Cutaneous Myeloid Sarcoma

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Abstract

Introduction: Myeloid Sarcomas (MS) are rare neoplasms occurring at extramedullary sites. They are typically found in the setting of Acute Myeloid Leukemia (AML) either concurrently or at relapse. Less often, they may be associated with other hematologic disorders such as Myelodysplastic Syndromes (MDS) or Myeloproliferative Neoplasms (MPN). Rarely MS can present as an isolated leukemic tumor, without bone marrow involvement. The presentation of these isolated cases is greatly variable and can make diagnosis particularly challenging.

Case Presentation: A case report of a 79-year-old patient with rare and rapidly evolving cutaneous presentation of isolated MS, without bone marrow involvement.

Discussion: This case identifies the potential for isolated MS to present as a cutaneous skin infiltration in the absence of AML, MDS or MPN. Given the rarity of this neoplasm and the wide variation in symptomology, it is prudent to be aware of aberrant presentations of isolated MS. This case highlights the need for physicians to consider MS in the differential diagnosis, even in the context of negative bone marrow, as early diagnosis and treatment with chemotherapy has been demonstrated to improve survival outcomes.

Keywords: Isolated myeloid sarcoma; Cutaneous infiltration; Skin infiltration

Introduction

Myeloid Sarcoma (MS), also known as granulocytic sarcoma, chloroma, or myeloblastoma, is a rare extramedullary proliferation of myeloblasts thought to be a variant of Acute Myeloid Leukemia (AML) [1]. The initial manifestation of the disease is highly variable and can present at different stages, such as preceding or coinciding with AML, arising from plastic transformation of a Myelodysplastic Syndrome (MDS), or developing from a chronic Myeloproliferative Neoplasm (MPN) [2]. However, MS rarely occurs in the absence of bone marrow involvement [3], and it is identified as isolated MS.

Case Presentation:

A 79-year-old male with past medical history of atrial fibrillation, benign prostatic hyperplasia, and resected colon cancer in 2008, presented with new onset of shortness of breath, difficulty ambulating and a diffuse progressive skin rash. On initial examination, skin exam revealed innumerable, indurated, non-pruritic, non-tender, red and purple papules and nodules on the arms, chest, back and abdomen (Figure A). By day 6 of admission, the rash had progressed to the neck and face, and the discrete lesions on the arms had coalesced into large indurated plaques (Figure B and C).

Initial blood work was significant for leukocytosis (white blood cell count: 15.2 x 10^9/L with normal differential without immature cells), anemia (hemoglobin: 8.4 g/dl MCV: 89), and thrombocytopenia (platelets: 82 x 10^9/L). Computed Tomography (CT) revealed innumerable, indurated, non-pruritic, non-tender, red and purple papules and nodules on the arms, chest, back and abdomen (Figure A). By day 6 of admission, the rash had progressed to the neck and face, and the discrete lesions on the arms had coalesced into large indurated plaques (Figure B and C).

Bone marrow biopsy revealed a mildly hyper cellular bone marrow for age, with trilineage hematopoiesis and erythroid hyperplasia, no increase in blasts was identified. Cytogenetic analysis showed abnormal karyotype with trisomy 8 (47, XY, +8(8)/46, XY (12 )). Flow cytometry did not reveal immunophenotypic abnormalities.

Skin biopsy showed dermal infiltrate consisting of medium-sized to large atypical cells with evenly dispersed chromatin and variably prominent nucleoli. Sections were positive for CD4,
CD33 CD43, CD56, Myelo Per-Oxidase (MPO) (Figure D), lysozyme (Figure E), and negative for CD2, CD3, CD5, CD7, CD20 CD30, CD34, CD117, CD123, and TdT, confirming a clonal myeloid population consistent with AML. Cytogenetics revealed trisomy 8.

Induction chemotherapy for AML was planned, however patient’s clinical status deteriorated considerably. Patient developed refractory fever, delirium, and concurrently worsening leukocytosis, anemia, and thrombocytopenia. Patient died on day 12 of the hospital stay.

Discussion

Myeloid Sarcoma (MS) is an extramedullary tumor reported in 2% to 8% of patients with AML, or preceding a diagnosis of AML [1,3]. However, there are case reports without overt BM involvement [4]. While cases of MS have been described in all age groups, there is a slight male predominance. Frequent sites of involvement include skin, lymph nodes, as well as subperiosteal bone structures, gastrointestinal tract, bone, soft tissue, testis [3,5,6]. Clinical manifestations differ based on the site of involvement.

Research on pathogenesis of MS has shown the predominance of specific ligands and receptors, such as a set of chemokine receptors (CCR5, CXCR4, CXCR7, CX3CR1) was identified to be present only on MS blast cells in the skin, and absent on blasts from bone marrow [7]. Other studies suggested that ability of the blastic cells to migrate of can be attributed to interaction between Matrix Metallo Proteinase (MMP) 9 and leukocyte surface beta (2) integrin [8] and hinted that higher expression of MMP-2, membrane type 1 MMP and tissue inhibitor of MMP-2 play a role in the blast capability to survive and penetrate to other sites [9]. Diagnosis is based on morphological evaluation of tissue from involved sites and bone marrow biopsy. In cases without associated AML, this may be frequently misdiagnosed, most often as non-Hodgkin lymphoma, undifferentiated cancer, malignant melanoma, extramedullary hematopoiesis and inflammation [6,10,11].

Blasts are typically positive on immunohistochemistry for antibodies to MPO and lysozyme. Flow cytometry, essential for diagnosis, is positive for myeloid-associated antigens such as CD43, CD13, CD33, and CD117, as well as TdT, CD56, CD 61, CD34, but negative for lymphoid antigens such as CD3 and CD20 [5,12] as seen in our case.

Myeloid sarcoma has been associated with several cryptogenic abnormalities including t (8; 21) and, less often inv (16) (p13; q22) [10, 13, 14]. Fluorescence in situ hybridization analysis has revealed an array of chromosomal abnormalities including monosomy 5 or 7, trisomy 8, trisomy 11, del (5q), and del (20q) [6]. Molecular abnormalities reported were NPM1, FLT3 mutation, however the prognostic significance is unknown [15,16].
Due to the rarity of MS and lack of clinical trials, treatment for new onset myeloid sarcoma usually follows the strategy for AML [17]. Treatment planning takes into consideration, age of the patient, performance status, comorbidities, organ involvement, cytogenetics and molecular abnormalities and involves intensive chemotherapy and radiotherapy if warranted in limited disease. Overall patients with isolated MS, receiving systemic chemotherapy have slower progression than patients receiving only localized treatment [5]. The utility of hematopoietic stem cell transplant is yet to be studied prospectively but results from retrospective analyses are promising [6]. This case highlights an unusual form of MS without bone marrow or obvious organ involvement. Given the rapid progression of disease and poor prognosis, this case should prompt clinicians to consider MS early on in the differential.

References