An Uncommon Case of Non-leukemic Myeloid Sarcoma of the Face in a 71-year-old Filipino Female: A Case Report

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ABSTRACT

Myeloid sarcoma is a tumor that demonstrates extramedullary proliferation of myeloid blasts with or without maturation. It may present as an isolated tumor or may have peripheral or marrow involvement. The diagnosis of myeloid sarcoma is highly challenging as it may mimic other tumors.

A 71-year-old woman with an Eastern Cooperative Oncology Group (ECOG) performance score of 2 presented with a progressively enlarging right facial mass that had been growing for 18 months. Initially, it appeared as a 1x1 cm erythematous pustular lesion. A core biopsy suggested carcinoma, but COVID-19 delayed immunohistochemical (IHC) testing.

As the mass grew, eventually covering more than half of her face, a CT scan revealed a large, multilobulated mass involving the periorbital areas, nose, and upper lip. A repeat biopsy showed atypical round cell proliferation, and immunohistochemical staining confirmed myeloid sarcoma with CD34 and CD117 positivity. Bone marrow aspiration and biopsy ruled out leukemia.

The diagnosis of non-leukemic myeloid sarcoma was established. The patient was referred to plastic surgery, ophthalmology, and otorhinolaryngology for co-management of the mass. Initial treatment began with azacitidine, a hypomethylating agent. However, after completing only one cycle of chemotherapy, she declined further treatment for personal reasons, choosing not to continue with the planned therapeutic regimen.

Non-leukemic myeloid sarcoma of the face in an elderly patient is rare. Diagnosis was confirmed via biopsy and immunohistochemical studies. Treatment with azacitidine was chosen based on the patient's ECOG score of 2. However, there is no consensus on its management, and the role of systemic chemotherapy remains debated. Continuous monitoring for progression to acute myeloid leukemia (AML) is crucial, as early detection significantly impacts prognosis and informs treatment decisions.

Keywords: myeloid sarcoma, acute myeloid leukemia, non-leukemic

INTRODUCTION

Myeloid sarcoma is a pathologic diagnosis for an extramedullary proliferation of blasts of one or more of the myeloid lineages that disrupts the normal architecture of the tissue where it is found.[1] It remains in the classification as a unique clinical presentation of any subtype of acute myeloid leukemia (AML). It may present as de novo, may accompany peripheral blood and marrow involvement, may present as relapse of AML, or may present as progression of a prior myelodysplastic syndrome (MDS), myeloproliferative neoplasm (MPN) or MDS/MPN overlap.[2] It is reported to occur in 2-8% of patients with AML, either as a single or as a multifocal tumor. The most common sites involved

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are lymph nodes, skin and soft tissues, bone, testes, gastrointestinal tract, and peritoneum.[3]

Non-leukemic myeloid sarcoma is a rare condition with an incidence of two cases per million adults. Its clinical presentation is also diverse reflecting variation in the location and size of myeloid sarcoma. Therefore, much of the literature is restricted to case reports and small retrospective series, and clinical knowledge of the condition, and its presentation and treatment is limited.[4] Here, we report an unusual case of non-leukemic myeloid sarcoma that involved the face in an elderly patient.

CASE PRESENTATION

A 71-year-old woman with an Eastern Cooperative Oncology Group (ECOG) performance score of 2, known to have hypertension and heart failure with mid-range ejection fraction, and unremarkable family and environmental exposure histories presented with an 18-month history of a progressively enlarging right facial mass. Initially, the mass appeared as a 1 x 1 cm erythematous pustular lesion on her right cheek. After consulting a dermatologist, she was advised to consult a surgeon. A core biopsy was performed revealing a malignant tumor, likely carcinoma. Immunohistochemical studies with CK, S100, and LCA were recommended, but the patient faced challenges completing them due to COVID-19 restrictions. As the mass continued to grow, now occupying more than half of her face (Figure 1), she sought consult with another physician who ordered a CT scan of the head and neck. The scan revealed a large multilobulated heterogeneously enhancing mass in the cutaneous and subcutaneous portions centered in the maxillary regions measuring 3.4 x 11.5 x 6.9 cm Superiorly, there were extensions to the periorbital regions with involvement of the nose. Inferiorly, there was an extension to the upper lip. Minimal intranasal extension was noted in the right inferior nasal cavity with involvement of the inferior nasal septum.

