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Myeloid Sarcoma of Appendix, Presenting as Acute Appendicitis: A Rare Case Presentation

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Abstract Myeloid sarcoma is a malignant neoplasm, in which a tumor mass consisting of myeloid blasts with or without maturation occur at an anatomical site other than the bone marrow. Myeloid sarcoma is frequently, but not always, associated with acute myeloid leukemia, chronic myeloid leukemia, and other myelodysplastic disorders. Myeloid sarcomas involving the appendix are uncommon and myeloid sarcoma of the appendix presenting as acute appendicitis is rare. A 64-year-old Omani female presented to the emergency department with 1-day history of acute right lower abdominal pain. She was noted to have leukocytosis and thrombocytopenia in her pre-operative blood investigation, which prompted a 2-week prior history of a single episode of minor nosebleed. Abdominal imaging demonstrated findings suggestive of an acute appendicitis, with differential of mesenteric adenitis and/or focal fat infarction, for which she underwent laparoscopic appendectomy. Surgical pathology of the appendix showed myeloid sarcoma involving the entire appendix including the base. On further investigation, a peripheral blood smear revealed many circulating blasts. Patient was later diagnosed to have acute myeloid leukemia with inv (16) (p13.1 q22) genetic abnormality in a tertiary hospital. Acute appendicitis with leukemic infiltration in form of myeloid sarcoma as the initial manifestation of acute myeloid leukemia has been described in very few cases in the literature, and our case is the first case to be reported in Oman.

Keywords: *Myeloid sarcoma, appendix, acute appendicitis, acute myeloid leukemia (AML)*

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1. Introduction

Myeloid sarcoma, also known as extramedullary myeloid tumor, granulocytic sarcoma and chloroma, is a malignant neoplasm in which a tumor mass consisting of myeloid blasts with or without maturation, occurs in an anatomical site other than the bone marrow. [1] It is frequently, but not always, associated with acute myeloid leukemia (AML), chronic myeloid leukemia (CML) and other myelodysplastic disorders. [2] Myeloid blast infiltrates in leukemic patients without formation of tumor mass is not classified as myeloid sarcoma. [1] Myeloid sarcoma can occur in a wide variety of extramedullary sites, commonest being lymph nodes, skin and central nervous system. [3] Involvement of appendix is very uncommon and initial presentation as acute appendicitis is very rare, with very few cases reported in the published literature. [4] To our knowledge, we report the first case of myeloid sarcoma of appendix presenting as acute appendicitis in Oman. The patient was later diagnosed to have acute myeloid leukemia (AML).

2. Case Report

A 64-year-old Omani female, with no prior significant medical history presented to the emergency department of secondary hospital with 1-day history of acute right lower abdominal pain. She denied having any other clinical symptoms including fever, nausea, vomiting, change in bowel habits, weight loss or night sweats. In her pre-operative blood investigation, she was noted to have leukocytosis with a white blood cell count of 28.8 x 10^9/L (reference range: 2.4–9.5 x 10^9/L), with 21.4% neutrophils; 31.9% monocytes; and 25.6% basophils; and thrombocytopenia (platelet count of 86.86 x 10^9/L, reference range: 150-450 x 10^9/L). A peripheral blood smear later demonstrated numerous circulating blasts (67%) with high nuclear/cytoplasmic ratio and nucleus with open chromatin and 0-2 nucleoli. Occasional cells with binucleation and irregular nucleus were also noted. The impression on the blood smear was of an acute leukemia requiring further investigations. The

abnormal blood investigation also prompted the patient to remember a 2-week prior history of a single episode of minor nosebleed.

Abdominal computed tomography imaging demonstrated findings suggestive of an acute appendicitis with appendix not filling with oral contrast and lack of intraluminal air. Multiple right-side mesenteric lymphadenopathies were noted. Radiological differential diagnosis of mesenteric adenitis and focal fat infarction was considered. Patient underwent laparoscopic appendectomy.

Surgical pathology of the appendix revealed a myeloid sarcoma involving the entire appendix including the base, with the appendix showing transmural infiltration by sheets of discohesive malignant cells with round vesicular nuclei, prominent nucleoli, and scant cytoplasm [Figure 1 (A)]. The malignant cells were positive for immunohistochemical stains myeloperoxidase (MPO), CD34, CD117 and CD45 [Figure 1 (B)].

