

Case Report

Radiotherapy for Myeloid Sarcoma of the Breast: A Case Report and Review of the Literature

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Abstract

While the role of systemic therapy in the treatment of myeloid sarcoma is well documented, the evidence for the use of radiation therapy is sparse. We present a case of isolated myeloid sarcoma to the breast. Following treatment for myelodysplastic syndrome. Myeloid Sarcomas (MS) are also known as chloromas and granulocytic sarcomas. They are extramedullary tumours of immature myeloid cells that develop in the setting of Acute Myeloid Leukaemia (AML), Chronic Myeloid Leukaemia (CML) and accelerated phase Myelodysplastic Syndrome (MDS) [1]. Treatment options include systemic therapy, localised radiation treatment or surgery. Retrospective series have identified that radiotherapy provides safe and reliable local control and symptom palliation [2]. We conducted a review of literature to assess the rationale, role, and dose of radiotherapy for this rare leukemia manifestation in the breast.

Keywords: Myeloid sarcoma; Chloroma; Granulocytic sarcoma; Breast; Radiotherapy

Methods

A literature search was performed in MEDLINE and Pubmed for articles on myeloid sarcoma to the breast published between 1972 and August, 2020 using the following keywords and phrases: myeloid sarcoma, chloroma, granulocytic sarcoma, extramedullary sarcoma, breast, radiotherapy, radiation therapy. Additional evaluated articles were identified by back referencing from bibliographies of original articles. The search was limited to English language articles.

Case Presentation

We present a case of a 52-year-old woman with myeloid sarcoma of the left breast and axillary nodes following allogeneic matched unrelated bone marrow transplant for Myelodysplastic Syndrome (MDS) two years prior.

This patient was initially diagnosed with MDS, treated with azacitidine followed by matched unrelated bone marrow transplant 10 months following diagnosis.

20 months following her transplant she self-detected a left breast mass, evident on mammogram which confirmed a 28mm dense mass in the upper outer quadrant. Ultrasound showed a 30mm poorly defined mass with heterogenous echotexture, and enlarged left axillary lymph nodes.

Core biopsy of breast lesion showed Myeloid Sarcoma (MS), with mixed phenotype. Bone marrow aspirate and trephine revealed slightly hypercellular marrow with reactive changes, showing no evidence of excess blasts and the chimerism was 99% donor. There was no evidence of systemic relapse. Staging PET scan showed a solitary FDG-avid left breast lesion and two ipsilateral axillary lymph nodes. No abnormal FDG avidity was seen elsewhere to suggest metastases.

Treatment options presented to the patient included systemic therapy, localised radiation treatment or close surveillance. The patient opted to proceed with localised involved field radiation therapy, with the aim of locoregional control and delaying time to systemic therapy, accepting that this treatment approach was unlikely to result in cure.

Radiotherapy was delivered using a Deep Inspiration Breath Hold technique (DIBH) to minimise cardiac dose with a left sided breast malignancy, and utilised IMRT treatment to deliver a dose of 40Gy in 20 fractions over 4 weeks. The treatment volume included the entire left breast, and left axilla. Coverage of >95% was achieved for all volumes.

The patient tolerated treatment well, with a good clinical response in both the breast and axilla at completion of treatment.

