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Isolated Mesenteric CD20-positive Myeloid Sarcoma

Maro Ohanian¹, Richard Sheng Poe Huang², Tatiana V. Yakoushina², Zeev Estrov¹, Harinder Juneja³, Lei Chen², Modupe Idowu⁵, and Lynne V. Abruzzo⁴

¹Department of Leukemia, The University of Texas MD Anderson Cancer Center, Houston

²Department of Pathology and Laboratory Medicine, The University of Texas Health Science Center at Houston

³Department of Hematology, The University of Texas MD Anderson Cancer Center, Houston

⁴Department of Hematopathology, The University of Texas MD Anderson Cancer Center, Houston

⁵Department of Hematology, The University of Texas Health Science Center at Houston

Keywords

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Introduction

Extramedullary manifestations of acute myeloid leukemia (AML) include myeloid sarcomas (MS), which are tumor masses composed of myeloid blasts, with or without maturation, arising in any anatomic location other than the bone marrow (BM) [1]. With only case reports and small retrospective studies available, the incidence of MS is unclear [2, 3]. We present an unusual, diagnostically-challenging case of isolated mesenteric MS without BM involvement [2, 3].

Case Report

A 54-year-old man with a 2 month history of abdominal pain underwent an abdominal CT scan that revealed a 9 × 6.9 cm mesenteric root mass (Figure 1a). Complete blood count (CBC) demonstrated an elevated white blood cell count (WBC) of $14.2 \times 10^9/L$ (normal range, $4.5\text{--}12.0 \times 10^9/L$) with neutrophilia (78%). Histologic examination of a CT-guided biopsy specimen revealed large discohesive cells, with oval to slightly irregular nuclear contours, finely dispersed chromatin, single small eosinophilic nucleoli, and a moderate

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Corresponding author: Modupe Idowu MD, modupe.idowu@uth.tmc.edu, Assistant Professor, Division of Hematology, Department of Internal Medicine, 6431 Fannin Street, MSB 5.287, Houston, TX 77030, Telephone: 713-500-6764.

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amount of eosinophilic cytoplasm, in a background of necrotic cellular debris and scattered small, mature-appearing lymphocytes (Figure 2a). Immunohistochemical (IHC) stains performed on formalin-fixed, paraffin embedded tissue sections demonstrated that the tumor cells expressed CD45, CD20, CD68 (weak), and myeloperoxidase (MPO) (Figure 2b-2e). They were negative for CD3, CD21, CD43, CD34, CD117, CD138, PAX-5, MUM-1, BCL6, cyclin D1, TdT, and lysozyme. Fluorescence *in situ* hybridization (FISH) analysis for *BCR/ABL1* rearrangement was negative, but demonstrated extra copies of the *BCR* and *ABL1* signals, consistent with a hyperdiploid cell population. Molecular diagnostic testing for *NPM1* mutation was negative. Insufficient material was available for immunophenotypic analysis by flow cytometry or karyotypic analysis. Taken together, the results were consistent with MS.

A bone marrow (BM) specimen obtained concurrently showed normocellular marrow with trilineage hematopoiesis, slight eosinophilia, and <1% blasts by morphology and flow cytometry. Karyotypic analysis demonstrated a normal diploid male karyotype. FISH analyses for common abnormalities associated with myeloid neoplasias, i.e., deletions of 5q31 or 7q31, or translocations involving *EVII* (3q26), *MLL* (11q23), *RUNX1T1/RUNX1* (t(8;21)(q22;q22)), *BCR/ABL1* (t(9;22)(q34;q22)), *PML/RARA* (t(15;17)(q22;q21.1)), or *CBFB* (inv(16)(q22)), were negative.

The patient received treatment with idarubicin and cytarabine, and his abdominal symptoms improved. After 2 courses of consolidation with high-dose cytarabine (HDAC), a CT scan demonstrated that the mass had decreased to 6 × 4 cm (Figure 1b). Subsequent peripheral blood and BM evaluations remained negative. Due to severe sepsis, additional treatment with HDAC was deferred. Follow-up positron emission tomography (PET)/CT scan 86 days after HDAC course 2 was negative for fluoro-D-glucose PET-avid disease. However, the size of the mass remained stable (Figure 1c). The patient's clinical course has been evaluated every 3 months with routine CBCs and PET/CT scans. He is alive without evidence of disease 18 months since presentation. Should he relapse, we will resume cytarabine-based chemotherapy, possibly with rituximab.

Discussion

The clinical diagnosis of MS is challenging, particularly as the initial manifestation of disease with focal symptomatology. In our case, the gastrointestinal (GI) symptoms justified investigation for a malignant neoplasm. While MS may occur at any site along the mesentery and GI tract, or at any point during the course of AML [3], it rarely causes GI symptoms. Only two cases of isolated non-mesenteric abdominal MS have been reported [4, 5], and isolated mesenteric MS occurring at initial diagnosis without BM involvement has been reported only once [2].