A core biopsy of the mass was repeated demonstrating atypical round cell proliferation, suspicious for malignancy. Immunohistochemical staining was strongly positive for CD34, weakly positive for CD117, and negative for LCA, CD3, CD5, CD20, PAX5, TdT, CD56, MPO, CD15, CD68, pancytokeratin, S100, p63, EMA, CD30, and desmin. The biopsy was signed out as most compatible with hematolymphoid neoplasm favoring myeloid sarcoma (Figures 2 and 3). Complete blood count was normal: hemoglobin 121 g/L, hematocrit 36%, white blood cell count 10 x 10^9/L, and platelet count of 464 x 10^9/L.

A bone marrow aspiration and biopsy revealed normocellular marrow with trilineage hematopoiesis, with no evidence of hematolymphoid neoplasm involvement (Figure 4). Flow cytometry for the basic leukemia panel showed no significant abnormal blast population. Cytogenetic testing was not pursued due to financial considerations, but with the available findings, a diagnosis of non-leukemic myeloid sarcoma was confirmed. Referrals to plastic surgery, ophthalmology, and otorhinolaryngology were also facilitated for further management.

She was treated with the hypomethylating agent azacitidine, administered at a dose of 90 mg, equivalent to 75 mg/m^2 for a body surface area (BSA) of 1.2 m^2 given subcutaneously once a day for seven days. She received only one cycle and refused any further chemotherapy because of financial constraints.

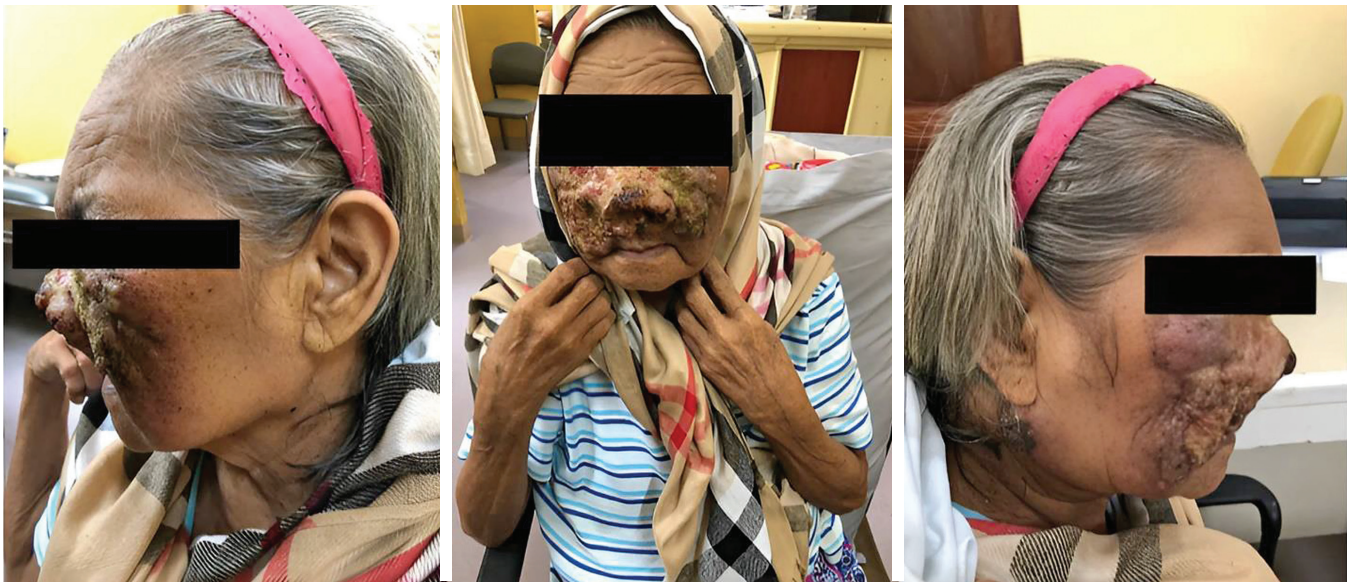

Figure 1. Photograph showing the extent of the mass in the face. The mass occupies the periorbital area, nose, maxillary region extending up to the upper lip.

