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Case Report

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A Rare Coexistence: Pulmonary Langerhans Cell Histiocytosis and Pulmonary Tuberculosis in a Young Male

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SUMMARY

Pulmonary Langerhans Cell Histiocytosis (LCH) is a rare disorder affecting the lung parenchyma with an unclear underlying cause. The condition is marked by isolated or multiple proliferations of histiocytes, which resemble dendritic Langerhans cells in phenotype. The progression of LCH varies significantly, ranging from isolated eosinophilic granulomas in the bone to widespread involvement of multiple organs. Although rare, LCH has been observed in conjunction with other conditions, like pulmonary tuberculosis. We describe an uncommon case involving a 34-year-old male patient who presented with fever, dry cough, and progressively worsening dyspnea, accompanied by an unintentional weight loss of 15 kg over the preceding 20 days. He was diagnosed with both pulmonary tuberculosis (TB) and Pulmonary Langerhans Cell Histiocytosis (P-LCH). The diagnosis was corroborated by radiological imaging, which displayed multiple nodules and small cysts in the upper and middle lung lobes on both sides, consistent with P-LCH. Additionally, sputum CBNAAT testing confirmed the presence of Mycobacterium tuberculosis.

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Background

Pulmonary Langerhans Cell Histiocytosis (PLCH) is an uncommon disease, histologically characterized by granulomas densely populated with Langerhans cells. [1]. The illness has a very unpredictable natural history. The clinical severity of the disorder varies, ranging from a single bone eosinophilic granuloma to a multi-organ disease. Although tuberculosis is one of the most common respiratory infectious, pulmonary Langerhans cell histiocytosis (PLCH) is relatively rare and is defined histopathologically by granulomas containing a high concentration of lung-localized Langerhans cells (LCH) . The disease's course is unpredictable, with clinical severity ranging from isolated bone eosinophilic granuloma to multi-organ involvement. Although tuberculosis is one of the most frequently encountered respiratory infections, it can occur infrequently alongside PLCH, making differentiation between the two challenging. This report outlines a case involving the coexistence of pulmonary tuberculosis and pulmonary Langerhans cell histiocytosis. Diseases can rarely co-exist with PLCH, and the differentiation between the two is difficult [2,3]. Here, we describe a case of active pulmonary tuberculosis coexisting with pulmonary Langerhans cell histiocytosis.

Case Presentation

A 34-year-old, active smoker and alcoholic male shopkeeper from North India, presented at AIIMS, Rishikesh. He reported having a high-grade fever (up to 102°F) for 20 days along with chills, body aches, weakness, and a non-productive cough. He mentioned losing 15 kg over the past month. He did not have any headaches, eye pain, sinusitis, sore throat, or chest pain. Upon examination, he appeared malnourished, exhibited tachycardia (110 bpm), tachypnea (28 breaths per minute), had a temperature of 101.2°F, and an oxygen saturation of 96%. The physical exam revealed bilateral pitting pedal edema, pallor, and a 2 cm lymph node in the left axilla. His abdomen was distended and non-tender, displaying shifting dullness, and chest auscultation showed reduced air entry in the right infra-scapular area.

Investigations

A complete hemogram was suggestive of pancytopenia with Hemoglobin of 6.4 g/dl, total leucocyte count of 3500 cells per cumm, and platelet count of 4000 cells per cumm. Liver function test revealed elevated transaminases and alkaline phosphatase (SGOT= 216 U/L, SGPT= 108 U/L, ALP= 1668 U/L), ESR was 40 mm/hr, hypoalbuminemia with serum albumin of 1.2 g/dl, coagulopathy with PT: 18, INR: 1.6 . Ascitic fluid analysis revealed low SAAG ascites with ascitic fluid albumin= 0.2, serum albumin= 1.2. Contrast-enhanced CT scan of the thorax revealed Innumerable miliary nodules seen diffusely scattered in bilateral lungs, predominantly in bilateral upper and right middle lobes with cavitation to form multiple variable-sized cysts in bilateral upper and right middle lobes- features suggestive of Langerhans cell histiocytosis (Figure 1.) For pancytopenia, a bone marrow aspiration and biopsy were done, suggesting a cellular marrow with granulomatous inflammation, suggestive of tuberculosis (Figure 2). Sputum CBNAAT was positive for Mycobacterium tuberculosis.

