

## CASE REPORT

### Myeloid sarcoma of the breast in an aleukemic patient: a rare entity in an uncommon location

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#### Abstract

Myeloid sarcoma (MS) is an extramedullary solid neoplasm of immature myeloid cells. These tumours usually develop in concurrence with or following acute leukemia. The breast is an uncommon site for presentation of this tumour, where it is often misdiagnosed as lymphoma or carcinoma. A 33-year-old female presented with a right breast lump in a private hospital, which was diagnosed as ductal carcinoma on lumpectomy. Subsequently she developed a lump in the left breast and a similar diagnosis of carcinoma was made on biopsy. A left mastectomy was performed. Histopathological examination revealed a tumour composed of mononuclear cells arranged in sheets and cords with round to oval vesicular nuclei and occasional prominent nucleoli. IHC for CK was very weak and focal. The tumour cells were immunonegative for ER, PR, Her2neu, epithelial membrane antigen, e-cadherin, CD3 and CD20. Diffuse immunopositivity for myeloperoxidase, CD34 and CD117 established a diagnosis of myeloid sarcoma. A histopathological review of the right breast lesion, with immunohistochemistry, also confirmed the diagnosis of myeloid sarcoma. Investigatory work-up for acute myeloid leukemia, including bone marrow aspirate and biopsy and karyotypic studies, proved negative. The patient was treated with high dose cytarabine (HDAC) regimen and was disease free during the 12-month follow-up. Although extremely rare, awareness of such a presentation is crucial. This case also illustrates that careful histopathological review along with an expanded panel of immunohistochemistry is extremely important for recognizing such cases as a misdiagnosis can lead to unnecessary surgery and inappropriate therapy.

**Keywords:** aleukemic patient; bilateral breast lump; immunohistochemistry; myeloid sarcoma

#### INTRODUCTION

Myeloid sarcomas (MS) are extramedullary solid neoplasms of immature myeloid cells. This entity was first described by Burns in 1811.<sup>1</sup> The common sites of presentation are lymph nodes, bone, soft tissue and skin.<sup>2,3</sup> These neoplasms are known by various synonyms such as granulocytic sarcoma, chloroma, monocytic sarcoma, extramedullary myeloid cell tumour and myeloblastoma.<sup>4</sup> Myeloid sarcoma commonly develops in concurrence with acute myeloid leukemia. However, there are instances where it has been reported without blood or bone marrow involvement.<sup>5</sup> Many reports of myeloid sarcoma occurring in the breast in patients with AML have been published, but the presence of myeloid sarcoma as an isolated breast mass

without any history or subsequent development of AML is rare.<sup>4</sup> We report a case of myeloid sarcoma involving both breasts without any evidence of a myeloid neoplasm within a 12-month follow-up. We emphasise the importance of immunohistochemistry (IHC) and careful consideration of histological features to avoid a misdiagnosis.

#### CASE REPORT

A 33-year-old female presented with a lump in the right breast to a private hospital. Contrast enhanced CT scan showed a mass in the right breast (Fig. 1a). Lumpectomy was performed and a histopathological diagnosis of an invasive carcinoma was made. No further treatment was undertaken at the private hospital. Two months

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later, she developed an induration at the scar and was referred to a tertiary care centre with suspected tumour recurrence. On examination an indurated scar was noted in the right breast. Also multiple hard nodules were palpable in the left breast. Ultrasound examination showed well-defined hypoechoic lesions beneath the areola in the left breast (Fig. 1b). Core biopsy of the left breast lesions was performed.

Histology showed an infiltrating tumour composed of cells arranged in sheets and cords. The cells were round to oval with vesicular nuclei showing weak immunoreactivity for cytokeratin (CK). The tumour cells were immunonegative for oestrogen receptor (ER), progesterone receptor (PR) and Her2neu proteins. Based on immunopositivity for cytokeratin, a diagnosis of an infiltrating carcinoma was made. The patient underwent a left breast mastectomy with axillary lymph node dissection.

*Pathology*

On histological evaluation of the mastectomy specimen, haematoxylin and eosin stained sections showed a tumour composed of mononuclear cells arranged in sheets and cords. The cells were round to oval with vesicular nuclei and occasional prominent nucleoli. Some of the cells show nuclear convolutions. Interspersed among them, many cells were seen having eosinophilic granules in their cytoplasm (Fig. 2A). IHC for CK was very weak and focal (Fig. 2B) and the tumour cells were immunonegative for ER, PR and Her2neu. Thus, a second panel of IHC with antibodies to epithelial membrane antigen (EMA), e-cadherin, CD3 and CD20 was performed. The tumour

cells were immunonegative for these markers (Fig. 2C-F), thus ruling out the possibility of an infiltrating carcinoma or a lymphoma. A third panel of IHC was done which showed diffuse immunopositivity of the tumour cells for myeloperoxidase (MPO), CD34 and CD117, thus establishing a diagnosis of myeloid sarcoma (Fig. 2G-H).