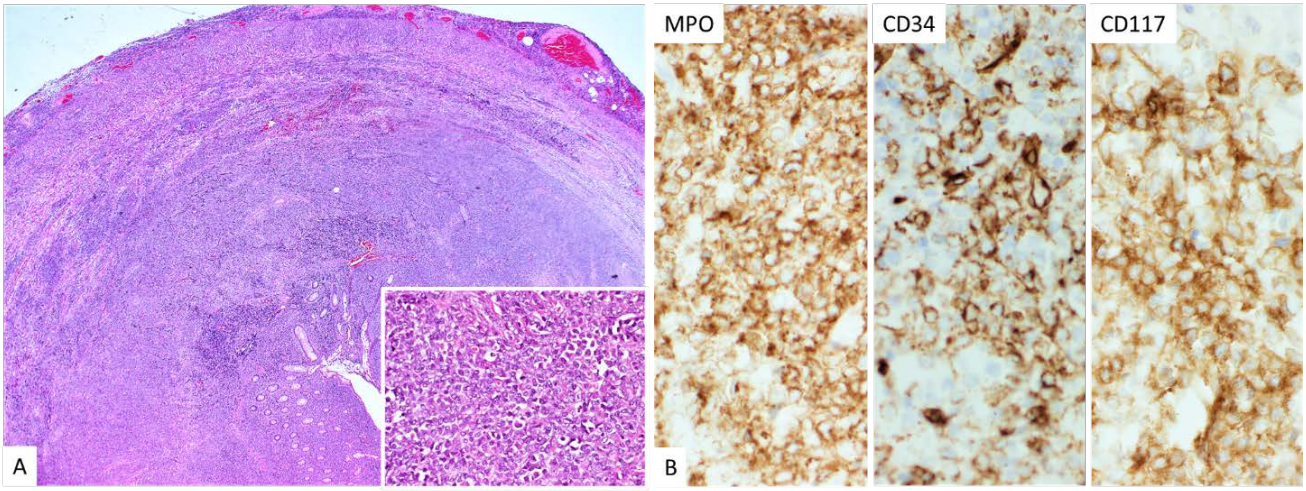

Figure 1. Appendix with Myeloid sarcoma. **A.** Appendix showing transmural infiltration by sheets of discohesive malignant cells (Hematoxylin and Eosin, Magnification 2X), with malignant cells showing round vesicular nuclei, prominent nucleoli, and scant cytoplasm (Bottom right Inset A, Hematoxylin and Eosin, Magnification 40X). **B.** The malignant cells were positive for immunohistochemical stains myeloperoxidase (MPO), CD34 and CD117 (Magnification 40X)

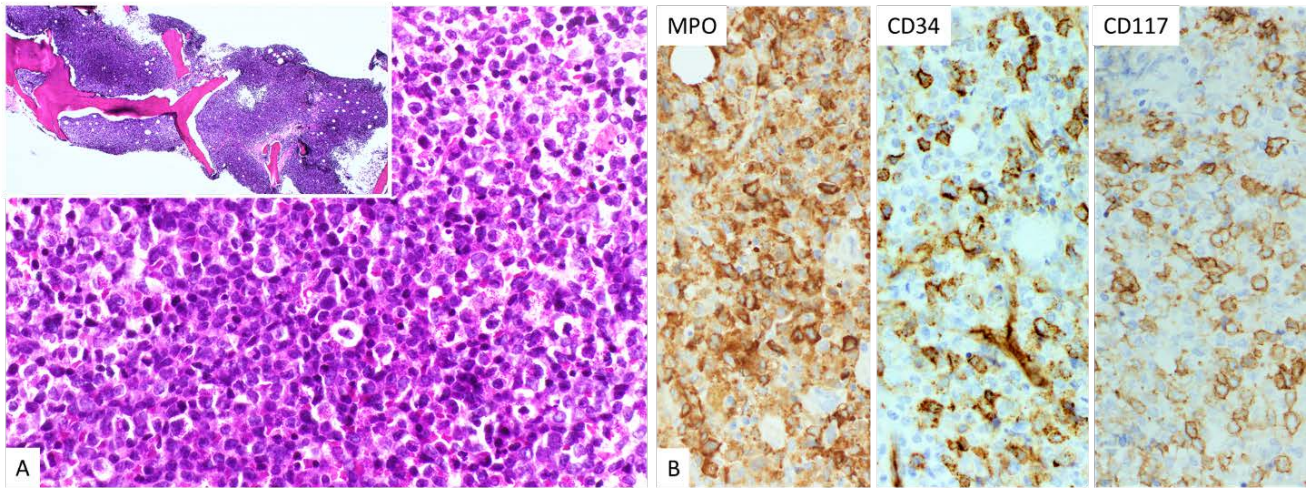

Figure 2. Bone Marrow with Acute myeloid leukemia (AML). **A.** Hypercellular bone marrow (Top left Inset A, Hematoxylin and Eosin, Magnification 2X), with marrow spaces filled with malignant cells showing vesicular nuclei with irregular nuclear contours, coarse chromatin, and granular cytoplasm (Hematoxylin and Eosin, Magnification 40X). **B.** The malignant cells were positive for immunohistochemical stains myeloperoxidase (MPO), CD34 and CD117 (Magnification 40X)

