lymphocytes (13%), and eosinophils of 72%. A peripheral smear showed normocytic normochromic blood with eosinophilic leucocytosis. The absolute eosinophil count (AEC) was 25,920 cells per cubic mm. Liver function tests (LFT) and renal function tests (RFT) were normal. Hepatitis B surface antigen, anti-hepatitis C antibody, and Human Immunodeficiency Virus (HIV-1 and HIV-2) ELISA results were all negative. Mantoux’s skin test was negative. He underwent additional tests, including a peripheral smear for microfilaria, the Widal test, the Dengue NS1 antigen test, toxoplasmosis serology, and sputum fungal staining, all of which were negative. Blood, urine, and stool cultures were also negative. The bone marrow aspiration performed to rule out eosinophilic leukaemia showed a negative result.

A chest X-ray revealed diffuse nodular calcifications in bilateral lungs involving all zones (**Figure 1**) . High-resolution computed tomography (HRCT) chests show multiple tiny (2-3 mm) centrilobular and peribroncho-vascular branching nodular densities noted scattered diffusely and equally in bilateral lungs, both in the upper and lower lobes (**Figure 2**) . Ultrasound (US) of the chest showed mild left-sided pleural effusion with lung consolidation and collapse. The US neck detected sub-centimetrically enlarged cervical lymph nodes (7-8 mm). ZN stain and cartridge-based nucleic acid amplification test (CBNAAT) tests on sputum samples produced normal results.

The child was initially started on amoxicillin and clavulanic acid (a combination antibiotic). Due to his raised eosinophil count, the child was given diethylcarbamazine. Other symptomatic and supportive treatment was given with intravenous fluids, pantoprazole, paracetamol, Lactic Acid Bacillus (a probiotic), and nebulisations with 3% normal saline and levo salbutamol. Chest physiotherapy and spirometric exercises were advised. In view of radiologically diagnosed pulmonary tuberculosis, the patient’s regimen shifted to anti-tubercular therapy (ATT) with a fixed-dose combination of isoniazid, rifampicin, pyrazinamide, and ethambutol with pyridoxine. Complaints of coughing and difficulty breathing subsided at the time of discharge. At one-month follow-up, his eosinophil counts returned to normal levels.

Test	Result	Units	Normal Range	Method
Hemoglobin	11.6	gm/dl	11.5-15.5	Colorimetric
Total Count	36,000	cells/cu mm	5000-13,000	Impedance
Neutrophils	11	%	40-80	Light Microscopy
Lymphocytes	13	%	20-40	Light Microscopy
Eosinophils	72	%	01-06	Light Microscopy
Monocytes	04	%	02-10	Light Microscopy
Basophils	00	%	0-2	Light Microscopy
Packed Cell Volume (PCV)	35.7	Vol %	35-45	Calculation

Test	Result	Units	Normal Range	Method
Mean Corpuscular Volume (MCV)	87.5	Fl	77-95	Calculation
Mean Corpuscular Haemoglobin (MCH)	28.4	Pg	25-33	Calculation
Mean Corpuscular Haemoglobin Concentration (MCHC)	32.5	%	31.0-37.0	Calculation
Red Blood Cell count	4.08	millions/cu mm	4.0-5.2	Impedance
Platelet count	4.4	lakhs/cu mm	1.4-4.1	Impedance