Twelve lymph nodes obtained from the axillary dissection showed metastatic tumour deposits. A review of previous slides from the core biopsies of right and left breast lesions with the extended panel of immunohistochemical markers confirmed the diagnosis of myeloid sarcoma in these biopsies.

*Investigations and clinical course*

The patient underwent a work-up for acute myeloid leukemia (AML). Complete blood count showed a hemoglobin level of 12.5 g/dL with 5,940 leucocytes/ $\mu$ L; 72.8% neutrophils, 19.2% lymphocytes and 250,000 platelets/ $\mu$ L. Peripheral blood smear, bone marrow aspirate and biopsy were normal. Karyotype analysis showed normal 46, XX chromosomes.

Patient was started on high dose cytarabine (HDAC) regimen and was disease free during the 12-month follow-up.

**DISCUSSION**

Myeloid sarcomas of the breast are uncommon neoplasms. The presence of MPO gives these tumours a “green tint,” hence the basis of the name “chloroma” (Greek: chloros). Rappaport renamed them as granulocytic sarcomas in 1966.<sup>6</sup> The occurrence of myeloid sarcoma in the breast

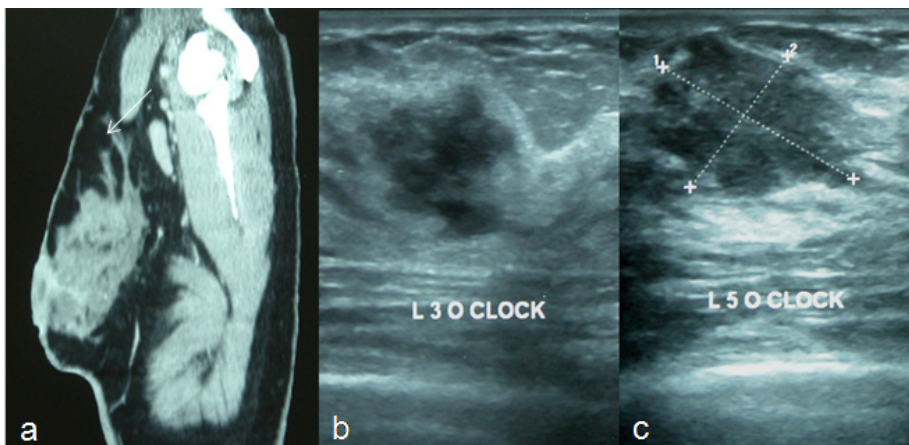


FIG. 1: (a) Contrast-enhanced sagittal CT image showing right breast mass (white arrow). Follow-up ultrasonography shows two lesions in the left breast at (b) 3 and (c) 5 o’ clock respectively.

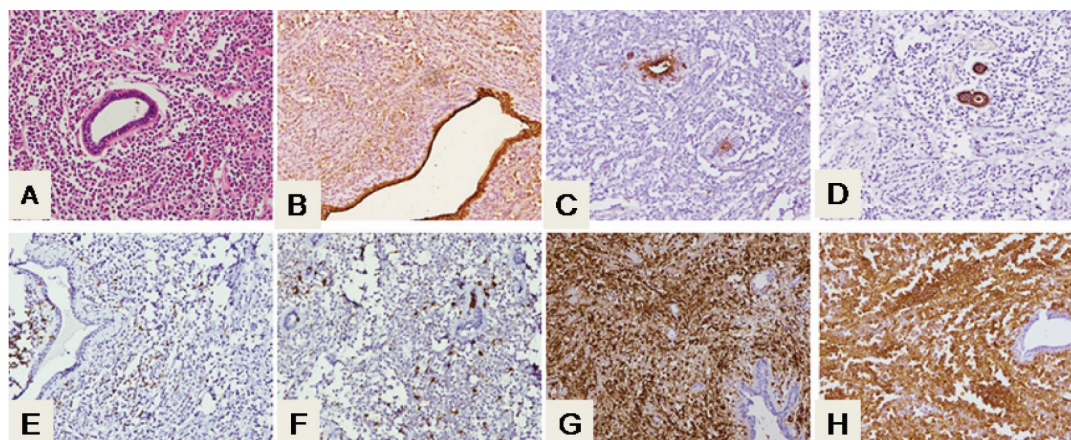


FIG. 2: Photomicrographs showing (A) tumour composed of mononuclear cells in a sheet-like pattern with normal ducts (H & E x100). Immunohistochemistry revealed weak and focal staining for (B)cytokeratin, and immunonegativity for (C) EMA, (D) e-cadherin, (E) CD3 and (F) CD20. The tumour cells were diffusely immunopositive for (G) MPO and (H) CD34.

without leukemic presentation is extremely rare and poses a diagnostic and therapeutic dilemma to both clinicians and pathologists.

