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CASE REPORT

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An intriguing case of a paravertebral extramedullary erythropoiesis presenting as tumor-mimicking lesion in a patient with eosinophilia with FIP1L1-PDGFRA rearrangement

Sassi Farah[1] | **Houcine Yoldez**[1] | **Ayadi Rahma**[1] | **Mlika Mona**[1] | **Braham Emna**[1] | **Abdennadher Mahdi**[2] | **El Mezni Faouzi**[1]

[1]Pathology Department, Abderrahmen Mami Hospital, Ariana, Tunisia

[2]Cardiovascular and Thoracic Surgery Department, Abderrahmen Mami Hospital, Ariana, Tunisia

Correspondence
Sassi Farah, Abderrahmen Mami Hospital, 2080 Ariana, Tunisia.
Email: sassi.farah@outlook.fr

Abstract

Extramedullary hematopoiesis in the posterior mediastinum is rare. Our case interested a 28-year-old man with a history of eosinophilia with FIP1L1-PDGFRA fusion gene who had a mediastinal mass surgically excised. Pathological examination concluded to an extramedullary erythropoiesis. This case is original by its location and the presence of only the erythroblastic line rearrangement.

KEYWORDS

eosinophilia, erythropoiesis, FIP1L1-PDGFRA, mediastinum, myeloproliferative neoplasm, tyrosine kinase inhibitor

1 | INTRODUCTION

The term "extramedullary hematopoiesis" (EMH) refers to hematopoiesis that takes place outside the medulla of the bone. Although EMH may manifest anywhere in the body, the liver, spleen, and/or lymph nodes are where it most frequently manifests as diffuse lesion.[1] Rarely, EMH manifests as a solitary mass in an unusual site mimicking a tumor and, thus, is usually misdiagnosed.[2] The posterior mediastinum is an uncommon localization of EMH. It is typically recognized as a bilateral, multiple, well-circumscribed mass with soft tissue density during radiological screening using computed tomography (CT) and/or magnetic resonance imaging (MRI).[2] Through pathological analysis, trilineage hematopoietic cells are clue features to validate the diagnosis of EMH.[3] However, the presence of only erythroblasts in extramedullary sites has never been described before.

EMH develops when there is myelofibrosis and insufficient erythropoiesis, such as in thalassemia, hereditary spherocytosis, and sickle cell disease.[3] However, extramedullary erythropoiesis (EME) as a complication of a myeloproliferative neoplasm with eosinophilia with FIP1L1–PDGFRA fusion gene has never been reported in the literature to the best of our knowledge.

We, herein, report the first case of an EME presenting as a paravertebral tumor-like mass in a 28-year-old man with a history of myeloproliferative neoplasm with prominent eosinophilia with FIP1L1–PDGFRA fusion gene.

2 | CASE REPORT

A 28-year-old man was admitted to the respiratory department for chronic dyspnea for one year which worsened suddenly. On investigation, he had a 13-year history

of myeloproliferative neoplasm with eosinophilia with FIP1L1–PDGFRA fusion gene diagnosed by real-time polymerase chain reaction (RT-PCR), BCR-ABL negative with an initial absolute eosinophil count (AEC) of 78.06×10^9/L and white blood cells (WBC) of 91.87×10^9/L. He has been treated with Imatinib with gradual dose escalation (100 mg/d then 3×100 mg/wk) since 2010 with a moderate decrease in eosinophils count (5.690×10^9/L, in 2019) supporting the use of second-generation tyrosine kinase inhibitors (TKI), Nilotinib. No strict plan for molecular monitoring was established.