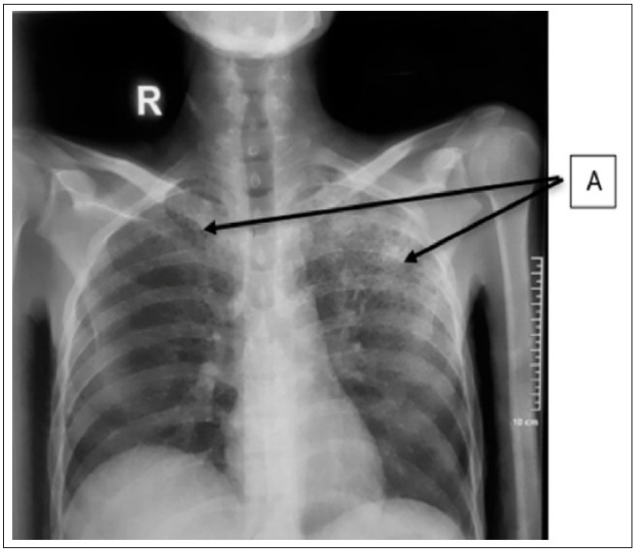

Figure 1: Xray of the Patient

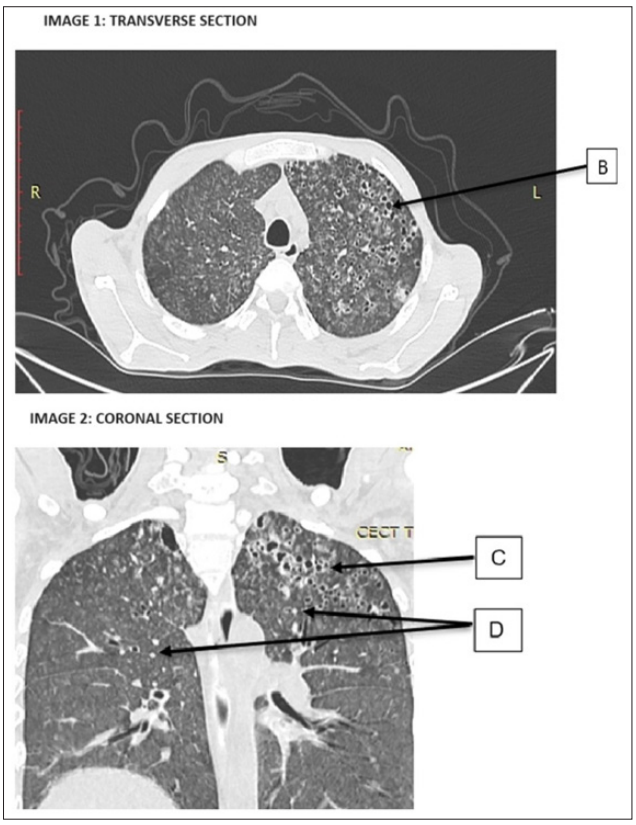

Figure 2: Contrast-Enhanced CT Scan Chest

Figure 2 Showing Transverse Sections (Image 1) and Coronal Sections (Image 2) of the CECT chest of the Patient Showing Multiple Small Cystic lesions, More in the left upper lobe (arrows B and C), and Multiple Nodular Lesions (arrow D)