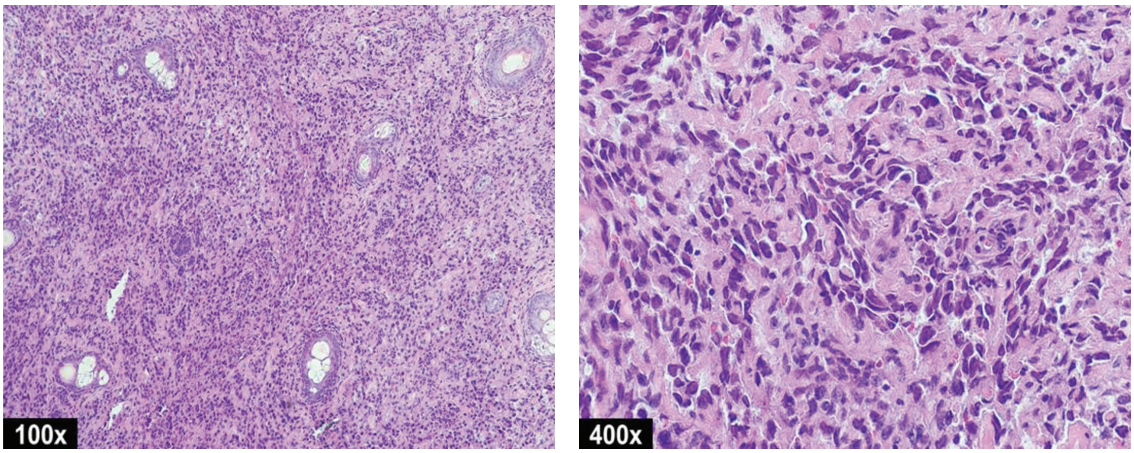

Figure 2. Photomicrographs of the face mass biopsy with H&E stain described as mild to moderate atypical pleomorphic cells with eosinophilic cytoplasm and irregularly folded hyperchromatic nuclei infiltrating the dermal tissues.

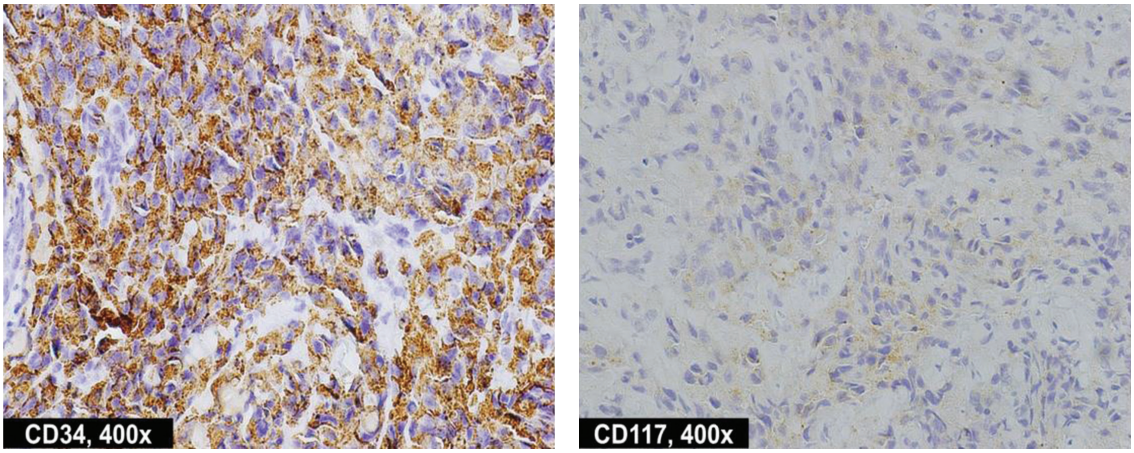

Figure 3. Immunohistochemical stain of the biopsy sample. The tumor cells were strongly positive for CD34 and weakly positive for CD117.

