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HAIRY CELL LEUKAEMIA WITH AN UNCOMMON PULMONARY PRESENTATION: A CASE REPORT AND REVIEW OF THE LITERATURE

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ABSTRACT

Introduction: Hairy cell leukaemia (HCL) is a rare B-cell neoplasm and pulmonary involvement in HCL is exceedingly rare, often leading to diagnostic challenges. Non-resolving pulmonary infiltrates have a broad differential, including infections, malignancies, and autoimmune diseases, requiring a multidisciplinary approach for diagnosis.

Case report: We report the case of a 61-year-old man who presented with fever, dyspnoea, weight loss, and bicytopenia. Initial chest imaging showed bilateral lower lung opacities, and empirical antibiotic therapy was administered. Despite treatment, symptoms persisted, prompting further investigations. High-resolution computed tomography scan revealed consolidations and ground-glass opacities. Extensive infectious workup was negative. Bronchoscopy with endobronchial ultrasound biopsy showed organizing pneumonia, and a bone marrow biopsy confirmed HCL with pulmonary involvement. The patient declined a surgical lung biopsy, but his pulmonary infiltrates and bicytopenia improved with corticosteroid and cladribine chemotherapy.

Conclusion: This case highlights the importance of considering haematologic malignancies in non-resolving pulmonary infiltrates and persistent bicytopenia. A stepwise diagnostic approach, including bone marrow biopsy and bronchoscopy, was crucial in establishing the diagnosis. Successful treatment with cladribine reinforces its efficacy in HCL and suggests similar cases may benefit from this approach. Further research is needed to optimize diagnostic and treatment strategies for HCL with pulmonary involvement.

KEYWORDS

Hairy cell leukaemia, bicytopenia, pulmonary lymphoma

LEARNING POINTS

- Hairy cell leukaemia with initial pulmonary manifestation is very uncommon.
- The timing for bone marrow examination to persisted bicytopenia is uncertain.

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INTRODUCTION/BACKGROUND

Hairy cell leukaemia (HCL) is a rare, indolent B-cell lymphoproliferative disorder that accounts for approximately 2% of all adult leukaemias. It typically presents pancytopenia, splenomegaly. Most cases are diagnosed incidentally or during evaluation for cytopenia. Pulmonary involvement in HCL, however, is extremely rare and not commonly recognized as part of the initial disease presentation. This case of a rare disease with uncommon presentations emphasizes the importance of physician awareness regarding hematologic malignancy in atypical clinical scenarios. This case exemplifies the need for a multidisciplinary, algorithmic approach in evaluating persistent pulmonary and hematologic abnormalities

CASE DESCRIPTION

A 61-year-old man with fatigue, poor appetite and a 9 kg unintentional weight loss (from 65 to 56 kg) for 2 months, presented with fever, dry cough and progressive dyspnea for 1 week. He denied recent travel or a history of bleeding. He worked in the electronics industry with frequent exposure to chemicals. His medical history included type 2 diabetes mellitus managed with oral hypoglycemics. He had a 30-year smoking history.

Upon arrival at our emergency room, his body temperature was 38.1°C, and his heart rate was around 141 bpm, without hypotension. Peripheral capillary oxygen saturation was 90% with a shallow breathing pattern under ambient air. Chest auscultation revealed bilateral basilar crackles. There was no palpable adenopathy, skin rashes, bruising or petechiae. Chest X-ray disclosed patchy opacities in the lower lobes bilaterally *(Fig. 1A)*. Laboratory data showed anaemia (haemoglobin, Hb 9.6 g/dl) and leukopenia (white blood cell, WBC count 2600/µl), with elevated C-reactive protein (31.84 mg/dl). The platelet count was within normal limits (309 $\times 10^3$/µl). COVID-19 polymerase chain reaction (PCR) testing was negative. Renal and liver functions were normal. He was then admitted to the Chest Medicine ward with a tentative diagnosis of bilateral lower lung community-acquired pneumonia.

