Pulmonary Extramedullary Hematopoiesis

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Introduction

Myelodysplastic syndrome (MDS) and myeloproliferative neoplasms (MPNs) are two broad categories of disease under the even broader umbrella of myeloid neoplasms. These two categories of pathology can have multiple overlapping features, including blood cell abnormalities and bone marrow inadequacy or failure, and often present with derangements in blood cell counts and splenomegaly. Their similarities lead to difficulty in accurate diagnosis and treatment.

In rare cases, patients can develop extramedullary hematopoiesis, leading to even more unusual clinical presentations. Liver and spleen are the most common sites of extramedullary hematopoiesis, but other sites have been noted. Herein, we describe such a case of a patient who presented with new lung nodules and overlapping risks for multiple etiologies.

Case Presentation

A 70-year-old gentlemen with a past medical history of coronary artery disease, tobacco use disorder, chronic cough, anemia, and myelofibrosis presented to a regional Pennsylvania hospital with complaints of fever (103.0°F at home), chills, and increasing dyspnea for three weeks. In the ED, the patient was afebrile, with normal heart rate and respiratory rate, normotensive, and with adequate oxygen saturation on room air. Physical exam was noncontributory. Labs revealed a severe leukocytosis with neutrophilic predominance and anemia.

Complete Blood Count	Value (ref range)
Hemoglobin	7.9 g/dL (14.0-17.0 g/dL)
Red blood cells	2.87/L (4.50-6.00/L)
White blood cells	149.9 x 10^3/L (4.0-11.0 x 10^3/L)
Neutrophils, absolute	83.94 x 10^3/L
Bands, absolute	10.49 x 10^3/L
Lymphocytes, absolute	6.00 x 10^3/L
Monocytes, absolute	17.99 x 10^3/L
Metamyelocytes, absolute	10.49 x 10^3/L
Myelocytes, absolute	4.50 x 10^3/L
Other cells, absolute	16.49 x 10^3/L

Table 1. Complete blood count on presentation. Of note, patient has anemia and leukocytosis with neutrophilic predominance.

The patient had previously been on momelotinib, a JAK2 inhibitor, with normalization of his blood counts.

Due to the above findings and patient's history of myelofibrosis, a peripheral blood smear was reviewed. The smear showed atypical granulocytes with immature myelocytes, Pelgeroid and hypersegmented neutrophils, and promonocytes consistent with known history of myeloproliferative/myelodysplastic disorder.

In the setting of worsening dyspnea and concern for pulmonary embolism or infection, a computed tomography (CT) angiogram of the chest was obtained (Figure 1).

Clinical Course

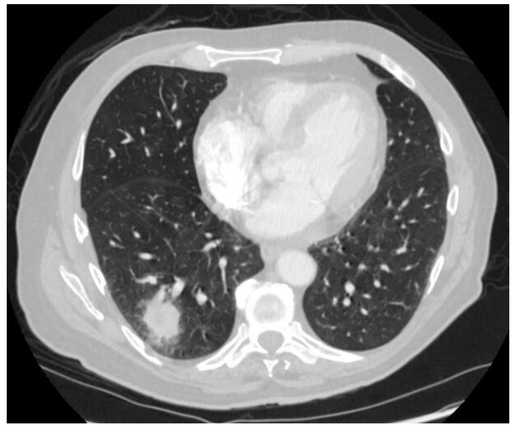

Figure 1. CT angiography of the chest. Notable findings include bilateral lower lung spiculated nodules measuring up to 2.9 cm, associated mediastinal and hilar lymphadenopathy, and centrilobular emphysema. No pulmonary embolism was seen. In this view, only the right lung nodule is visible.

Out of concern for lung malignancy versus infection, Pulmonology was consulted and performed a bronchoscopy for biopsy. Bronchoalveolar lavage was also performed and Mycobacterium avium complex was isolated. Despite this, acid fast staining and cultures were unrevealing.