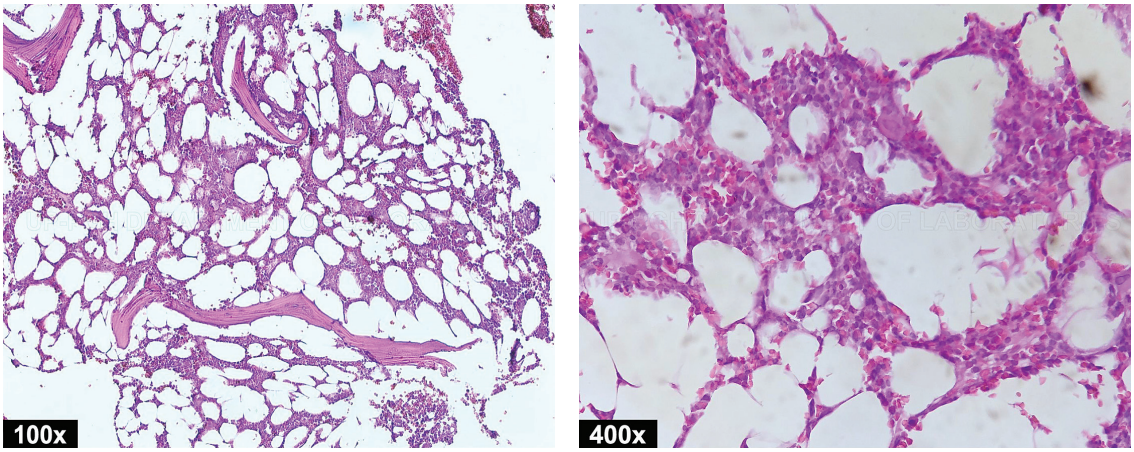

Figure 4. Photomicrograph of bone marrow core biopsy described as normocellular for age, with 20-30% cellularity. Erythrogranulopiesis with maturation is present. Megakaryocytes are adeqauate. No extraneous cells seen.

DISCUSSION

Myeloid sarcoma is a rare neoplastic condition consisting of immature myeloid cells and occurring at an extramedullary site. It is composed of myeloblasts, monoblasts, or megakaryocytes, that partially or totally efface the tissue architecture.[3,5]

Myeloid sarcoma may herald AML by a few months or even years in approximately in 25% of cases, appear concurrently with AML in 15-35% of cases, or after the diagnosis of AML in almost 50% of cases.[6] There is no established predilection to either sex. In one study, it has a slight male predominance with a male-to-female ratio of 1.2:1 while another study reported male-to-female ratio was 1:1.9.[4,8] It may occur at any age and the organs or sites usually involved include the skin, lymph nodes, breasts, vagina, and cervix.[5,7] Its size ranges from 2 to 20 cm. Depending on the size and localization, the most common signs and symptoms associated with the myeloid tumor are compression signs accompanied by severe pain and abnormal bleeding.[7]

The pathogenesis of myeloid sarcoma is believed to be due to aberrant homing signal for the blasts interdicting its bone marrow localization.[7] One study noted that AML blasts isolated from the skin has a unique set of chemokine receptors compared to the blasts from the bone marrow and blood. The study suggested that different chemokine/chemokine receptor interactions underlie the homing and retention of AML blasts in the skin.[9]

The diagnosis of myeloid sarcoma is based on a clinical presentation, radiological investigations, and tissue biopsy.[10] Computed tomographic imaging is usually the imaging of choice. MRI may also be used as this can exclude other differential diagnosis such as hamartomas and abscesses.[11] FDG PET/CT is also a useful and safe tool to detect extramedullary AML with a sensitivity of 77% and specificity of 97%.[12] Core biopsy is done to confirm the diagnosis with its microscopic growth pattern as either a diffuse or an Indian file pattern. It can be subclassified according to the predominant cell type (monoblastic, myelomonocytic, granulocytic). The Ki-67/MIBI score ranges from 50 to 95%.[13]

In addition to core biopsy, immunohistochemistry is added as this is an important method for establishing the diagnosis of myeloid sarcoma.[9] CD68-KP1 is noted to be the most commonly expressed marker followed by MPO, CD117, CD99, CD68/PG-M1, lysozyme, CD34, terminal deoxynucleotidyl transferase (TdT), CD56, CD61/ linker of activated T lymphocyte/ factor VIII-related antigen, CD30, glycophorin, and CD4.[4]