On the day of admission, a complete blood count (CBC) was done showing hemoglobin level at 15.5 g/dl, platelets count at 256×10^9/L, WBC at 11.7×10^9/L, AEC at 4.030×10^9/L, and normal levels of lymphocytes, neutrophils, monocytes, and basophils. Laboratory studies, including liver function tests, random blood sugar, renal function tests, alkaline phosphatase, and serum calcium, were within normal limits. Infectious serologies (Hepatitis A, B, or E and HIV) were negative. Peripheral smear examination showed no blasts. Bone marrow aspirates revealed a blast percentage <3%. A computed tomography (CT) of the chest showed in the upper mediastinum a 50×54 mm left latero-vertebral mediastinal mass with subpleural development with a heterogeneous density without calcified or fatty cystic component in contact with the left sub-clavian artery without signs of invasion. The mass was located at T2 and T3 and was not accompanied by costovertebral osteolysis (Figure 1). In the abdominal area, the spleen was of normal size, measuring 12 cm in long axis, with notches and calcification of sequellar appearance. Magnetic resonance imaging (MRI) of the chest was performed showing a mass of the posterior mediastinum lateralized on the left with an isosignal T1-weighted, hyposignal T2-weighted, enhanced after injection of Gadolinium. The differential diagnosis based on radiological features was Castelman disease, a mesenchymal tumor, or a neurogenic tumor. A surgical excision was undergone. Grossly, the mass was well circumscribed, brownish with a homogeneous cut surface. The entire surgical resection was included. The histological examination showed a loose fibrous connective tissue, with numerous fibroblasts and dystrophic vessels. Numerous erythroblasts were observed at different stages of maturation, associated with small areas of extravasated erythrocytes and many siderophages (Figure 2). Focal zones of hemosiderin and dystrophic calcification forming Gamna–Gandy nodules were observed. No megakaryocytes or granulocytic cells have been observed as evidenced by immunohistochemistry which showed no staining with myeloperoxidase (MPO). Glycophorin A was focally positive (Figure 3). With the final diagnosis of EME, the patient was discharged with a prescription for inhaled corticoids and referred to hematology department. Physical examinations and additional radiographs were used to evaluate

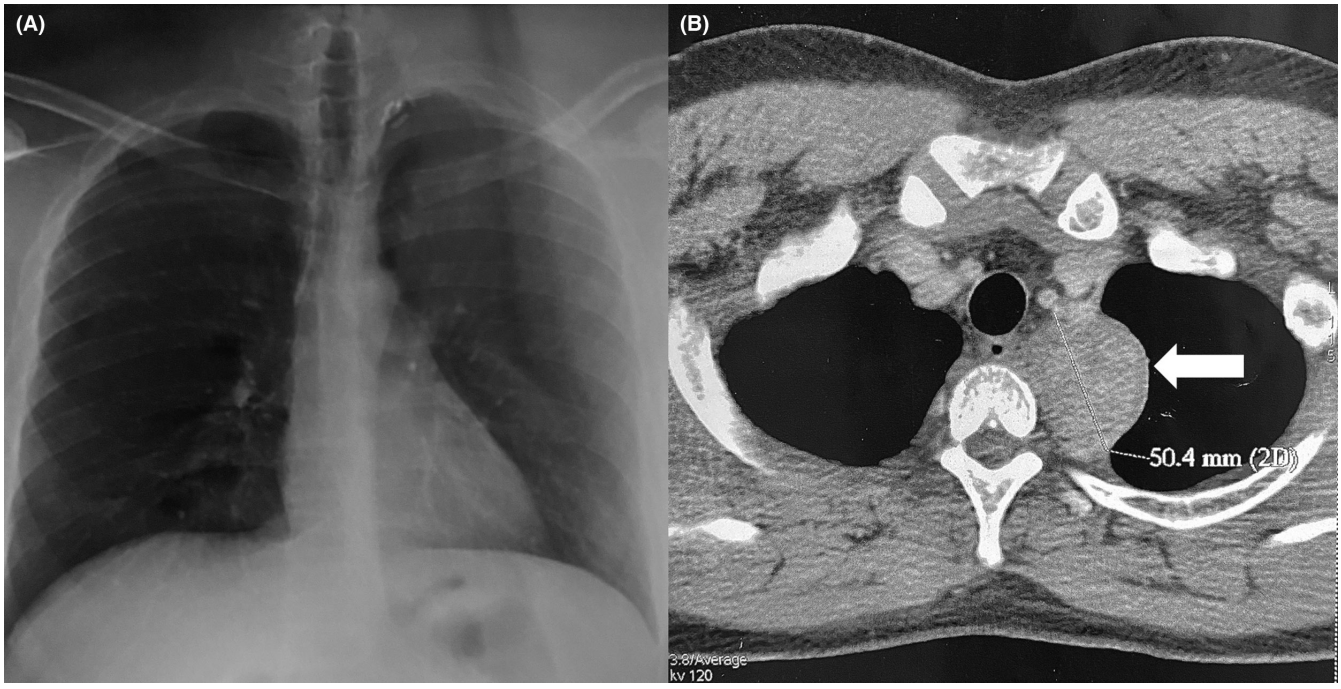

FIGURE 1 (A) Chest radiography showing no sign of tumor. (B) Computed tomography of the thorax showing a 50×54 mm left latero-vertebral mediastinal mass (arrow) with an heterogeneous density without calcified or fatty cystic component in contact with the left sub-clavian artery without signs of invasion.

