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Review article

Myeloid diseases in the lung and pleura

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ABSTRACT

Myeloid diseases detected as primary or secondary lesions in the lung and pleura are rare. Clinical presentations and radiographic results may vary significantly depending on the nature of the diseases. The most common diseases associated with lung and pleura involvement are myeloid sarcoma/acute myeloid leukemia (AML) and extramedullary hematopoiesis (EMH). AML typically represents localized involvement by systemic acute leukemia, while EMH is frequently secondary to underlying benign hematolymphoid disorders or myeloproliferative neoplasms. This review provides an overview of the pathogenesis, clinical presentations, radiologic/imaging studies, pathologic and genetic findings, and treatment/outcomes associated with myeloid diseases in the lung and pleura.

Introduction

Myeloid diseases detected as primary or secondary lesions in the lung and pleura are rare. Clinical presentations and radiographic results may vary significantly depending on the nature of the primary disease. Despite their rarity, case reports or small case series of myeloid diseases involving the lung and pleura have been reported. A review of the literature indicates that the most common myeloid diseases associated with lung and pleura involvement are myeloid sarcoma/acute myeloid leukemia (AML) and extramedullary hematopoiesis (EMH).[1–15] These cases could mimic lymphoma, non-hematolymphoid tumors, or infection.

This article aims to provide an overview of the salient features of myeloid sarcoma and EMH in the lung and pleura, including pathogenesis, clinical presentations, radiologic/imaging studies, pathology, and treatment/outcomes. We hope this article will be of interest to the *Seminars in Diagnostic Pathology* readership.

Myeloid sarcoma and acute myeloid leukemia

Acute myeloid leukemia (AML) is a malignant neoplasm characterized by the proliferation of leukemic cells (blasts) with myeloid differentiation. AML is a heterogeneous disease that can affect individuals in any age group, albeit it is more common in adults and its incidence increases with age. Patients might develop AML *de novo*, or the disease could arise secondarily in the context of an antecedent myeloid neoplasm such as myeloproliferative neoplasm (MPN), myelodysplastic syndrome (MDS), or MDS/MPN. A subset of patients exposed to chemotherapy and/or radiation therapy develops therapy-related AML (or MDS).[16] Each of these broad AML subgroups is associated with different prognostic properties, further modulated by cytogenetic and molecular genomic factors that impart added clinical, therapeutic, and prognostic complexity.

Pathogenesis

Localized tissue involvement by AML outside the bone marrow resulting in architectural tissue alteration is termed myeloid sarcoma, and it is generally reported to be seen in 2.5-9% of cases.[17] Goyal *et al* reported a lower incidence of 0.8% myeloid sarcoma in a cohort of 94,185 patients in the National Cancer Database diagnosed with AML between 2004 and 2013.[18] In this study, patients had a median age of 59 years (range, 41-73 years), and 56.1% were men; 32/746 (4.3%) patients had cardiopulmonary and mediastinal involvement (not parsed out further). Movassaghian *et al* identified 345 patients in the Survival, Epidemiology, and End Results database aged ≥15 years diagnosed with isolated myeloid sarcoma between 1973 and 2010.[19] This cohort included only 3 cases involving lung and 1 involving pleura (Table 1).

Extramedullary manifestations of AML have been divided into 4 clinicopathologic subgroups: 1) isolated myeloid sarcoma; 2) myeloid sarcoma with concurrent AML; 3) myeloid sarcoma as a relapse lesion; 4) blast phase/transformation of an underlying MPN, MDS or MDS/MPN.[20] AML with monocytic differentiation and with recurrent translocations involving core binding factor (*CBF*) – t(8;21)(q22;q22)/

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Table 1
Selected recent studies describing cases of myeloid neoplasms involving the lung and pleura