Table 1: Investigations

Investigation	units	Range	Day 1	Day 3	Day 7	DAY 13	**Ascitic fluid Analysis:** Cells – 90/ mm3 (Differential count – 70 % lymphocytes and 30% polymorphs Protein –0.7 mg/dl Gram stain and culture – Negative. KOH and acid-fast bacilli stain – Negative CBNAAT - negative **CECT Thorax:** Innumerable miliary nodules are seen diffusely scattered in bilateral lungs, predominantly in bilateral upper and right middle lobes, with cavitation to form multiple variable-sized cysts in bilateral upper and right middle lobes- features suggestive of Langerhans cell histiocytosis.
Hb	g/dl	13-17	7.4	6.4	9.3	9.4	
TLC (x1000)	$\times 10^3$ cells/mm^3	4-11	3.7	2.8	2.53	13.34 k	
DLC (N/L/M)	%	40-70/20-40/2-8/1-6	88/7/2	80/7/4	91/6.3/1.6	98/0.5/0.9	
Platelet	×103 cells/ mm3	150 -450	1 k	4 k	7 k	29 k	
TB	mg/dl	0.3 – 1.2	1.53	1.7	5.08	12.04	
DB	mg/dl	0 – 0.2	1/02	1.14	3.31	0.42	
SGPT	U/L	0-50	108	138	106	76	
SGOT	U/L	0-50	216	238	532	331	
ALP	U/L	30-120	1668	1201	538	1015	
GGT	U/L	0-55	248	184	74	122	
Total Protein	g/dl	6.6-8.3	3.9	4.1	4.2	5.2	
Albumin	g/dl	3.5-5.2	1.2	1.6	1.9	2.4	
Globulin	g/dl	2.5-3.2	2.7	2.6	2.3	2.7	
Urea	mg/dl	17-43	61	48	97	112	
Creatinine	mg/dl	0.72-1.18	0.87	0.87	1.6	1.92	
Sodium	mmol/L	136-146	124	133	140	138	
Potassium	mmol/L	3.5-5.1	4.3	3.4	3.9	3.7	
Chloride	mmol/L	101-109	97	99	101	99	
Calcium	mg/dl	8.8-10.6	6.8	6.6	7.3	7.9	
Uric acid	mg/dl	3.5-7.2	3.9	1.63	5.3	5	
Phosphorus	mg/dl	2.5-4.5	3.5	2.7	6.6	4.9	
PT/INR			18.6/1.66		28.4/2.6	20.8/1.87	
D-dimer				3.94	>180		
aPTT				60.1			
Fibrinogen				69.2	127		
Ferritin			>1650				
Procalcitonin	ng/ml	<0.5			2.2		

Hb – Haemoglobin, TLC – Total Leukocyte count, DLC – differential leukocyte count, RDW – red cell distribution width, ALT – alanine Transaminases, AST – Aspartate transaminases, ALP – alkaline phosphate, GGT – gamma-glutamyl transferase, PT – prothrombin ratio, INR – International standardised ratio.

Treatment

The patient was started on ATT for pulmonary tuberculosis. His HRCT thorax revealed features of pulmonary tuberculosis and Langerhans cell histiocytosis coexisting together. He was planned for lung biopsy for pulmonary Langerhans cell histiocytosis, but could not be done as the patient was vitally unstable for the procedure. He developed worsening oxygen requirement during his hospital stay, likely due to hospital-acquired pneumonia; he was initially managed with NRBM (15L/ min); later on, NIV support was given in medicine HDU. He was shifted to the medicine ICU due to worsening oxygen requirement, where non-invasive ventilation was tried but failed. Later, he was intubated in view of respiratory distress. He went into septic shock for which broad-spectrum antibiotics (Inj Meropenem 1g TDS, Inj Vancomycin 1g BD and Inj Levofloxacin 750 mg OD- later doses were modified as per creatinine clearance) and inotropes (Inj Noradrenaline, later Inj Vasopressin) were started, but the patient succumbed to his illness.

Discussion

Langerhans cell histiocytosis (LCH) is an uncommon infiltrative disorder of the histiocytes, marked by the accumulation of tissues by Langerhans cells, a unique form of dendritic cell. Formerly known as histiocytosis X or eosinophilic granuloma., it is now recognized that the so-called "X" cells are actually LCH cells [4]. These cells can be distinguished from other dendritic cells by their surface expression of CD1a and the presence of intracellular Birbeck granules. Lung involvement is more common in adults and can present as either isolated pulmonary LCH (PLCH) or as a multisystem illness that affects many organs [5]. Incidental PLCH was found in roughly 4–5% of 502 patients in a study who underwent surgical lung biopsies for diffuse lung disease [6]. The condition is closely linked to smoking, which is thought to encourage the accumulation and activation of histiocytes in the small airways. About 70% of those affected have a reduced diffusing capacity of carbon monoxide (DLCO) on pulmonary function testing (PFT). High-resolution CT (HRCT) scans of the chest typically reveal small nodules and cysts with thin or thick walls, mostly located in the upper and middle lung regions.

PLCH presents with a broad spectrum of clinical manifestations [5,7,8]. Even with widespread lung involvement, symptoms may be either absent or mild, causing many patients to initially link their respiratory problems to smoking. While a lung biopsy is usually needed for a definitive diagnosis, it may not be required if HRCT results strongly point to PLCH. In our case, HRCT findings highly indicated pulmonary Langerhans cell histiocytosis. Birbeck granules can be seen by electron microscopy or Langerin (CD207) immunohistochemical staining to identify LCH cells in inflammatory lesions [9]. While immunohistochemical markers such as CD1a and S-100 can aid in identifying LCH cells, they are unable to make a conclusive diagnosis of PLCH on their own.