Cytogenetic analysis can also be done on bone marrow, tissue or peripheral blood. Cytogenetic abnormalities were seen in approximately 50% of patients.[14] Mutated NPM1 is the most common mutation reported while the most common translocation is t(8;21) (q22;q22), although the inv (16)(p13;q22) translocation is also associated with extramedullary disease in AML, particularly at abdominal sites.[10]

Non-leukemic myeloid sarcoma is characterized by the absence of leukemia, myelodysplastic syndrome or myeloproliferative neoplasm, and a negative bone marrow biopsy.[15] It has been described in limited case reports. In one retrospective analysis of non-leukemic myeloid sarcoma, it was diagnosed in 2.2% of patients with AML.[5] The age of detection for non-leukemic myeloid sarcoma and the classic AML were similar, but inverse male-to-female ratio were observed for these two diseases for unclear reasons. Myeloid sarcoma can affect various body sites, with common locations being the skin, lymph nodes, breasts, vagina, and cervix. Facial involvement is rare, with only one reported case in a study.[5,6] The median time to the development of AML in non-leukemic myeloid sarcoma ranges from 5 to 12 months.[15]

The prognosis on patients with non-leukemic myeloid sarcoma remains unclear.[5] There are still no large prospective studies to answer this question due to the rarity of non-leukemic myeloid sarcoma and variations in presentation and genetic profile.[12] Tsimberidou et al. suggest that patient with myeloid sarcoma has longer event-free survival than patients with AML. However, their study does not address the issue of comparability between the myeloid sarcoma and AML patients.[14]

There is currently no consensus on the treatment of non-leukemic myeloid sarcoma due to its rarity. Based on observation of its high rate of progression to AML, the current recommendation is to treat them similarly to AML.[5,10] In the study of He et al., patients with non-leukemic myeloid sarcoma treated with intensive chemotherapy had an overall response rate of 91.3% and complete remission of 56.5%.[5] Local therapy for myeloid sarcoma includes radiotherapy, surgery, or both.[16] Radiotherapy in addition to systemic therapy is often given to patients with non-leukemic myeloid sarcoma, although its role is not yet established. For some patients, debulking of the sarcoma may also be an option prior to starting systemic chemotherapy.[16] However, there is no evidence that combining these approaches produces better outcome.[14] For the elderly, it is vital to assess for their performance status in choosing whether to give intensive chemotherapy or a less-intensive modality of treatment such as hypomethylating agents.[17] Currently, there are few case reports on elderly patients with myeloid sarcoma treated with hypomethylating agents with maximum response as either clinical resolution or decrease in size of the myeloid sarcoma.[18]

Although upfront chemotherapy in patients with myeloid sarcoma retards development of AML, its effect on overall survival in non-leukemic myeloid sarcoma has not been extensively investigated. In a study by Lontos et al., there is no significant difference in the overall survival among non-leukemic myeloid sarcoma given local treatment plus chemotherapy versus local treatment alone. Since chemotherapy in myeloid sarcoma has been associated with high treatment-related mortality, the data from this study suggests that some myeloid sarcoma patients can avoid upfront induction chemotherapy and its related complications.[19]

CONCLUSION

Non-leukemic myeloid sarcoma of the face is an exceedingly rare occurrence, particularly in the elderly Filipino population. For our patient, reaching the right diagnosis was made possible by obtaining an adequate biopsy and performing comprehensive immunohistochemical tests. Considering her age, existing health conditions, and overall physical state, we opted to treat her with azacitidine, a hypomethylating agent. Although she only completed one cycle, she handled the treatment remarkably well, suggesting that azacitidine can be an appropriate and tolerable option for elderly patients with myeloid sarcoma. However, this positive response is nuanced by the short duration of treatment and potential variability in individual responses to azacitidine. Unfortunately, she declined further therapy. While no clear consensus exists regarding the optimal approach to non-leukemic myeloid sarcoma, systemic chemotherapy is still being evaluated, with some advocating early intervention and others favoring localized treatments. Close monitoring for potential progression to AML remains crucial in managing these patients.

Informed Consent

Informed consent was secured from the patient.

Statement of Authorship

Both authors certified fulfillment of ICMJE authorship criteria.

Author Disclosure

Both authors declared no conflicts of interest.

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