Study	Cases	Age/Sex	Underlying diseases	Involved anatomic locations	Pathology/Genetics	Follow up
Fang L *et al.* (2020)[46]	1	37/M	Isolated myeloid sarcoma	Mediastinum, pleura, lung and pectoralis major	*ASXL1* p.R693X	Remission
Goyal *et al.* (2017)[18]	32*	59 (range, 41-73) 56% M	Myeloid sarcoma, not otherwise specified	Cardiopulmonary and mediastinal area	n/a	n/a
Chandra *et al.* (2017)[47]	1	45/M	Chronic myeloid leukemia	Humerus and pleura	n/a	Positive for disease by imaging
Movassaghian M *et al.* (2015)[19]	4	n/a	Isolated myeloid sarcoma	Lung or pleura	n/a	n/a
Faiz et al. (2012)[22]	28	65 (range, 17-85) 55% M	AML (25) and MDS/MPN (3)	Pleura	n/a	n/a
Tsimeridou AM et al. (2008)[48]	1	n/a	Isolated myeloid sarcoma	Pleural and chest wall	n/a	n/a

*Cardiopulmonary and mediastinal (not detailed further). Abbreviations: n/a, not available

RUNX1-RUNX1T1; inv(16)(p13;1q22) or t(16;16)(p13.1q22)/*CBFB-MYH11* – have a higher predilection for extramedullary involvement at presentation.

Radiologic/Imaging studies

Imaging findings of lung involvement by AML include leukostasis, hyperleukocytosis, and pulmonary alveolar proteinosis.[21] Pleural involvement is comparatively less common but can be also seen in AML, manifest as pleural effusion, pleural masses, or pleural thickening.[21] Faiz *et al* conducted a thorough analysis of pleural effusions in a cohort of 111 patients with acute leukemia and MDS/MPN.[22] Pleural effusions were due to an infectious etiology in most patients. Among 45 patients with pleural effusion directly attributed to the underlying malignant hematologic disease, 25 (56%) had AML, and 3 (6%) had MDS/MPN.

Pathology

Histologic evaluation to determine the nature of the myeloid proliferation is essential for appropriate diagnosis and disease classification, particularly in patients who have myeloid sarcoma as a relapse lesion, blast transformation of an underlying hematologic malignancy, or - much less commonly in lung and pleura - isolated myeloid sarcoma. Histologic identification of a neoplasm comprised of immature neoplastic cells with blastoid features should prompt evaluation for myeloid sarcoma or AML (Figs. 1, 2, and 3). Typically, myeloid sarcoma is comprised of intermediate-sized to large cells with scant to moderate amounts of somewhat eosinophilic cytoplasm, irregular nuclear

Fig. 1. Acute myeloid leukemia involving lung tissue. (A) Leukemic involvement is primarily peribronchial and perivascular. (B) Leukemic cells are immature, and they have scant to moderate cytoplasm, irregular nuclear contours, and blastoid chromatin pattern. [A, 200x hematoxylin and eosin; B, 600x hematoxylin and eosin]