PLCH is typically a single-system disease; most patients do not exhibit extrapulmonary involvement at diagnosis [10]. When other organs are involved, the most common sites are the bones affecting 4%–15% of cases, the pituitary gland 5%–15%, and the skin in less than 5% cases. Isolated PLCH confined to the regional lymph nodes is exceptionally rare. Although cervical lymphadenopathy has been documented in LCH cases, it usually manifests as isolated lymph node LCH or as a component of a systemic disease that is broad rather than confined to the lungs. A frequent side effect of PLCH is spontaneous pneumothorax, which is most likely caused by cystic destruction of the lung parenchyma. Younger people seem to be more at risk, with 15% of PLCH patients reporting a history of pneumothorax [Figure 3].

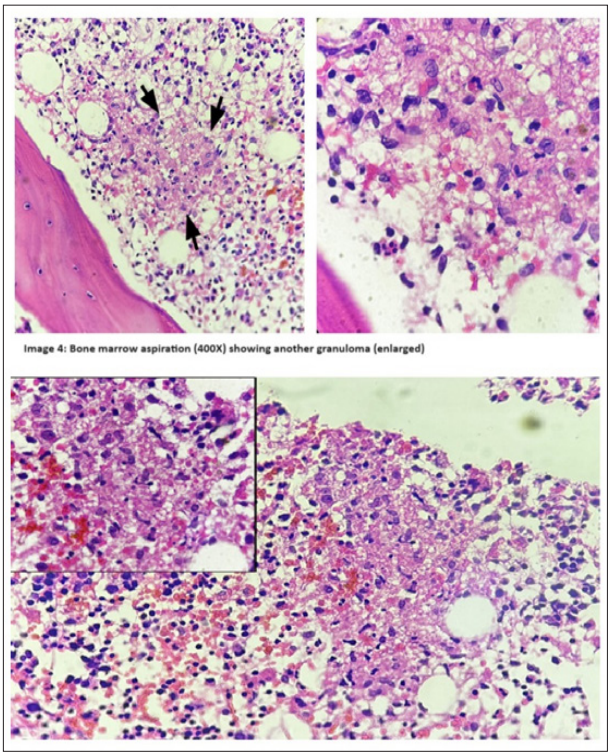

Figure 3: Bone Marrow Biopsy of the Patient

Figure 3 Shows the Patient's Bone Marrow Biopsy Report, Showing a Well-Formed Granuloma (black arrows). Image 4 Shows the Magnified Image Highlighting the Granuloma with Multiple Giant Cells and Lymphocytic Infiltration (square enlarged).

Additionally, tuberculosis-related lung damage can predispose patients to pneumothorax [11]. Managing PLCH requires quitting smoking, given the strong link between cigarette use and the progression of the disease. The overall prognosis is usually good , especially for patients who maintain stable lung function throughout the course of the disease. However, those with severe disease or declining pulmonary function may require immunosuppressive therapy [12]. Corticosteroids, frequently prescribed for the treatment of PLCH, have the potential to greatly enhance the virulence of tuberculosis if given without simultaneous antituberculous therapy, presenting significant dangers in cases where TB has not been diagnosed. Thus, in individuals diagnosed with both PLCH and tuberculosis, the primary focus should be on treating tuberculosis first. In instances of pneumothorax, recurrence is most effectively treated with tube thoracostomy and pleurodesis, rather than relying solely on chest tube drainage.

This method reduces the risk of recurrent pneumothorax, which is a well-established complication of PLCH.

Learning Points

- PLCH should be considered in smokers presenting with dry cough and breathlessness, especially when HRCT shows characteristic cystic and nodular changes in upper and middle lung zones. While lung biopsy is the gold standard, highly characteristic HRCT findings may be sufficient for diagnosis in some cases.
- Spontaneous pneumothorax is a common complication of PLCH, occurring in approximately 15% of patients, particularly younger ones, and preventive interventions should be considered after the first episode.

- In regions with high tuberculosis prevalence, clinicians should consider the possibility of coexisting tuberculosis in patients with PLCH-like presentations and be cautious when

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