Myeloid Sarcoma of the Breast of a Young Boy: A Case Report

Mahfuz H1, Hossain ME2, Uddin MM3, Karim MM4, Robbani MG5

Abstract
Granulocytic sarcoma also called myeloid sarcoma (MS) is an extramedullary tumour of immature granulocytic cells. It is a rare entity and most frequently associated with acute myeloid leukaemia (AML) but can occur with other myeloproliferative disorders. It may occur at any site, leading to very varied clinical presentations. Although it can occur in a number of areas of the body, the involvement of the breast is uncommon. We present a rare case of MS in a 14 year old boy with a non-tender lump in the left breast that had been apparent for five months. Available diagnostic techniques, including ultrasound and magnetic resonance imaging were systematically performed. After mastectomy, biopsy and immunohistochemistry was done. Immuno-histochemical stains were positive for CD45 (haematological marker) and myeloid markers, such as myeloperoxidase (MPO), and CD68, CD43 suggesting the diagnosis of MS. Although MS is a rare tumour in breast and its diagnosis is usually difficult, the clinician must know about its existence to make differential diagnosis.

Introduction
The myeloid sarcoma is an extramedullary solid tumour composed of immature cells of the granulocytic lineage.1 It was first described in 1811 by Burns and was initially called a chloroma by King in 1853, for the green colour of the tumour when exposed to air, due to the presence of myeloperoxidase in the tumour cells.2 As this colour was inconsistent and the lesion consisted of immature cells of granulocytic lineage Rappaport suggested to designate this neoplasm as granulocytic sarcoma.3 In 1892, Dock associated MS to leukaemia and more recently this tumour has been associated to myeloid leukaemia and other myeloproliferative disorders, such as polycythaemia vera and myeloid metaplasia, as well as in the evolution of myelodysplastic syndrome.3 MS is shown to precede acute myeloid leukaemia at which the bone marrow aspiration and biopsy reveal no haematological disease. This type of MS is called isolated, primary or non-leukaemic MS. It occurs with an incidence of 2 14% in AML.4 It has been identified to be solitary or multiple.5 MS occurs at any age both in paediatric and elderly patients.5 The bones, lymph nodes, soft tissues and skin are the most common sites of presentation of MS, with involvement of the breast being rare.4 Since the locations are diverse, clinical presentation of the disease is also diverse with signs and symptoms determined by the size and localization of the tumour.5

Case Report
A 14 years old boy presented to a tertiary care Military Hospital on May 29, 2017, with an enlarged, painless and palpable mass in the left breast that had been present for five months. Physical examination revealed a fixed mass 10.0 x 8.0 cm in diameter, hard in consistency which was located in central quadrant of the left breast, with no palpable axillary lymph nodes. The chest radiography was normal. CT scan of chest revealed mass lesion over anterior chest wall at the level of left breast. MRI of breast showed fairly large well-defined signal intensity change area (7.0 cm X 8.0 cm) in left breast, hyper-intense on T1 FS and iso to hyper-intense on T2 and STIR sequences. Post contrast scan showed enhancement of the area. Underlying pectoralis muscle was intact. A whole-body bone scan finding was normal.

On June 11, 2017 simple mastectomy was done with axillary dissection (Lt). Gross examination revealed a relatively well demarcated nodular lesion, which was grayish-white in colour, measuring 11x10x4 cm and covered by fibro-adipose tissues. Histopathology revealed there was diffuse infiltrate of medium sized round to oval cells in fibro-collagenous and fatty tissues with indented oval nuclei, 1-2 nucleoli and dispersed chromatin. Cytoplasm was small in amount and eosinophilic.
Case Report

Figure 1: Breast lump (Left)

There were very few small lymphocytes and plasma cells admixed with them. Mitoses were few. No necrosis was seen. Immunohistochemical analysis revealed that the tumor was positive for TDT, CD34, CD99, MPO, CD43 and CD15 but negative for CD20, CD3, Pax-5, CD2, CD1a, CD117, CD56, CD61, CD30, Glycophorin A, CD4, estrogen receptor, progesterone receptor, human epidermal growth factor receptor 2 and p120. Ki-67 was 75%. Watch and wait approach was adopted and the patient was on monthly follow up. Later on, local recurrence was identified in the soft tissue via fine needle aspiration cytology. Subsequently systemic chemotherapy was started on September 16, 2017 with Inj. Daunorubicin 60 mg/m\(^2\) on day 1, 3, 5 and Inj. Cytarabine 100 mg/m\(^2\) on day 1-7 as per 3+7 induction protocol.