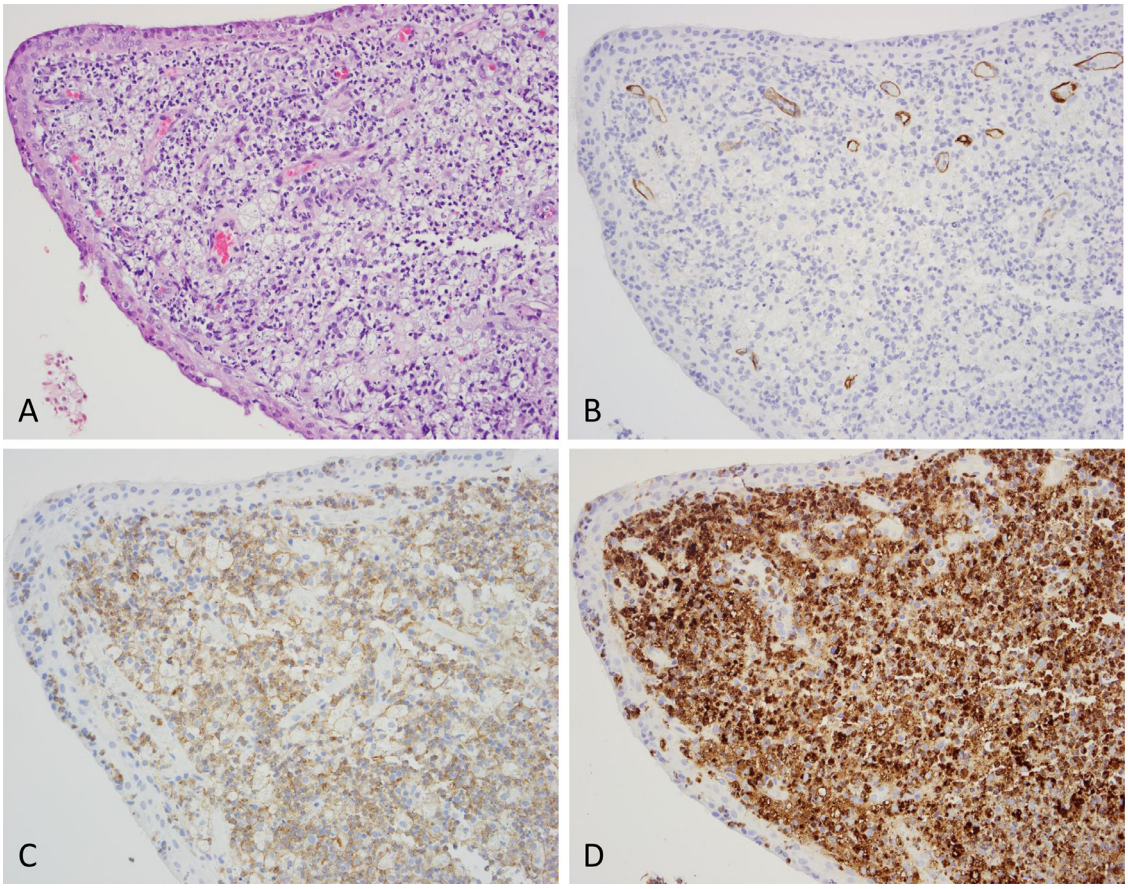

Fig. 2. Endobronchial biopsy showing acute myeloid leukemia involving lingula. (A) Leukemic cells are admixed with inflammatory cells. (B) CD34 immunohistochemistry shows lack of expression in leukemia infiltrate. (C) and (D) CD33 and lysozyme immunohistochemistry show diffuse expression in mature and immature cells, respectively. [A, 200x hematoxylin and eosin; B-D, 600x immunohistochemistry with hematoxylin counterstain]

contours, open chromatin, and variably prominent nucleoli. In the majority of cases, a subset of neoplastic cells exhibits some degree of maturation, manifest as cells with deeply clefted nuclei in keeping with differentiation to metamyelocyte or even band stage of granulocytic maturation, or with irregular/folded nuclei in keeping with differentiation to promonocytes and mature monocytes. Mitotic figures are usually easily identified, and some cases have a starry-sky pattern.[23] Eosinophils are present in a subset of cases. Immunohistochemistry provides the most useful adjunct tool (Figs. 2 and 3), as it is not uncommon for myeloid sarcoma to be identified unexpectedly, precluding an opportunity to collect fresh material for flow cytometry immunophenotyping.