Table 1: Routine blood investigations on admission

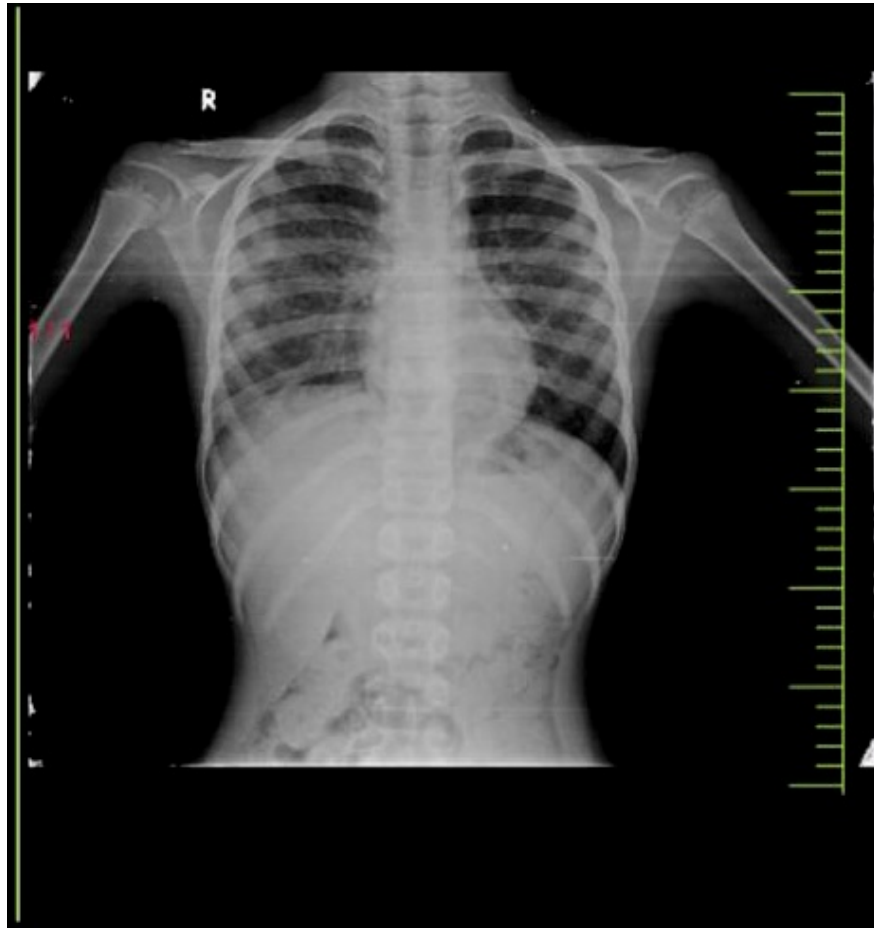


Figure 1: Chest X-ray showing diffuse nodular calcifications in both lungs, involving all zones



Figure 2: HRCT showing Numerous tiny (2–3 mm) nodules in both lungs, with branching patterns in both the upper and lower lobes.

DISCUSSION:

The most prevalent reasons for increased eosinophil count are parasitic infections, allergy/atopy, urticaria, eczema, allergic rhinitis, angioneurotic oedema, reactive eosinophilia subsequent to T-cell lymphoma, acute leukaemia, B-cell lymphoma, eosinophilic leukaemia, allergic drug reactions, idiopathic hyper-eosinophilic syndrome, and collagen vascular diseases such as rheumatoid arthritis, eosinophilic fasciitis, or allergic angitis [9].

Although TB is not a well-known cause of eosinophilia in the medical literature, it was identified in our case. Based on current evidence, there have been few reported instances of this phenomenon in recent years. Flores et al. described a similar case of peripheral blood eosinophilia and TB, which included symptoms such as lethargy, weight loss, and lymphadenopathy and was confirmed by a lymph node biopsy that revealed a granulomatous lesion [10]. Gill et al. reported a case of abdominal tuberculosis with peripheral eosinophilia. The patient was diagnosed with abdominal tuberculosis based on a histopathological examination of peritoneal tissue [8]. Similarly, Garg et al. reported a case of peripheral blood eosinophilia and TB, which included symptoms such as cough, generalized weakness, and significant weight loss and was

confirmed by endoscopic bronchial ultrasound-guided fine-needle aspiration of the mediastinal lymph node that revealed acid-fast bacilli [5].

Ray et al. proposed that after experiencing an early hypersensitive reaction to the Mycobacterium antigen, susceptible people can develop florid tropical pulmonary eosinophilia [11]. IL-5 has been shown to be the main cytokine driving the development of peripheral eosinophilia in people with pulmonary TB. The release of toxic eosinophil products is closely associated with tissue pathology. Examples of such by-products are eosinophil cationic protein, major basic protein, and eosinophil-derived neurotoxin. Potentially, the emission of reactive oxygen species may cause tissue injury [12]. The normal range of eosinophils in blood is between 0.0 and 6.0 %, and between 30 and 350 is the typical range for the AEC. AEC between 0.5 and 1.0 x10⁹/L (SI units) or 0.5 and 1.0 x10³ cells/microliter (conventional units) is considered to be mild blood eosinophilia, whereas AEC greater than or equal to 1.5 x10⁹/L is considered to be hyper-eosinophilia [13]. Our patient presented with an AEC of 70%, accounting for 25,920 cells, and a TLC of 36,000.

Hsu et al. reported that patients undergoing peritoneal dialysis had modest peripheral blood and peritoneal fluid eosinophilia. The eosinophilia persisted despite the cessation of dialysis, but it disappeared following the initiation of anti-tuberculous treatment [14]. Similarly, Haftu et al. reported a rare case of hepatic TB with significant peripheral eosinophilia [15]. Our patient's imaging results aided in clinching the diagnosis. Further evidence supporting the link between TB and peripheral eosinophilia is the patient's positive clinical response to anti-TB therapy with Ethambutol, Rifampicin, Isoniazid, and Pyrazinamide for the initial two months, followed by Rifampicin and Isoniazid for the next four months (2ERHZ/4RH). Patients with peripheral eosinophilia should have TB considered as a differential diagnosis, particularly after more prevalent reasons have been ruled out.