Our case also demonstrates that the pathologic diagnosis of MS can be challenging. On routine histology, the features were consistent with a high-grade hematopoietic neoplasm. However, the lack of granulocytic differentiation or admixed eosinophils, particularly in the absence of BM involvement, suggested a diagnosis of high-grade non-Hodgkin's lymphoma (NHL). In fact, MS is misdiagnosed initially as high-grade NHL lymphoma in 46% of cases,

often due to its poorly-differentiated appearance [6, 7]. Misdiagnosis as lymphoma may also result from weak or absent expression of MPO or other markers of myeloid differentiation, or from aberrant expression of markers of lymphoid differentiation, such as the B-cell marker, CD20, a feature of our case [1]. A relatively high proportion of lineage-committed acute leukemias aberrantly express an antigen of a different lineage, i.e., lineage infidelity. For example, in a study of 106 AML cases, Khalidi and co-workers detected CD20 expression by flow cytometry in 17% of cases [8]. However, CD20 expression by MS has been reported rarely, in only 5 cases [6, 9, 10], possibly because it is evaluated infrequently in these neoplasms. Thus, the current case is the first reported case of CD20-positive isolated mesenteric MS.

MS is often associated with trisomy 8 or with the AML translocations involving core-binding factors, i.e., t(8;21)(q22;q22) and inv(16)(p13;q22) [3]. In fact, t(8;21) and inv(16) have been reported in abdominal MS [11]. Mutated *NPM1* is the most common mutation reported in MS [12]. The abdominal mass in the current case was negative for *NPM1* mutation. Unfortunately in our case insufficient material was available for karyotypic analysis.

In this case, even though we had only a needle biopsy for diagnosis, the vast majority of the small specimen was composed of tumor cells that strongly expressed MPO. Although we did not stain for the B-cell markers CD19 and CD79a/b, we stained for four other markers of B-cell differentiation that span the spectrum of maturation (PAX5, BCL-6, MUM-1, and CD138)-all were negative. Ki-67 is a marker of proliferation that we would expect to be expressed by both myeloid and lymphoid tumors with a high proliferative fraction [1]. Positivity for this marker would not have helped us distinguish between the two lineages. It is worth noting that differential diagnosis also includes a composite lymphoma and extra-medullary myeloid cell tumor. On H&E sections, the cytology of the neoplastic cells was relatively uniform throughout the tumor. We did not identify two components on immunohistochemical stains. Thus, we had no morphologic or immunophenotypic evidence that this tumor was a composite lymphoma and extra-medullary myeloid cell tumor.

The prognostic significance of *de novo* MS without BM disease is uncertain; interpretations of retrospective data vary. Some studies suggest that survival rates for patients with MS are similar to AML without MS, ranging from 20% -30%, [11, 13], while others suggest that MS may have superior survival [13, 14]. Retrospectively, Lan and co-workers showed that MS patients treated with systemic chemotherapy had better 5-year overall survival rates than those who received other treatments, such as radiotherapy or surgery without chemotherapy [13]. Tsimberidou and co-workers demonstrated that MS patients without BM disease who received systemic chemotherapy had better event-free and overall survival than patients with classical AML [14]. Since patients with isolated MS generally develop BM involvement over a median of 5 to 12 months [3], systemic chemotherapy is recommended for patients who present with isolated MS [14, 15].

This rare case of isolated mesenteric MS was diagnostically challenging due to its unusual clinical, morphologic, and immunophenotypic features. Because MS may occur without BM involvement, imaging studies, in addition to monitoring of the BM response to

chemotherapy, are necessary. This case also raises the possibility that patients with CD20-positive MS or AML may benefit from targeted anti-CD20 immunotherapy.

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Clinical Practice Points

- Myeloid sarcoma is misdiagnosed as high-grade non-Hodgkin lymphoma in up to 46% of cases, often due to its poorly-differentiated histologic appearance.
- Misdiagnosis of myeloid sarcoma as lymphoma may also result from weak or absent expression of myeloperoxidase (MPO) or other markers of myeloid differentiation, or from aberrant expression of markers of lymphoid differentiation, such as the B-cell marker, CD20.
- Because myeloid sarcoma can occur without bone marrow involvement, imaging studies, in addition to monitoring the bone marrow response to chemotherapy, may be necessary.
- A relatively high proportion of lineage-committed acute leukemias aberrantly express an antigen of a different lineage, i.e., lineage infidelity.

Figure 1. Imaging studies. Abdominal CT scans performed (A) before, and (B) after chemotherapy treatment demonstrate a large mass that decreased in size. (C) A PET/CT scan performed 86 days after 2 courses of HDAC was negative for PET-avid disease.

Figure 2.

Histologic features of the mesenteric mass. (A) The mass is composed of sheets of poorly-differentiated cells in a background of necrotic debris (hematoxylin and eosin, 400×). The neoplastic cells express (B) CD45, (C) CD20, (D) CD68 (weak), and (E) myeloperoxidase (immunohistochemistry, 400×).