Immunohistochemical markers useful in the evaluation of myeloid diseases in the lung and pleura are summarized in Table 2. The diagnosis of myeloid sarcoma with initial pulmonary presentation in a patient without a known history of leukemia can be challenging. As such, it should be in the differential diagnosis when a patient presents *de novo* with round cell neoplasm involving the lung. While CD45 (leukocyte common antigen) expression may help to demonstrate the hematopoietic origin of the neoplastic cells, it should be noted that CD45 expression level may occasionally be dim enough to be below the detection limit of immunohistochemistry. Furthermore, myeloid sarcoma may express B-cell, T-cell, or NK-cell markers, such as CD19, CD7, and CD56, respectively. Reactivity of tumor cells with CD43, a nonspecific marker that is often positive in T-cell lymphoma, without CD3 coexpression should always prompt consideration of a myeloid neoplasm. In an analysis of immunohistochemistry markers for myeloid sarcoma, Chen *et al* demonstrated that the most frequently expressed

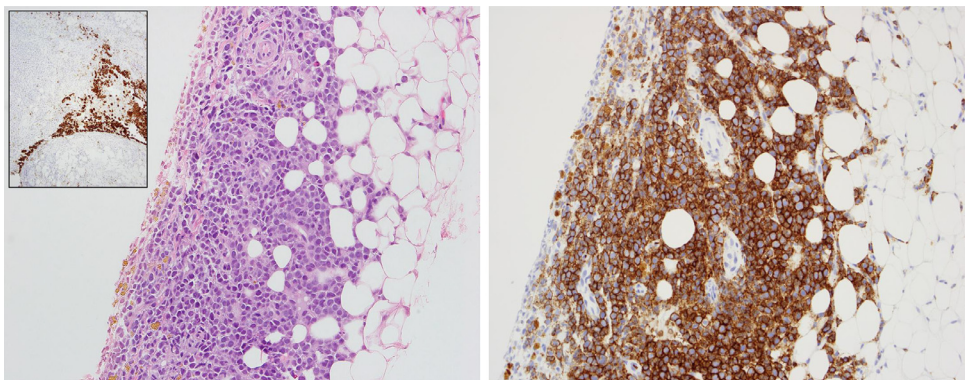

Fig. 3. Pleural biopsy showing acute myeloid leukemia. (A) Leukemic cells involve the full thickness of the parietal pleura. Inset shows mesothelial cells highlighted by pancytokeratin, with absence of staining in underlying leukemic infiltrate. (B) CD34 immunohistochemistry shows positive staining in leukemic cells. [A, 200x hematoxylin and eosin; B-D, 600x immunohistochemistry with hematoxylin counter

Table 2
Markers useful in the evaluation of hematolymphoid lesions involving lung and pleura. Markers in bold font are usually positive in extramedullary hematopoiesis, myeloid sarcoma or acute myeloid leukemia

Markers	Target population	Remarks
CD34	Blasts	Positive in most myeloid sarcomas, albeit not all
CD45	Any hematolymphoid cells	Not infrequently dimmer expression in blasts relative to mature elements
CD3, CD5, CD7	T-cells	Usually negative, but may be occasionally aberrantly expressed in myeloid neoplasms or in T/myeloid acute leukemia
CD4	T-helper lymphocytes and monocytes	May be aberrantly expressed in myeloid neoplasms, particularly those with monocytic differentiation
CD11c, CD33	Broad hematolymphoid expression	
CD14, CD64, CD68, CD163, lysozyme	Monocytes	
CD15	Mature granulocytes	
CD19, CD20, CD22, CD79a	B-cells	Usually negative, but may be rarely aberrantly expressed in myeloid neoplasms (especially CD19 in t(8;21)/*RUNX1-RUNX1T1*) or in B/myeloid acute leukemia
CD56	Aberrant monocytes	Positive in blastic plasmacytoid dendritic cell neoplasm (BPDCN) and some cases of acute myeloid leukemia
CD61	Megakaryocytes	
CD71, glycophorin A	Erythroid cells	
CD117	Broad expression, including immature myeloid precursors	Positive in most myeloid sarcomas, but not specific
CD123, TCF4	Broad expression, including plasmacytoid dendritic cells and immature myeloid precursors	Positive cases must be distinguished from BPDCN. TCF4 is uniformly positive in BPDCN and negative in other myeloid processes.[26,27]
Myeloperoxidase	Granulocytes (lineage-specific marker)	Positive in most myeloid sarcomas, albeit not all
MNDA (myeloid nuclear differentiation antigen)	Myelomonocytic cells	

markers include myeloperoxidase (97%), CD43 (97%), lysozyme (93%), CD68 (93%), followed by CD117 (87%).[24] Similarly, Chang *et al* demonstrated that myeloperoxidase, CD68, lysozyme, and CD34 represented a useful panel for myeloid sarcoma.[25] In the latter study, the authors reported that CD68 clone KP-1 was expressed across all subtypes of myeloid sarcomas, whereas clone PG-M1 was less sensitive in general and stained cases with monocytic differentiation.