Reference	Study	Level of evidence	Presentation	Clinical picture	Systemic disease	Treatment	Radiotherapy	Outcome
[8]	Barloon et al, 1993	Case report	Palpable breast masses	Isolated relapse post treatment for AML	No	Radiotherapy alone	24Gy/10#	No evidence of local disease at 10 weeks
[12]	Breccia et al, 1995	Case report	Palpable breast and ipsilateral neck masses	Primary localised myeloid sarcoma	No	Radiotherapy, chemotherapy	36Gy/18#	No clinical evidence of disease post radiotherapy. Disease free at 19 months
[13]	Au et al, 1999	Case report	Palpable slow growing unilateral breast mass	Isolated relapse post multiple relapses of AML	No	Chemotherapy, radiotherapy, autologous SCT	30Gy	No clinical response in breast, progressive disease at 4 months
[14]	Guerhazi et al, 2000	Case report	Palpable unilateral breast mass	Isolated relapse post treatment for AML	No	Chemotherapy	-	No clinical evidence of local disease at 5 weeks
[7]	Quintas-Cardama et al, 2003	Case report	Palpable right breast mass	Primary unilateral breast MS	No	Lumpectomy, chemotherapy, consolidative radiotherapy	36Gy/18#	Disease free at 37 months
[15]	Shea et al, 2004	Case report	Screening detected bilateral breast masses	Primary bilateral breast MS	No	Chemotherapy, autologous SCT, radiotherapy to bilateral breasts	Dose not reported	Disease free at 24 months
[16]	Roy et al, 2004	Case report	Palpable left breast mass	Primary unilateral breast MS	No	Biopsy, chemotherapy	-	-
[5]	Fu et al, 2014	Case reports	Clinical left breast mass	Primary MS	No	Lumpectomy + chemotherapy	-	Disease free at 4 years
			Clinical left breast mass	Relapsed AML with MS to breast	Unknown	Lumpectomy + chemotherapy	-	Overall survival 38 months
[17]	Gunduz et al, 2014	Case report	Palpable right breast mass	Isolated relapse post treatment for AML	No	Chemotherapy, autologous SCT	-	Deceased 24 days post chemotherapy due to sepsis
[18]	Goncalves et al, 2014	Case report	Palpable left breast mass	Primary unilateral breast MS	No	Lumpectomy, chemotherapy, radiotherapy	30Gy/15#	Disease free at 26 months
[19]	Huang et al, 2015	Case report	Clinical mass left breast	AML treated with chemotherapy, solitary relapse to breast	No	Lumpectomy, Chemotherapy	-	Local control at 1 year
[20]	Nalwa et al, 2015	Case report	Clinical right breast mass	Primary bilateral breast MS	No	Mastectomy + axillary lymph node dissection, chemotherapy	-	Disease free at 12 months
[21]	Gomaa et al, 2018	Case report	Clinical left breast mass	Primary MS breast	No	Chemotherapy, radiotherapy	Dose not reported	No systemic disease at 6 months
[22]	Sharma et al, 2018	Case report	Palpable right breast mass	Primary unilateral MS	No	Lumpectomy, chemotherapy	-	Disease free at 12 months
[4]	Dominguez Rullán et al, 2018	Case report	Asymptomatic chest mass	Isolated myeloid sarcoma	No	Local excision, radiotherapy, chemotherapy	40Gy/20#	Progression to AML
[23]	Bubulac et al, 2019	Case report	Ultrasound detected breast masses	AML with MS relapses to breast x3	No	Chemotherapy, allogenic SCT, chemotherapy for relapses x2, last relapse treated with radiotherapy	Dose not reported	OS 36 months
[24]	Wu et al, 2019	Case report	Palpable right breast mass	Primary unilateral breast MS	No	Mastectomy, sentinel lymph node biopsy, chemotherapy	-	Disease free at 1 year
[25]	Minoia 2019	Case report	Clinical left breast mass	Primary bilateral breast MS	No	Chemotherapy, radiotherapy	30Gy/15#	Disease free at 27 months



Figure 1: FDG PET showing MS left breast mass.



Figure 2: FDG PET showing MS in axillary lymph node.

She suffered only a mild skin reaction with intact skin and grade 1 erythema.

At clinical follow up 6 weeks post completion of radiotherapy the patient had a significant clinical response, with decrease in size of the breast mass and no palpable axillary adenopathy. Her post-treatment PET scan obtained 10 weeks post completion of radiotherapy showed a complete metabolic response in both the left breast and axilla, with an absence of any distant disease evident.

Discussion

Haematological malignancies may manifest as extramedullary soft tissue masses known as myeloid sarcomas, granulocytic sarcomas, extramedullary sarcomas or chloromas and are a rare extramedullary tumour of immature myeloid cells [3]. These may occur in isolation, or more commonly in patients with a history of Acute Myeloid Leukemia (AML), MDS, or in blast phase of Chronic Myeloid Leukemia (CML) [4].

The reported cases of myeloid sarcomas localised to the breast are scarce in the literature [5]. In a series of 96 cases of MS reported by Mayo Clinic, only 3% of cases were within the breast [6]. Cases have been treated with chemotherapy, autologous stem cell transplant, surgery and radiotherapy.

Treatment strategies include systemic therapy while Radiotherapy (RT) and surgery have been used to improve local control [4]. RT alone is effective for local control but unlikely to provide long term disease control or cure. Systemic chemotherapy is recommended to achieve long term remission or, in some cases, to prevent progression to AML [7]. While it is uncommonly treated with radiotherapy alone, there are reports of low dose radiotherapy achieving complete mammographic response of isolated MS to the breast [8].