A review of scientific literature revealed 12 cases (Table 1) of isolated myeloid sarcoma without any history of subsequent AML having unilateral breast involvement and only two cases, including ours, with bilateral breast involvement.<sup>2,4,5,7-13</sup> The age of presentation in isolated MS cases ranged from 29-72 years with a mean age of 42.4 years. This was similar to reported cases with leukemic presentation.<sup>4</sup> Patients usually present with a lump and associated symptoms like pain, breast

engorgement, nipple inversion and discharge are usually absent.<sup>4</sup>

The radiological appearance of MS is varied making it difficult to differentiate it from breast carcinoma or metastatic tumours. Mammographic studies have shown that the lesions can have both regular and irregular borders and are usually large and non-calcified. Homogenous hypochoic masses with well-defined or ill-defined margins are noted on ultrasonography.<sup>4,8,14</sup>

The tumor on histopathology shows various infiltrative patterns like diffuse, Indian file, targetoid and starry sky thus, mimicking lobular carcinoma, lymphoma, neuroendocrine tumour,

**TABLE 1: Isolated myeloid sarcoma involving breast reported in the literature with no history of hematological disorder or concomitant AML.**

Author , Year	Age of patient (years)	Side of presentation	Clinical follow-up
Eshghabadi et al,1986	45	R	ANED at 64 mo
Pettinato et al,1988	56	L	ANED at 11 mo
Jung et al,1998	28	R	Dead at 30 mo
Breccia et al,2000	71	L	ANED at 19mo
Quintas-Cardoma et al,2003	31	R	ANED at 37 mo
Shea et al, 2004	55	B	ANED at 24 mo
Valbuena et al,2005	31	R	ANED at 96 mo
Valbuena et al,2005	60	R	ANED at 96 mo
D'Costa et al, 2007	45	L	AML after 6mo
Azim et al,2008	52	L	ANED a 12 mo
Chavez et al, 2009	29	R	DNED at 16 mo
Present case	33	B	ANED at 12 mo

Key: R-right; L-left; B-bilateral; ANED- Alive, no evidence of disease; DNED- Dead, no evidence of disease; AML- acute myeloid leukemia; mo – months.



melanoma or at times a sarcoma<sup>4,13</sup> as in our case, where the first specimen was a core biopsy and due to tiny nature of the specimen and weak focal IHC positivity for CK it was misdiagnosed as an invasive carcinoma. In children, small round cell tumours like Ewings sarcoma, lymphomas and rhabdomyosarcomas are the common mimics.<sup>4</sup> On histology, the presence of immature eosinophilic precursors with preserved ductal and lobular structures is a clue for suspecting a MS.<sup>4</sup>

A panel of immunohistochemical markers comprising of MPO, CD34, CD43, CD117 and CD68 is positive in the majority of cases and these are extremely useful to ascertain the myeloid differentiation. 75% of cases are immunopositive for CD45.<sup>4,13</sup>

Due to the rarity of MS, there have been no large studies for analyzing the prognosis. Few reports compare the prognosis of isolated MS in patients with concomitant AML or AML without MS. Event-free survival in isolated cases has been found to be longer than AML patients.<sup>15</sup> Usually, patients with isolated MS develop a myeloproliferative disease within 6-12 months.<sup>13</sup> However, treatment with induction and consolidation chemotherapy can limit the disease as in our case where the patient has been on follow-up for the past one year and is doing well.

There is no consensus on the treatment of MS as there have not been many randomized prospective trials. The current treatment regimen is the conventional AML-type chemotherapeutic protocol in patients presenting with isolated MS or with concomitant AML. Some studies have suggested that HDAC may be an important agent in treatment and achieving longer disease-free survival of patients.<sup>15</sup> Radiotherapy along with chemotherapy in comparison to chemotherapy alone has no effect on survival. However, Tsimberidou and colleagues suggested that radiotherapy may prolong failure-free survival. Hematopoietic stem cell transplantation had a significant impact on overall survival of MS patients.<sup>15</sup>

### Conclusion

Isolated myeloid sarcomas presenting as breast masses have a varied appearance on imaging which can often be misleading. Careful histopathological review along with an expanded panel of immunohistochemistry is extremely useful for recognizing such cases as a misdiagnosis can lead to unnecessary surgery and inappropriate therapy.

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