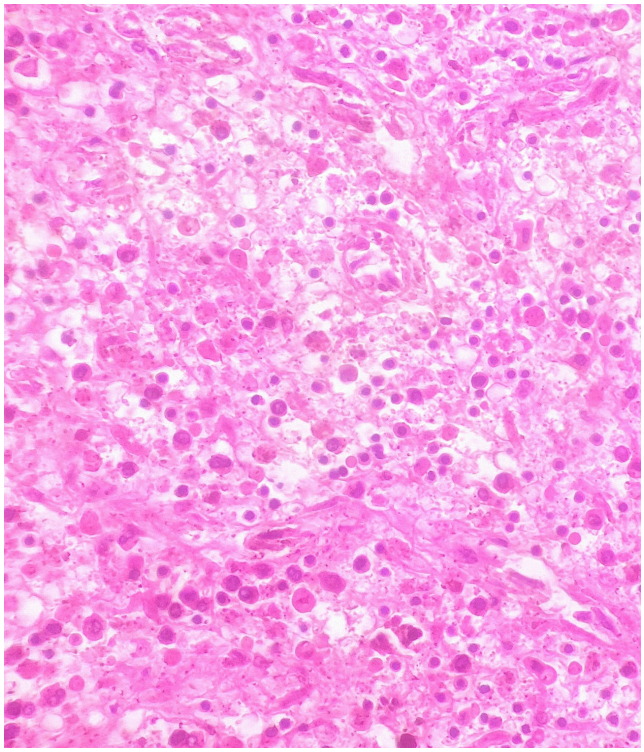

FIGURE 2 Numerous erythroblasts were observed at different stages of maturation, associated with small areas of extravasated erythrocytes and many siderophages (HE ×400).

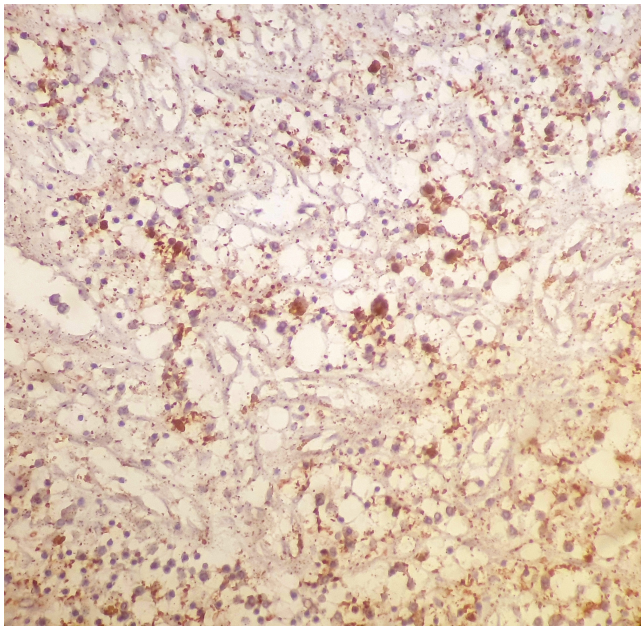

FIGURE 3 Staining in erythrocyte precursor cells with Glycophorin A.

the patient, who has now been asymptomatic for three years after initially presenting, with no local recurrence or distant disease.

3 | DISCUSSION

The WHO recognized that "Myeloid/lymphoid neoplasms with eosinophilia and PDGFRA rearrangement" usually manifest as hypereosinophilia (HE/AEC of $\geq 1.5 \times 10^9$/L) or hypereosinophilic syndrome (HES; HE with organ damage)[4] and less frequently as acute myeloid leukemia or T-lymphoblastic leukemia/lymphoma.[5] It involves the constitutive activation of tyrosine kinases that are highly responsive to TKI, Imatinib, as a result of the FIP1L1-PDGFRA (F/P) translocation.[5] Myeloid neoplasms with PDGFRA rearrangement are usually characterized by a cryptic deletion on chromosome 4q12 that results in a FIP1L1-PDGFRA gene fusion.[6]

Eosinophils may infiltrate tissues in myeloid neoplasms with PDGFRA rearrangement; however, involvement of the bone marrow is a hallmark, and the diagnosis is normally made by analyzing the blood and bone marrow. Although soft tissue masses including the scapula, chest wall, scalp, and spine have been recorded, extramedullary involvement by myeloid neoplasm with a PDGFRA rearrangement is relatively uncommon.[7]

