

Granulocytic sarcoma with unusual localizations (breast and stomach) without bone marrow involvement after the allogeneic transplantation

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Abstract

Granulocytic sarcoma (GS) is a rare extramedullary solid tumor composed of immature myeloid cell that is associated with acute myeloid leukemia or myelodysplastic syndrome. Especially, the involvement of the breast as a pattern of relapse after allogeneic bone marrow transplantation (allo SCT) is extremely rare. We report the case of a 57-year-old woman who palpated a painless lump in the superior quadrant of her right breast. Her past medical history was a myelodysplastic syndrome (MDS) treated with bone marrow transplantation. Imaging work-up by mammogram and ultrasonography (US) showed solitary mass suspect of malignancy in breast. Tru-cut biopsy was performed from the suspect palpable mass of the right breast. Histologic findings were compatible with a granulocytic sarcoma in breast. While she was also evaluated for mass in the breast, also investigated by endoscopy for the symptoms of gastrointestinal system. The endoscopic biopsy showed diffuse neoplastic infiltration similar the pathology of the breast. GS of the breast is a rare extramedullary involvement of hematologic diseases. There are no the specific radiologic features in the presentation with GS of the breast. Our case also showed that careful histopathological review along with all panel of immunohistochemistry is extremely important for diagnose.

Keywords: Myelodysplastic syndrome; Granulocytic Sarcoma; Allogeneic bone marrow transplantation.

Introduction

Granulocytic sarcoma is a rare extramedullary solid tumor composed of immature myeloid cell and is associated with acute myeloid leukemia or myelodysplastic syndrome [1]. It was first reported by Burns in 1811 and was described as chloroma by King in 1853 [2, 3]. The common sites of presentation are lymph nodes, bone, soft tissue and skin [4, 5]. The breast is an uncommon site for presentation of this tumour. Despite of its importance for the initial assessment of the disease, breast imaging also lacks specificity and GS can mimic several other tumors, including breast carcinoma and lymphoma [6]. However, there are instances where it has been reported without blood or bone marrow involvement [7]. Especially, the involvement of the breast as a pattern of relapse after bone marrow transplantation is extremely rare. We report case of high risk myelodysplastic syndrome (MDS) with relapse 18

months after allo SCT as a granulocytic sarcoma in the right breast without bone marrow involvement. We also discuss the clinicopathologic features of granulocytic sarcoma in the breast and stomach after alloSCT.

Case

A 56 year-old woman was applied to our center due to cytopenia, and the diagnosis of high risk myelodysplastic syndrome (MDS) was made in January 2016. At the time of diagnosis hemoglobin was 8,5 mg/dl, white blood cell count was 6x10⁹/l and platelet count was 93x10⁹/l in the peripheral blood count. Biochemical tests were normal. Blasts in the bone marrow aspirate were 12%. There was positive for cluster of differentiation (CD)34 (12%), for CD117 (20%) and for P53(30-40%). Cytogenetic analysis showed normal karyotype. She was treated with decitabine 20 mg/kg/day intravenously (iv) on days 1-5. She received 4 courses of decitabine treatment.

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The patient underwent an alloSCT from her human leukocyte antigen (HLA)- matched brother after a conditioning regimen of busulfan (16mg/kg) and cyclophosphamide (120 mg/kg) in June 2016. Graft-versus-host disease (GVHD) prophylaxis consisted of cyclosporine and methotrexate. Full donor chimerism was obtained on 30th day after transplantation. Acute skin GVHD disappeared with methylprednisolone. Chronic GVHD was not observed in the patient during follow-up period. She was admitted with a palpable mass in the right breast that had been increasing in size for the past 3 months in December 2017. She had been a firm mass that was palpated on the right breast with 3.0x3.0 cm in diameter. There were no signs of retraction or skin abnormalities. Mammography planned to patient because of examined palpable mass. Mammography showed a single, irregular, poorly defined mass that was 2,5x3,5x4 cm in diameter, without calcification on the right breast with axillary lymph node that have 1,5 cm in diameter and thick cortexed (**Figure 1**). She has diagnosed as granulocytic sarcoma of the breast with a tru-cut biopsy of the right breast. The results of immunohistochemistry were positive for CD34, lysozyme, and myeloperoxidase (MPO), CD117, CD33 and were negative for CD3, CD20, CD30 and PAX5 (**Figure 2**). Her bone marrow aspiration and biopsy revealed no blast. Endoscopy has been planned due to abdominal pain and vomiting that persisting for 1 month. Endoscopy revealed a mass in the fundus area, 3,5 cm in size, from which a biopsy sample was taken. The gastroscopic biopsy showed diffuse neoplastic infiltration that the cluster of tumor cells expressed CD43, CD117, CD33, CD34 and MPO (**Figure 3**). GS was diagnosed in the stomach also. Later, she was treated with idarubicin at 12mg/m²/day iv on days 1-3 and cytarabine (ara-C) at 100 mg/m²/day iv on days 1-7. DLI was planned following chemotherapy.