A nasal cannula at 3 l/min was applied upon hospitalization for oxygen support, and amoxicillin/clavulanate with azithromycin were administered as empirical antibiotics. Treatment was switched to levofloxacin after 3 days due to progressing lower lung infiltrates *(Fig. 1B)*. Testing for several pathogens was performed and results were negative, including *Streptococcus pneumoniae*, *Haemophilus influenzae*, *Legionella pneumophila*, *Mycoplasma pneumoniae*, herpes simplex virus, Cytomegalovirus and *Mycobacterium tuberculosis*. PCR tests for Influenza A and B were also negative. Follow-up laboratory data showed persistent anemia (Hb 9 g/dl), leukopenia (WBC count 2000/µl).

Despite 10 days of antibiotic therapy, the patient remained hypoxemic with unresolved pulmonary infiltrates. High-resolution computed tomography (HRCT) revealed bilateral lower lungs consolidations and ground-glass opacities (GGO) *(Fig. 1C)*. A ventilation/perfusion scan showed a low probability of pulmonary embolism. Anemia was macrocytic (mean corpuscular volume, MCV 103.8 fl; reticulocyte index: 0.56) without gastrointestinal bleeding

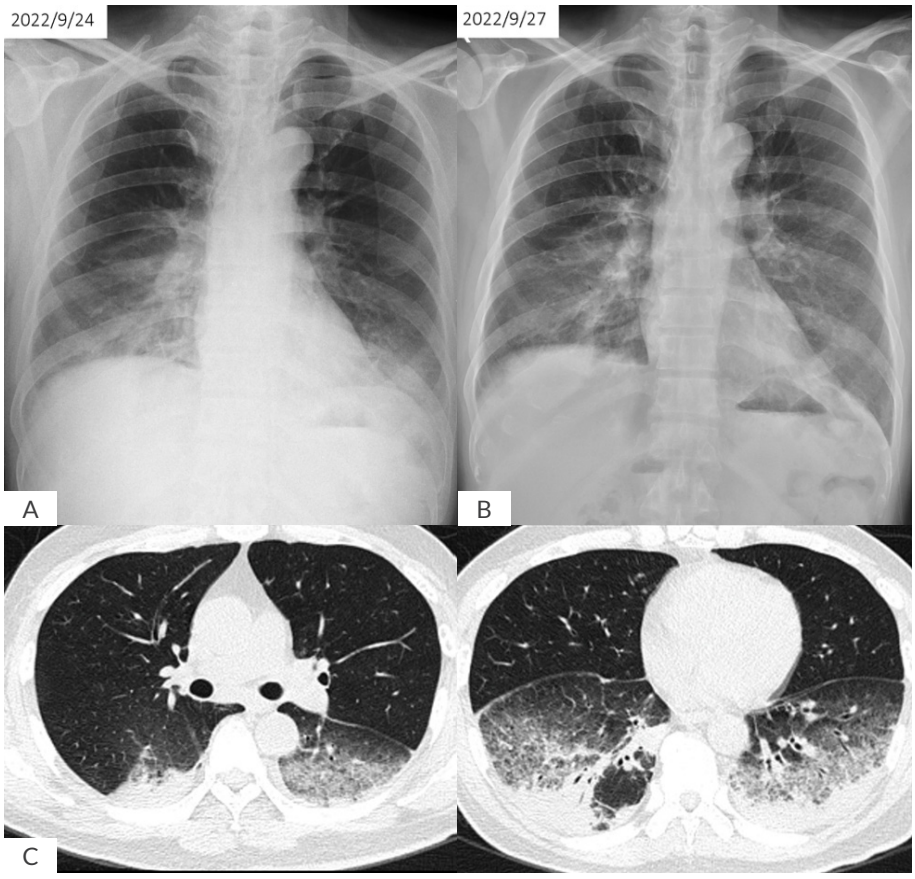


Figure 1. A) Chest X-ray disclosed patchy lung opacities in the lower lobes bilaterally; B) Chest X-ray showed progressing lower lung infiltrates after using 3 days of previous antibiotics; C) High-resolution computed tomography scan showed mixed consolidation and ground-glass opacity involving bilateral lower lungs without endobronchial lesions.