Figure 2: H & E stain: The cells are of medium size with scanty cytoplasm and oval nuclei.

Figure 3: Immunohistochemistry-TDT positive

Figure 4: Immunohistochemistry-CD34 positive

Figure 5: Immunohistochemistry-MPO positive

Discussion

The term myeloid sarcoma was first used to describe an extramedullary mass composed of immature granulocytic cells and later used to encompass all forms of leukaemic infiltrates. MS is now identified as a wide spectrum of manifestations characterized by the occurrence of one or more extramedullary masses with or without bone marrow leukaemic involvement. MS is more common in men than in women, with a male/female ratio of 1.2:1.2 The most commonly reported median age is 56 years.2 It can occur in any anatomic site and exhibits rapid growth. MS in the breast is uncommon and may be misdiagnosed as lymphoma or carcinoma, particularly in the absence of infiltration of the bone marrow.4 Viadana et al reported only 4 cases (1.7%) of breast involvement among 235 patients with AML.6

Patients with MS of the breast mainly present with a painless mass and exhibit no other associated symptoms, such as nipple discharge or inversion.4 In the present case, the patient exhibited no evident symptoms with the exception of a rapidly growing mass.

The clinical presentation of MS can also be very
variable. It is now believed that this condition is a tissue variant of AML, and its diagnosis is equivalent to a diagnosis of AML.² It can manifest de novo in healthy patients, who then go on to develop AML months to years later.² This disease can occur in known AML in the active phase or as the first manifestation of relapse in previously treated patients. It may also present as a blastic transformation in chronic myeloid leukaemia, chronic myeloproliferative disorder, or myelodysplastic syndrome.² Misdiagnosis as non-Hodgkin lymphoma (NHL) can occur due to histologic similarities of the blasts to large-cell NHL, which is especially true in poorly differentiated MS.² Definitive diagnosis is based on immunohistochemistry, including stains for MPO, lysozyme, CD45, CD43, and CD68². Cytomorphology via fine needle aspiration of palpable masses or bone marrow biopsy can also be used to aid in the diagnosis.

In our case, in order to establish the diagnosis of MS of breast extensive immunohistochemistry panel was performed. Haematological origin was confirmed by the positivity for CD45, the myeloid lineage was identified by the positivity of MPO, CD68 and CD43. Therefore, based on the data presented, we concluded that the breast lump was compatible with MS.

Paradoxically, the presence of a normal bone marrow biopsy, as was seen in our patient, generally correlates with a worse outcome.⁷

Given the rarity of this disease, there are limited studies and currently no consensus on the treatment of myeloid sarcoma. Treatment is the same as that for AML, even for isolated tumour without haematologic involvement.² Currently, it is believed that systemic chemotherapy should be given to all patients. Additionally, surgical removal of the tumour and/or radiation is indicated if the tumour is massive or if there is spinal cord compression. Patients treated with surgery and/or local radiotherapy generally have a shorter survival as compared to those treated with systemic chemotherapy.³ Furthermore, aggressive therapy must be initiated for isolated myeloid sarcoma, because even after treatment, patients with MS are still at risk of developing AML.²

The therapeutic approaches for MS of the breast also remain controversial. The majority of studies have concluded that all patients with MS should receive mastectomy or lumpectomy plus standard systemic chemotherapy.⁵ Imrie et al reported that the overall survival was longer in chemotherapy treated patients compared with those who did not receive chemotherapy.⁹ Our patient was treated with mastectomy with axillary clearance followed by systemic chemotherapy.

**Conclusion**

The myeloid sarcoma is a rare neoplasm in the breast and it is frequently confused with other malignant tumours such as lymphomas. The diagnosis of the MS is always challenging for both the physician and the haematopathologist. The careful morphological analysis and the staining by immunohistochemistry are vital for establishing the diagnosis. A high degree of clinical suspicion to enable early diagnosis of this aggressive disease and subsequent intensive treatment with chemotherapy is imperative in this uncommon variant of AML.

**References**