The differential diagnosis of myeloid sarcoma includes neoplasms of histiocytic/dendritic derivation, such as blastic plasmacytoid dendritic cell neoplasm (BPDCN), tumors derived from Langerhans cells, histiocytic sarcoma, interdigitating dendritic cell sarcoma (IDCS), and dendritic sarcoma not otherwise specified. The distinction between BPDCN and myeloid sarcoma is critical for appropriate therapy selection.[26] Sukswai *et al* have demonstrated that coexpression of TCF4 and CD123 by dual-color immunohistochemistry provides a highly sensitive and specific marker for BPDCN.[27] Tumors derived from Langerhans cells, including Langerhans cell histiocytosis and Langerhans cell sarcoma, are characterized by CD1a, langerin, and/or S100 expression, both of which are typically negative in myeloid sarcoma. The distinction between histiocytic sarcoma and myeloid sarcoma should rest on both morphologic and immunophenotypic grounds; namely, histiocytic sarcoma is characterized by uniform sheets of epithelioid or sometimes spindle-shaped neoplastic cells, often with high-grade nuclear features and lacking maturing elements. Histiocytic sarcoma cells are characteristically positive for CD68, CD163, and lysozyme, but they lack expression of myeloid markers (e.g. myeloperoxidase and CD13) as well markers of Langerhans cells. Interdigitating dendritic cell sarcoma and dendritic sarcoma not otherwise specified are exceedingly rare neoplasms that usually present as large solid masses comprised of dense spindle cell proliferations forming storiform patterns, a finding that is not seen in myeloid sarcoma. These neoplasms are positive for S100 but lack expression of myeloid markers, markers of Langerhans cell tumors, or markers of follicular dendritic cell derivation (e.g. CD21, CD23, CD35). Loghavi *et al* have reported an unusual case of chronic myelomonocytic leukemia that mimicked a dendritic cell tumor, so this possibility should be kept in mind.[28]

In the bone marrow and peripheral blood, a 20% blast count is used as a cutoff to establish a diagnosis of AML, with the exception of cases with recurrent chromosomal translocations. No such cutoff is established to distinguish myeloid sarcoma from extramedullary hematopoiesis, wherein the identification of a significant blast population and absent trilineage hematopoiesis provides a discretionary basis to make a diagnosis of the former.[29,30]

Extramedullary hematopoiesis

Extramedullary hematopoiesis (EMH) refers to a proliferation of myeloid elements in extramedullary sites, and is typically associated with hematological diseases. EMH can be broadly divided into benign/reactive myeloid proliferation and neoplastic/clonal myeloid proliferation. The most common sites are spleen and liver followed by lymph node, skin, paravertebral region, small intestines, breast, dura, and brain.[31,32] On occasion, they can present in unusual sites, such as the lung and pleura.[1–6,33–36] Table 3 outlines the clinicopathologic features of published cases of pulmonary and pleural EMH. Awareness of the differential diagnosis of EMH within the thorax from other solid tumors or infectious process is important to avoid an erroneous diagnosis.