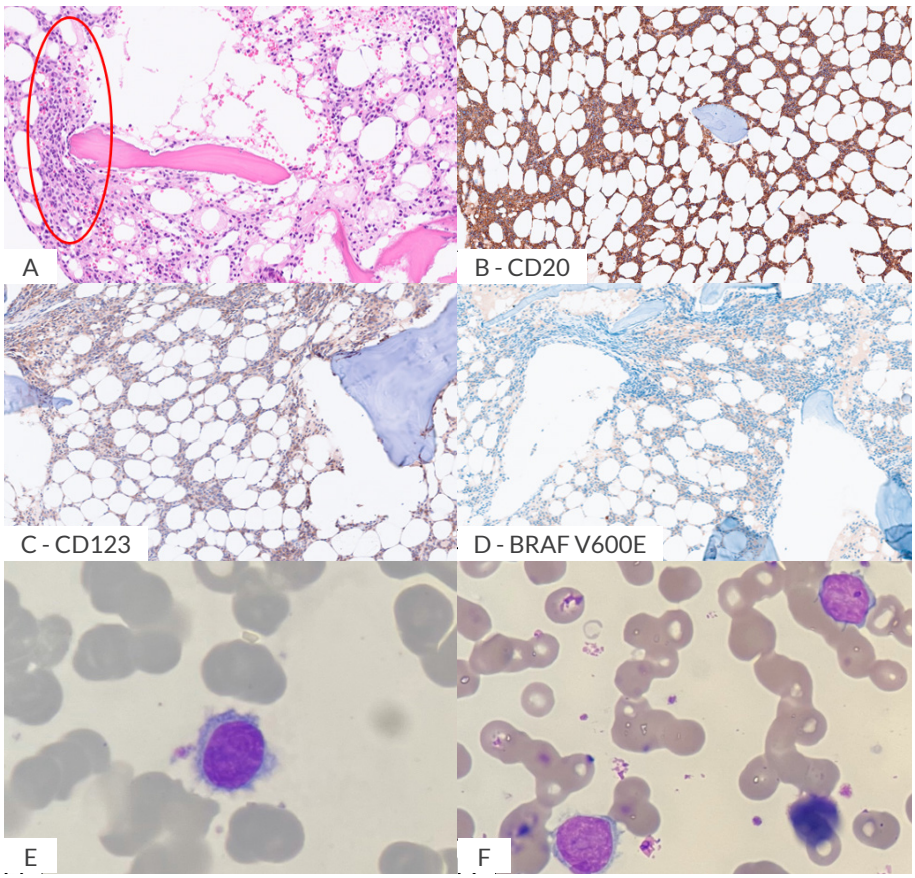


Figure 2. Bone marrow analysis: A) Small B cell lymphoma with plasmacytic differentiation; B-D) Immunohistochemistry staining showed positive with CD20, CD123, BRAF V600E; E) Cytoplasmic projections noted from lymphocytes in the bone marrow smear; F) Cytoplasmic projections noted from lymphocytes in the peripheral blood smear.

or nutritional deficiencies. Abdominal ultrasound showed no hepatomegaly or splenomegaly, and hepatitis markers were negative. Adrenal and thyroid function tests were normal, and autoimmune evaluations showed no remarkable findings. The diagnosis of the patient remained elusive, so we decided to arrange bronchoscopy and consult a hematologist. The bronchoscopy disclosed normal endobronchial mucosa without visible lesions; however, endobronchial ultrasound (EBUS) revealed a concentric lesion with a "blizzard sign" at RB9. Biopsy and bronchoalveolar lavage (BAL) were conducted. Comprehensive microbiological studies, including the Film Array Respiratory Panel for common respiratory pathogens, routine sputum culture, acid-fast stain, KOH stain, and India ink preparation, yielded negative results. Histopathological examination of the tissue revealed organizing pneumonia, with no evidence of malignancy.

The bone marrow biopsy was performed for unexplained bicytopenia, which reported diffuse infiltrate of small B-cell lymphoma. Immunohistochemistry staining showed positive markers including CD20, CD123, BRAF V600E *(Fig. 2A-D)*. The flow cytometry indicated that these abnormal B cells were positive for CD19, CD20, CD11c, CD103, CD123, Cyclin D1, and negative for CD3, CD5. The bone marrow smear presented the lymphocytes with cytoplasmic projections *(Fig. 2E)*, which also presented in peripheral blood *(Fig. 2F)*. Chromosome analysis revealed a normal male karyotype. The diagnosis of hairy cell leukemia was proved.