Patient was later seen at a tertiary hospital, where she underwent further investigations including repeat peripheral blood smear, bone marrow aspirate, flow cytometry, bone marrow trephine biopsy and cytogenetic analysis of the bone marrow and was diagnosed to have acute myeloid leukemia (AML). The bone marrow aspirate was hypercellular, showing suppression of trilineage hematopoiesis and replacement by sheets of blasts. The blasts accounted for 61% of total nucleated cells. Flow cytometry of the bone marrow aspirate identified 43% events in the blast region having low side scatter and dim expression of CD34. The blasts expressed immunopositivity for CD34, HLA-DR, MPO, CD117, CD13, CD33 and CD15 (weak), and immunonegativity for CD56, TdT and monocytic B and T cell markers. The bone marrow trephine revealed a hypercellular marrow with marked reduction in erythropoiesis and granulopoiesis, and the marrow spaces were filled with malignant cells showing vesicular nuclei with irregular nuclear contours, coarse chromatin, and granular cytoplasm [Figure 2 (A)]. The malignant cells were immunopositive for CD34, CD117 and MPO [Figure 2 (B)].

Finally, the cytogenetic analysis of the bone marrow revealed AML with inv(16)(p13.1q22) genetic abnormality. The cytogenetic investigations included nested-PCR for detection of *CBFB-MYH11* fusion gene transcript, which detected 2-3 fusion signals of *CBFB/MYH11* (16q22/16p13) in 88% of analyzed cells, indicating inv(16), and fluorescence in situ hybridization (FISH) which revealed a final karyotype of the AML as 46, XX, inv(16)(p13.1q22) [16]/46, XX [4], with the abnormal clones showing inversion of chromosome 16 at 16p13 and 16q22 in 80% of the analyzed metaphase cells. Patient is currently undergoing treatment for AML.

3. Discussion

Myeloid sarcomas can involve almost any site in the body including skin, lymph nodes, gastrointestinal tract, bone, soft tissue and testis. [1] Gastrointestinal involvement accounts for about 7-11% of reported myeloid sarcoma cases, with ileum being the most common site.[3] Myeloid sarcoma in the appendix is very uncommon, and presentation of it as acute appendicitis is even rarer, with less than 10 cases reported in the published literature. [4,5,6] Myeloid sarcomas may occur *de novo.* They may precede or coincide with AML or represent acute blastic transformation of a myelodysplastic syndrome. [1,7] Therefore, investigation and further follow up for systemic hematological malignancy is essential. Myeloid sarcoma may also occur as an initial manifestation of relapse of a previously diagnosed and treated AML. [1]

Acute myeloid leukemia (AML) is an aggressive hematological malignancy commonly associated with recurrent genetic abnormalities, which include balanced translocations or inversions. These genetic abnormalities have distinctive clinicopathological features and prognostic significance. [8] WHO classification requires a minimum of 20% of blasts in the bone marrow or blood for diagnosis AML. [9] AML patients may present with non-specific clinical symptoms of fatigue, breathlessness, frequent infections, weight loss and diarrhea, and occasionally with symptoms unique to acute leukemias such as unusual bleeding from the nose and gums. [10] Clinical laboratory findings usually reveal leukocytosis, anemia, and thrombocytopenia. [10] Less than 1% of patients with AML present with prominent extramedullary disease i.e., myeloid sarcoma. [11]

AML with inv(16)(p13.1q22) genetic abnormality resulting in *CBFB-MYH11* gene fusion, which is present in our patient, is found in 5-8% of younger patients with AML, with its frequency being lower in older adults. [7] This genetic abnormality is associated with a high rate of complete remission and favorable overall survival with treatment. [12]

4. Conclusion

It is unusual for myeloid sarcomas to present as acute appendicitis as the initial manifestation of acute myeloid leukemia (AML). It has been described in very few cases in the literature, and our case is the first case to be reported in Oman.

Disclosure

The authors declared no conflicts of interest.

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