With local therapy alone, progression usually occurs within 10–12 months after the diagnosis, suggesting that isolated MS should be considered as a systemic disease and initial treatment should include chemotherapy with or without transplantation [4,9]. A retrospective study from 1986 showed that 25% of patients initially treated without systemic therapy did not progress to haematological diseases during follow-up ranging from

3.5–16 years [10]. Collated retrospective data demonstrate that 88–100% of patients progressed to AML with exclusive local therapy, compared to 42% when given systemic chemotherapy [11].

A review of the published case reports specifically for breast myeloid sarcoma without systemic leukaemia or myelodysplastic syndrome, their presentation, treatment and radiotherapy doses (if reported) are summarised below.

The role of RT in the treatment of MS has not been well established. Overall, RT without systemic treatment is not considered an optimal therapy for primary MS patients. It can be used in conjunction with systemic therapies, primarily in patients who need rapid relief of symptoms, or as a consolidation therapy [26]. It has been suggested that radiotherapy may prolong failure free survival but not overall survival in patients presenting with isolated MS. This study also included one case of MS successfully treated with RT alone with 12 months failure-free-survival [27]. A series of 21 patients with isolated MS demonstrated that disease recurrence was lower in a group that received chemoradiotherapy than those receiving radiotherapy alone, with local control rates of 97% [2]. Small, retrospective reviews where radiotherapy is used in combination with chemotherapy have failed to show an overall survival advantage, and did not report on failure-free survival or local control [28,29]. Due to the rarity of this diagnosis, there are no randomised studies of radiation therapy for MS. Many retrospective studies only report the use of radiotherapy for MS in the urgent setting – progressive neurological failure in a patient with spinal MS, and superior vena cava syndrome in a patient with cardiac MS [30].

Radiotherapy should be considered in isolated MS, inadequate response to chemotherapeutic regimen, in recurrence following bone marrow transplantation, and when rapid symptom relief is needed. Additionally, radiation provides excellent palliation and is recommended when symptom relief is required [2].

There are few studies that have addressed the role of radiotherapy or defined an appropriate dose. When RT is used following inadequate response to chemotherapy, and for palliation in circumstances that require rapid symptom relief a low dose regimen of 24Gy in 12 fractions can be used for most patients and produces excellent disease control and minimal morbidity [2]. One retrospective case review of 20 patients with 43 separate radiotherapy courses identified a 65% completed response rate, 25% with partial response, and 10% with stable disease. Doses ranged from 6-35Gy, with a median of 20Gy. 95% of these patients achieved symptomatic relief of MS after RT [31]. Another retrospective review of 41 patients treated with radiotherapy for MS with a median dose of 24Gy (range 5–36Gy), report a local control rate of 93% [1]. Lower dose ranges have been reported to provide symptomatic relief and minimise disease burden if a more protracted course of treatment is not feasible [3].

Of the available published evidence on breast MS radiotherapy doses, when reported, range from 24-40Gy [4,7,8,12,13,18,25] and majority of these treatments were in conjunction with chemotherapy. Our dose of 40Gy in 20 fractions was selected as a monotherapy for this patient with the aim of providing durable local control and delaying systemic therapy. MS is considered radiosensitive and has been shown to have a dose-response relationship. The complete response rate in relation to dose has been reported as 43% with doses

of 10–19.99Gy, 86% with doses of 20–29.99Gy and 89% with doses above 30Gy [32].

While the treatment techniques for MS have been sparsely reported, there is documented successful use of electrons, photons including three-dimensional conformal techniques, intensity modulated RT which may be beneficial in treating head and neck areas, and adaptive radiotherapy [3,33]. Margins from 0.5cm to 3cm have been recommended [3,4,31]. Again, given the absence of systemic therapy treatment for this patient at this time, we opted for margins at the upper end of reported literature. Once a 3cm margin had been added, majority of the left breast tissue was within the clinical tumour volume to be covered, so a decision to treat the entire left breast was made. A deep inspiration breath hold technique was utilised due to the robust evidence in the primary breast cancer setting that this significantly decreases cardiac dose [34].

Isolated myeloid sarcoma is rare, and treatment modalities include surgical excision, RT and chemotherapy. Radiotherapy can be considered when MS presents isolated, when there is partial response to chemotherapy, or as a palliative measure to rapidly relieve symptoms. The proposed doses for isolated breast lesions range from 24-40Gy, however there is a significant dose-response correlation. These doses have a high likelihood of achieving local disease control with minimal morbidity. Radiotherapy may improve disease free survival or progression free survival, but due to a paucity of cases and a lack of randomised data this currently remains unproven.

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