Due to suspected lymphoma-related pulmonary involvement,

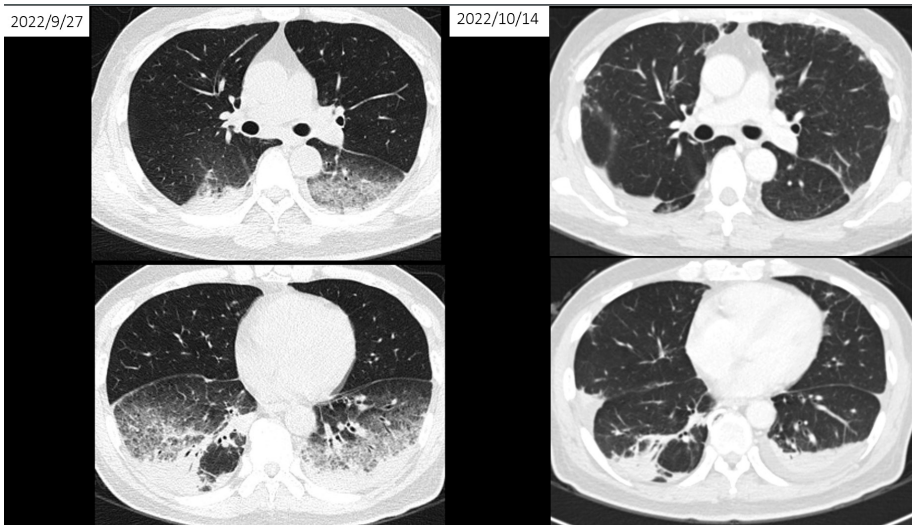


Figure 3. High-resolution computed tomography scan: right lower lobe/ left lower lobe consolidations without other solid organ tumours or enlarged lymph nodes, and the area of consolidations as well as ground-glass opacities decreased a lot compared with the computed tomography scan on 27 September.

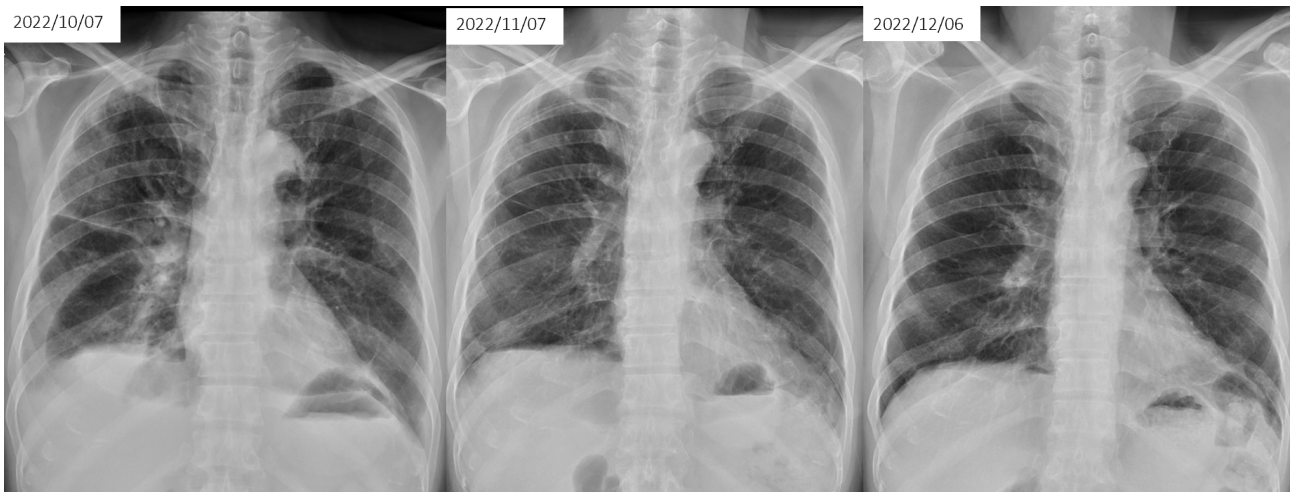


Figure 4. Chest X-ray: bilateral lower lung infiltrate almost resolved after treatment.