A few similar cases in the literature are described below (**Table 2**) :

Author	Case age/ Sex	Sign/symptoms	Radiographic findings	Laboratory Findings	Treatment plan	Outcome
Flores et al, 1983 [1]	61/M	Skin lesions, mild splenomegaly, cervical, axillary, and inguinal lymphadenopathy, fever, weakness, fatigue, and weight loss.	Abdominal Computed Tomography (CT) revealed retroperitoneal lymphadenopathy.	-White Blood cell (WBC), 8,200/cu mm, 26% neutrophils, 12% lymphocytes, 62% eosinophils; -Biopsies of skin lesions, liver, and lymph nodes revealed caseating granulomas with Langhans' giant cells and eosinophils. -A Ziehl-Neelsen (ZN) stain found acid-fast bacteria. -A needle-aspirated bone marrow specimen showed eosinophil infiltration	Isoniazid, Rifampin, Ethambutol, Streptomycin	The patient's health improved quickly.
Gill et al, 1940 [8]	19/M	Sharp chest pain, dry cough, sweating, upper abdominal discomfort, fever, and tachycardia.	Right-sided pleural effusion	- A chest fluid sample was cloudy and blood-stained, and a differential count indicated 80% eosinophil polymorphonuclear leukocytes. -Blood eosinophils 14 %	Laparotomy	The patient died eleven weeks after admission as his health worsened.

Author	Case age/ Sex	Sign/symptoms	Radiographic findings	Laboratory Findings	Treatment plan	Outcome
Hsu et al, 2000 [14]	66/F	Chronic renal failure, bilateral neck mass growth (1–3 cm) and malaise	CT showed numerous lym-phadenopathies and substantial central necrosis on both neck sides.	Peritoneal eosinophilia (54–85%) and peripheral eosinophilia (7–12%), pus-like material with unidentified non-fermentative Gram-negative bacilli in the biopsy.	Isoniazid, Rifampicin, Ethambutol, and Pyrazinamide	About 2 weeks later, her peripheral and peritoneal fluid eosinophilia subsided.
Garg et al, 2017 [5]	68/F	Cough, fatigue, weight loss, skinny, and pale	A contrast-enhanced CT of the chest and abdomen showed enlarged non-necrotic mediastinal lymph nodes with chronic liver disease features.	-Neutrophils 41%, lymphocytes 27%, and eosinophils 32%. -Needle-aspirated bone marrow and biopsies showed increased eosinophilic -Endoscopic bronchial ultrasound-guided fine-needle aspiration of mediastinal lymph nodes showed tubercular inflammation with bacilli-positive acid-fast stain.	Isoniazid, Rifampicin, Ethambutol, and Pyrazinamide	Eosinophil counts normalized within a week.

Author	Case age/ Sex	Sign/symptoms	Radiographic findings	Laboratory Findings	Treatment plan	Outcome
Haftu et al, 2020 [15]	9/F	Right upper quadrant stomach ache, decreased appetite, vomiting, weight loss, lethargy, and low-grade intermittent fever	-Abdominal Ultrasound (US) shows hepatomegaly with aberrant echo pattern and cystic change -Liver CT indicates several cystic and tiny daughter cysts as a connecting hypoechoic mass-like lesion	-Leucocytosis with severe eosinophilia with 50% -The biopsy showed partially encapsulated hepatocyte lobules with many epithelioid granulomas, large cells, necrosis, and micro abscesses and chronic inflammatory cells, mostly lymphocytes and eosinophils, confirming Liver TB.	Isoniazid, Rifampicin, Ethambutol, and Pyrazinamide	After six months of Anti-Tubercular Therapy (ATT), the patient was symptom-free, gained 5 kg, and with normal lab findings.

Table 2: List of similar cases published in literature

CONCLUSION:

The diagnostic process begins with a thorough history and physical examination. When collecting a patient’s history, it is important to ask about travel history as well as any diseases or conditions related to collagen vascular tissue, changes in immunological function, medication use, or blockage of the airway. Even with infectious disorders, the ultimate diagnosis will always depend on how well the patient responds to therapy. In light of these findings, we believe that further studies are required to determine the pathophysiology of severe eosinophilia in TB and to identify this condition as a potential causal factor.

CONFLICTS OF INTEREST:

None declared.

AUTHOR CONTRIBUTION:

All the authors contributed equally in drafting, editing, revising and finalizing the case report.

ETHICAL APPROVAL:

The ethical approval was not required for the case report as per the country’s guidelines.

CONSENT:

Written informed consent was obtained from the patient to publish this report.

DATA AVAILABILITY STATEMENT:

The data that support the findings of this article are available from the corresponding author upon reasonable request.

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