Pathogenesis

Benign EMH can be seen in patients with a variety of benign hematological diseases and rarely in patients with malignant solid tumors. The benign conditions include hemoglobinopathies, e.g. sickle cell anemia and thalassemia (2 cases in Table 3), where there are chronic anemia/hemolysis and physiological compensation for “ineffective marrow erythropoiesis” by proliferation of myeloid elements in extramedullary sites. Rare cases of EMH within the thorax have been reported in patients with solid tumors,[33] e.g. pleural EMH in a patient with esophageal carcinoma (Case 3 in Table 1). While the underlying mechanism of EMH remains unclear, the administration of potent hematopoietic growth factors, such as granulocyte colony-stimulating factor (G-CSF), may be a contributing factor,[37,38] as G-CSF can stimulate hematopoietic stem cells to produce granulocytes in the bone marrow, thereby increasing the release of granulocytes into the blood. Additionally, some abnormal cytokine or paracrine growth factors secreted by tumors may be able to mobilize stem/progenitor cells and stimulate myeloid proliferation in extramedullary sites as a part of paraneoplastic process.[31]

Neoplastic/clonal EMH can be seen in patients with a variety of

Table 3
Selected recent studies describing cases of extramedullary hematopoiesis (EMH) involving the lung and pleura

Cases	Age/sex	Underlying diseases	Locations of EMH /presentations	Radiographic Imaging	Pathology/Genetics	Follow up
		Benign/reactive EMH				
Case 1[1]	22/M	Thalassemia major	Lung/cough	Paracardiac lobulated masses, compressing spinal cord	N/A	SD
Case 2[36]	26/M	Sickle cell trait/beta thalassemia	Pleura/acute shortness of breath, chest pain; nodules on pleura ruptured and a fatal hemothorax	Large pleural effusion	B-EMH	DOD
Case 3[33]	48/M	Esophageal carcinoma	Pleura/staging	Pleural soft tissue mass, suspicious for metastasis	B-EMH	SD
		Neoplastic/clonal EMH				
Case 4/5/6[2]	N/A	Fibrotic stages of PV, ET, PMF	Lung/pre-HSCT assessment	Diffuse, multiple lung nodules in 3/11 (27%) patients/ regress after HSCT	One case with N-EMH	SD
Case 7[3]	69/W	Myelofibrosis (AAM)	lung/dyspnea	Bilateral lung interstitial infiltrates	N-EMH with fibrosis in lung including peribronchiolar fibrosis	DOD
Case 8[3]	68/W	Myelofibrosis (AAM)	Lung and pleura/dyspnea	N/A	N-EMH with fibrosis in lung and fibrosis in thickened pleura	DOD
Case 9[4]	76/F	Fibrotic stage of PV/*JAK2*^{V617F}, del(20q)	Lung/dyspnea, wheezing by central airway obstruction	Soft tissue mass encasing the left mainstem bronchus, mimicking metastatic cancer	N-EMH with increased blasts (by FNA)	SD
Case 10[5]	35/M	PMF/*JAK2*^{V617F} (homozygous)	Anemia, fatigue, low-grade fever and progressive abdominal distension	Perilymphatic nodules in right lung/pleural effusion, hepatosplenomegaly,	N/A (lung nodule)	SD
Case 11[6]	72/M	Advanced myelofibrosis	Bilateral lung/dyspnea	Bilateral diffuse pulmonary ground-glass opacity	N/A (hemorrhagic risk)	SD
Case 12[34]	72/M	MPN with myelofibrosis	Pleura/shortness of breath; Spleen/abdominal pain	Left pleural effusion and loculation	N-EMH in pleura/trisomy 8; no mutations in *JAK2* or *MPL*	SD
Case 13[35]	53/M	MDS/MPN with fibrosis	Lung/epistaxis and hemoptysis (pulmonary hemorrhage)	Pulmonary artery filling defect which extended into the right middle lobe	N-EMH (by FNA)	DOD

AAM, agnogenic myeloid metaplasia (also called primary myelofibrosis); DOD, died of disease; EMH, extramedullary hematopoiesis (B-EMH, benign EMH; N-EMH, neoplastic/clonal EMH); ET, essential thrombocythemia; HSCT, hematopoietic stem cell transplant; N/A, not available; PMF, primary myelofibrosis; PV, polythythemia vera; SD, stable disease.