	Before treatment	7 nov 22	17 nov 22	13 dec 22	28 jan 23	06 may 23
Hb (g/dl)	8.6	8.2	8.0	9.0	12.5	14.0
WBC (10^3/µl)	2.0	0.6	1.4	2.3	3.5	5.5
ANC (1/µl)	1420	480	1300	1380	1540	3108
Platelets (10^3/µl)	274	117	112	281	229	189
LDH (IU/l)	233	93	-	127	135	140
Uric acid (mg/dl)	4.2	4	-	3.9	5	7
Potassium (mEq/l)	5.6	4.1	-	-	-	-
Calcium (mg/dl)	8.95	9	-	-	-	-
Phosphate (mg/dl)	3.17	4.53	-	-	-	-

Abbreviation: Hb, haemoglobin; WBC, white blood cells; ANC, absolute neutrophil count; LDH, lactate dehydrogenase.

Table 1. Hemogram before and after chemotherapy.

surgical lung biopsy was suggested but declined by the patient over surgical risk concerns. Methylprednisolone 40 mg/q12h was initiated, and a follow-up computed tomography (CT) scan showed significant improvement in consolidation and GGO compared to the prior scan. *(Fig. 3)* Chemotherapy with cladribine for 7 days led to clinical complete remission by 28/01/2023. *(Table 1)* Chest X-ray showed near-complete resolution of lung infiltrates. *(Fig. 4)* Bone marrow examination on 21/02/2023 confirmed hematologic remission, with 0.06% abnormal cells.

DISCUSSION

This case highlights the importance of the management for patients with complex hematologic and pulmonary presentations. The overall prevalence of HCL is approximately 0.3 per 100,000 individuals per year, representing about 2% of all adult leukemias in the United States[1], with a lower incidence in Asia. HCL is a rare, indolent neoplasm of mature B cells with hairlike surface projections[2]. Most patients are asymptomatic, but classic HCL may present with pancytopenia, splenomegaly, and increased infection risk. Splenomegaly is common (present in 80 to 85% of patients), causing abdominal discomfort in the left upper quadrant and even splenic infarction[2,3]. However, our case did not present typical symptoms of splenomegaly at initial presentations.

Pulmonary involvement in lymphoma is also uncommon; while primary pulmonary lymphoma accounts for <1% of all lymphomas, secondary lung involvement occurs in ~24% of non-Hodgkin's lymphoma cases[4]. HCL with pulmonary infiltration is exceedingly rare, with only isolated case reports *(Table 2)*[5-7].

In this case, a multidisciplinary approach was essential because BAL excluded infection and bone marrow biopsy confirmed HCL.

However, EBUS biopsy revealed organizing pneumonia. It was unclear whether pulmonary involvement was due to leukaemia cell infiltration or secondary inflammation. While surgical lung biopsy could clarify this, risks such as bleeding and respiratory failure were of concern.

Many disorders that cause pancytopenia can also cause

Reference	Tissue-proved method	Treatment response
Fields and Harris, 1982[7]	Nil Mycobacterial infection	Nil
Hansen et al. 2019[6]	BAL cytology Positive for hairy cell leukaemia	Complete remission
Ecsiova et al. 2023[5]	Transbronchial biopsy Positive for hairy cell leukaemia	Complete remission

Abbreviation: BAL, bronchoalveolar lavage.

Table 2. Summary of previous case reports describing hairy cell leukaemia with pulmonary involvement.

bicytopenia, so the evaluations are similar. There are several causes of pancytopenia such as nutritional disorders, infections, drugs or autoimmune diseases[8]. After thorough work-up, prompt hematologic consultations are needed if there is no reasonable cause for more than 2 weeks. Bone marrow examination should be considered to identify aetiologies.

Non-resolving pulmonary infiltrations is defined as radiographic infiltrate that does not resolve within 12 weeks after using adequate antibiotic therapy[9]. We need to re-evaluate the microbiologic data because pneumonia caused by different pathogens still account for up to 40% of these cases[10]. The uncommon causes include pulmonary neoplasm, lymphoma or leukaemia, interstitial lung disease[9]. If CT scan or bronchoscopy cannot provide explanations for the pulmonary infiltrations, then surgical biopsy is needed to provide histopathological data[11].

We made the diagnosis of HCL following the above-mentioned algorithm, and the patient was successfully treated with cladribine. However, this case emphasizes that in the presence of pancytopenia accompanied by B symptoms and non-resolving pulmonary infiltrates, early bone marrow examination even before invasive lung investigations may facilitate identification of the underlying aetiology. The rarity of this presentation highlights the need for further research to better understand the optimal practices for similar cases.

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