EMH may have physiological or pathological origins. The development of extramedullary hematopoietic tissue when the normal blood-forming marrow is disturbed may be linked to a wide range of pathologic diseases. Spherocytic anemia, infant erythroblastosis, thalassemia, pernicious anemia during remission, macrocytic anemia of hepatic origin, carcinomas with bone marrow invasion, Hodgkin's disease, lymphoma, leukemia, osteosclerosis, and myeloproliferative syndrome are among the common causes of EMH.[2,8] As in our case, EMH is a physiological compensatory mechanism that is typically linked to hematologic diseases. There have also been reports of patients with EMH without a hematological disease.[2,9]

Intrathoracic EMH in myeloid neoplasm with FIP1L1-PDGFRA rearrangement is rare and forms a tumor-like mass in the posterior mediastinum, particularly in lower paravertebral space. Two cases have been reported. The first case interested a 63-year-old man with a FIP1L1-PDGFRA rearrangement confirmed by fluorescent in situ hybridization (FISH) in bone marrow and had a paravertebral mass at T4-T5, and L3 and sphenoidal mass with intraorbital extension. The second case was about a 53-year-old man with eosinophilia and a well-differentiated extramedullary myeloid tumor with a paravertebral mass at L3-L4 with extradural infiltration with evidence of FIP1L1-PDGFRA rearrangement by FISH in the extramedullary tissue.[10]

EMH in the posterior mediastinum is generally asymptomatic but can cause, when it has large dimensions,

pleural effusion, hemothorax, and fatal respiratory failure[2,11,12] which is similarly to our case where the patient presented with a dyspnea.

Chest CT typically shows a unilateral or bilateral, smooth, lobulated, and non-enhancing mass.[5,7] Our patient's non-specific contrast enhancement on the CT scan could be a sign of several other diseases, such as neural or mesenchymal tumors, neoplastic tumors, or EMH. As a result, samples from the tumor were necessary for a firm diagnosis and course of treatment. MRI is also very useful in the diagnostic's approach.[7]

Although biopsy is an undeniable tool to diagnose EMH, it remains an invasive tool because of the risk of hemorrhage. In our case, thoracoscopic excision of the tumor resulted in the first management and a valuable diagnostic data.

In our case, mediastinal EMH with only one cell lineage consisting of erythroblasts was seen. We do not fully understand the possible mechanism behind these two manifestations. The patient was not anemic. No blood transfusion was done. The spleen was of normal size. The entire surgical resection was included and was carefully examined to exclude granulocyte and megakaryocytic lineage. Immunohistochemical staining for MPO was negative, and Glycophorin A was positive. Such EME was described in 1995 in a patient's liver who have received a liver allograft with no evidence of bone marrow dysfunction. The authors explained that when the bone marrow is dysfunctional, EME is typically brought on by strong stimulatory signals for the formation of red blood cells. EME occurs under these circumstances mostly in the liver and spleen, demonstrating the potential for erythropoietic activity of these organs in adult.[13] In myeloid neoplasm with FIP1L1-PDGFRA rearrangement, this is the first case to report mediastinal EME.

Treatment for solid masses diagnosed EMH may vary based on the patient and the situation. Transfusion therapy, laminectomy, radiotherapy and the use of fetal hemoglobin, inducing agents that decrease the hematopoietic drive have been described.[14] Surgical excision reduces the frequency of transfusions and puts an end to the expansion of ectopic hematopoietic foci.

4 | CONCLUSION

To conclude, this is the first reported case of EME presenting as an isolated tumor-like lesion in the posterior mediastinum in a 28-year-old man with a myeloid neoplasm with FIP1L1-PDGFRA fusion gene successfully surgically treated. EME might be mistaken for other benign or malignant lesions. Collaboration between a clinician, radiologist, and pathologist is necessary to prevent misdiagnosis.

AUTHOR CONTRIBUTIONS

Farah Sassi (MD) involved in acquisition of data, literature research, conception, and preparation of the manuscript. Yoldez Houcine (MD) involved in conception, design, and preparation of the manuscript. Rahma Ayadi (MD) and Mouna Mlika (MD) revised the manuscript critically. Emna Braham (MD) involved in manuscript editing. Mahdi Abdennadher (MD) involved in acquisition of clinical data. Faouzi El Mezni (MD) involved in final approval of the version to be published. All authors read and approved the final version of this manuscript.

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None.

CONFLICT OF INTEREST

Not applicable.

DATA AVAILABILITY STATEMENT

Not applicable.

CONSENT

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

ORCID

Sassi Farah https://orcid.org/0000-0003-2078-6795
Mlika Mona https://orcid.org/0000-0003-2470-0012

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