myeloid neoplasms, typically with advanced fibrotic stages of MPN, such as primary myelofibrosis (PMF), polycythemia vera (PV), and essential thrombocythemia (ET), wherein there is a significantly diminished marrow hematopoiesis. MPNs are clonal hematopoietic stem cell neoplasms characterized by the proliferation of cells of one or more myeloid lineages (i.e., granulocytic, erythroid, and megakaryocytic). Acquired somatic mutations in *JAK2*^{V617F}, *CALR,* and *MPL*$^{W515L/K}$ have been shown to play a pivotal causative role in the pathogenesis of MPNs by constitutive activation of oncogenic signaling pathways, primarily the JAK/STAT pathway.[39] Splenomegaly and hepatomegaly, caused by sequestration of excess blood cells and/or proliferation of abnormal hematopoietic progenitor cells, are common. The most common sites of EMH are the spleen, liver, and rarely the lung and pleura (MPN cases in Table 3).[2–6,40] Notably, the actual incidence of pulmonary and pleural EMH may be higher than might be inferred from the number of rare cases reported in the literature. In a study of Chunduri *et al*[2], 4 of 11 patients (27%) with fibrotic stages of PMF, ET, or PV had multiple nodules in the lungs; one patient had a biopsy proven EMH. These nodules rapidly regress after allogeneic hematopoietic stem cell transplant. Less commonly, neoplastic EMH is seen in patients with MDS or MDS/MPN.

The postulated etiology of neoplastic EMH is displacement of pluripotent hematopoietic stem cells from the bone marrow, with subsequent homing and sequestration in various organs in which they undergo proliferation and myeloid differentiation, a mechanism presumably similar to that proposed for EMH in the spleen.[41] This hypothesis is supported by clinical observations of concordant abnormal cytogenetic/molecular findings detected in both bone marrow and neoplastic EMH, e.g. trisomy 8 detected in both pleural EMH and bone marrow in a study by Sonu et al[34], and *JAK2*^{V617F} detected in both splenic EMH and bone marrow in a study by Konoplev *et al.*[42] The alterative hypothesis of reactivation of embryonic rests of totipotent hematopoietic stem cells in various organs secondary to ineffective marrow hematopoiesis is less favored by current knowledge.

Clinical presentations

While the majority of pulmonary and pleural EMH masses are asymptomatic, patients may have variable clinical presentations depending on the nature of the underlying diseases and affected sites within the thorax. Pulmonary EMH may cause a pneumonia-like process and patients may present with cough, sputum, hemoptysis, and chest pain[35,43] or respiratory distress. Patients may present with dyspnea and shortness of breath with associated MPN-induced peribronchiolar fibrosis or interstitial lung fibrosis.[3,4] Rarely, patients may present with life-threatening complications such as pulmonary hemorrhage and hemothorax.[35,36] Several factors in addition to EMH in the pulmonary artery could further contribute to pulmonary hemorrhage, including thrombocytopenia and coagulopathy. Pleural EMH may result in pleural effusion and patients may present with chest pain and labored breathing.[3,5,34,36,43]

Radiologic/Imaging studies

Imaging modalities to detect thoracic EMH include computed tomography (CT), magnetic resonance imaging (MRI), ultrasonography, and/or technetium-labeled scintigraphy.[44] Pulmonary EMH may manifest as atypical diffuse ground-glass opacity, pulmonary nodules, multilobulated masses, interstitial thickening, and interstitial fibrosis.[3,6,45] Rarely, EMH tissue can compress the spinal cord leading to paraplegia.[1] Since their features on CT and MRI imaging could sometimes be atypical, EMH in patients with other solid tumors might be misdiagnosed as metastasis.[4,33] Pleural EMH can show pleural effusions, and/or pleural thickening.[34,36]

Pathology

Lung biopsy, the gold standard in establishing a diagnosis of pulmonary EMH, may not be needed in most clinical scenarios due to the high risk of hemorrhage and sampling error. A prior diagnosis of myeloid neoplasm by careful review of clinical history including bone marrow/peripheral blood findings, flow cytometry, immunohistochemistry, or cytogenetic/molecular testing may lead to a presumptive diagnosis of EMH followed by appropriate clinical management.