Multiple biopsy samples were obtained from lung nodules, lymph nodes, and bronchoalveolar lavage. Samples showed atypical hematopoietic cells consistent with MPN. Flow cytometry was performed on bronchoalveolar lavage and peripheral blood samples but did not identify blasts in either. The patient had further CT imaging of the head, abdomen, and pelvis which showed a nodule in the right lateral cerebral ventricle, splenomegaly, an adrenal nodule, and redemonstrated the previously noted lower lobe lung nodules.

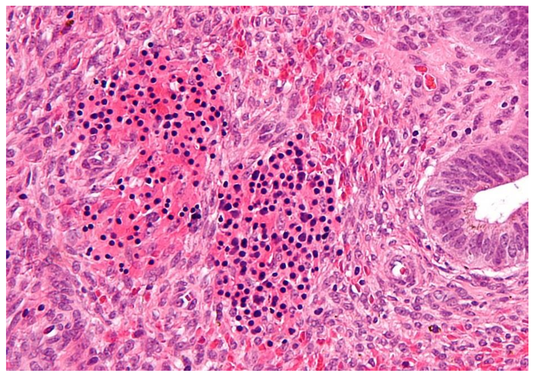

Figure 2. H&E stain of an endometrial polyp demonstrating extramedullary hematopoiesis, unrelated to our patient. Two foci of nucleated red blood cells are visible. Adapted from Wikipedia.org.

Due to persistent fever and dyspnea, patient was treated with course of antibiotics for pneumonia and oral steroids for bronchospasm. His symptoms improved and he was deemed to be stable for discharge. Upon deliberation with Hematology-Oncology, the patient was determined to have foci of extramedullary hematopoiesis in the lungs.

After discharge, biopsy samples were submitted for molecular analysis for gene variants. Molecular analysis showed pathologic variant in BRIP1 associated with an increased hereditary risk for cancer. Other noted mutations included CBL, IDH2, and SRSF2 variants, which elevated the patient's risk of progression to AML. His MPN was reclassified as a proliferative MDS at that time.

Discussion

Extramedullary hematopoiesis is a rare presentation of MDS. When present, usual sites of occurrence involve the liver, spleen, or paravertebral areas. The diagnosis of extramedullary hematopoiesis in rarer sites, such as the lungs, is challenging due to nonspecific symptoms that often mimic other pathologies. Differentials in these cases include infection, malignancy, and interstitial lung diseases.

Infectious	Pulmonary	Hematologic/Oncologic
Bacterial pneumonia	Idiopathic interstitial lung disease	Primary lung cancer
Tuberculosis	Pneumoconiosis	Metastatic cancer from alternate source
Nontuberculous mycobacteria	Sarcoidosis	MDS/MPN, Extramedullary hematopoiesis
Aspergilloma, invasive aspergillosis		

Table 2. A non-exhaustive list of differential diagnoses of our patient with fever, cough, leukocytosis, pulmonary nodules, and hilar/mediastinal lymphadenopathy in consideration of his risk factors. Differentials are roughly grouped by broad pathologic process.

Radiographic findings can help differentiate between these, but correct diagnosis often requires biopsy and pathology review. Even in cases where pathology is obtained, diagnosing extramedullary hematopoiesis requires a high degree of confidence to rule out other, more severe conditions. This case, which initially presented with seemingly obvious signs of infections with overlapping risks for primary lung malignancy, highlights this diagnostic challenge.

Conclusion

Myelofibrosis is a hematologic disorder that can present with rare features, such as extramedullary hematopoiesis, that obfuscate an accurate diagnosis. In patients with extramedullary hematopoiesis, workup often involves ruling out other pathologies such as infection, other primary malignancies, and inflammatory disorders. Often, biopsy is required to rule out and/or confirm clinical suspicions. Therefore, correct diagnosis requires a broad differential and awareness of atypical presentations.

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