When assessing pulmonary EMH presenting as a mass-like or nodular lesion, the main differential diagnosis is benign EMH versus clonal EMH. Benign EMH is characterized by well-differentiated myeloid cells, often with erythroid predominance, no increase in blasts, and absence of megakaryocytic dysplasia. Any history of a myeloid neoplasm, in particular one associated with myelofibrosis, can be a clue to the neoplastic nature of EMH. All cases reviewed in this article were present as a part of systemic myeloid neoplasm. Quite rarely, however, neoplastic EMH may represent an initial/presenting manifestation of a subsequently detected systemic myeloid disease.

The morphologic findings in neoplastic EMH typically recapitulate the features of the underlying disease. In patients with neoplastic EMH secondary to MPN, findings include trilineage hematopoiesis with megakaryocytic atypia. The latter could include increased/clustered megakaryocytes with hyperlobated and hyperchromatic nuclei. In patients with MDS/MPN, neoplastic EMH shows variably significant dysplasia, particularly notable on routine microscopy in megakaryocytes, which exhibit hypolobated or hyerplobated nuclei and nuclear fragmentation. The identification of myeloid components can be facilitated by immunohistochemistry stains (Table 2), such as CD34 and CD117 for immature myeloid blasts, CD61 for megakaryocytes, CD71 and glycophorin A for erythroid elements, and lastly CD64, myeloperoxidase, and lysozyme for granulocytic/monocytic cells.[31] An increase in myeloid blasts should prompt a careful examination to rule out myeloid sarcoma. The presence of concordant abnormal cytogenetic and molecular findings in the bone marrow and EMH would be further supportive of the neoplastic nature of EMH.[31,34,42] On rare occasions, significant fibrotic changes in EMH can mimic interstitial lung disease.[3] The identification of immature myeloid cells and dysplastic megakaryocytes supports a diagnosis of neoplastic EMH.

Pleural EMH may present as a pleural effusion. Careful cytomorphologic assessment in conjunction with immunohistochemical studies on cell block material, flow cytometry immunophenotyping, and/or cytogenetic/molecular studies can lead to a correct diagnosis.

Treatment and outcomes

It is usually not necessary to treat asymptomatic patients with EMH. The goal of treatment is aimed at treating the underlying disorder (i.e., cytoreductive therapy, targeted JAK2 inhibition).[4,5] Symptomatic patients are treated usually with supportive approaches such as transfusion or growth factors, and less commonly with radiotherapy and surgery. As hematopoietic tissue is extremely radiosensitive, palliative low-dose radiation therapy is usually effective in reducing the mass of EMH and relieving symptoms. Radiation therapy is used for paraspinal or intraspinal EMH and pleural or pulmonary EMH.[43] Significant respiratory distress caused by pleural effusion can be treated with thoracentesis and/or talc pleuridesis. EMH does not seem to affect the prognosis of patients, and the outcomes of EMH often align with those expected in the context of the underlying hematologic diseases.[43]

Conclusions

As pulmonary and pleural myeloid sarcoma and EMH are rarely encountered in routine pathology practice, on occasion they can present diagnostic difficulties. Pathologists and clinicians need to be familiar

with the clinical presentations of myeloid sarcoma and EMH with associated hematological diseases. A thorough morphologic and immunophenotypic assessment in conjunction with review of the clinical history and ancillary studies should lead to a correct diagnosis followed by appropriate clinical management.

CRediT authorship contribution statement

Joseph D. Khoury: Writing - review & editing. **Weina Chen:** Writing - review & editing.

Declaration of Competing Interests

The authors declare no conflict of interest.

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