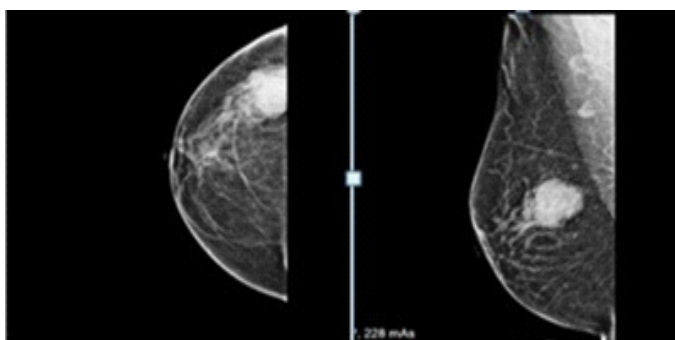


Figure 1: Mammography showed a single, irregular, poorly defined mass.

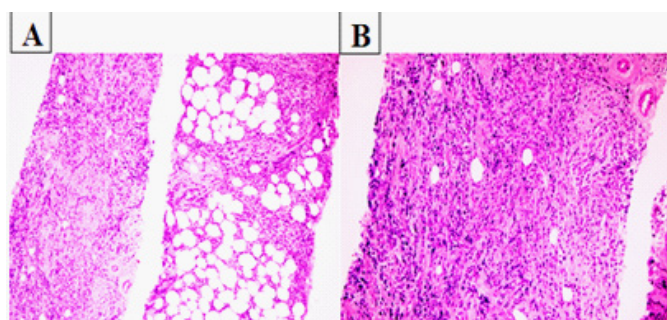


Figure 2: The granulocytic sarcoma of the breast with immunohistochemistry.

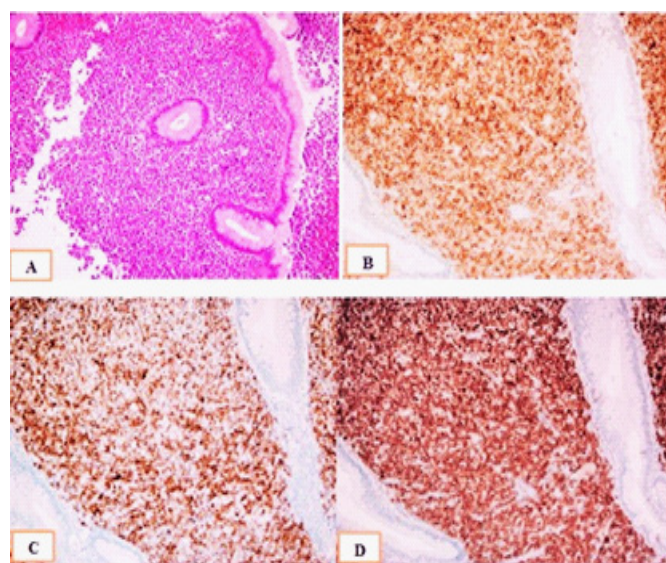


Figure 3: The gastroscopic biopsy showed diffuse neoplastic infiltration that the cluster of tumor cells expressed CD43, CD117, CD33, CD34 and MPO.

Discussion

There are four clinical presentations of granulocytic sarcoma; 1) Accompanied with AML; 2) could be the sign of AML; 3) could be associated with MDS transforming to leukemia and 4) solitary tumors [8]. Granulocytic sarcoma can occur concomitantly or can precede AML in 2%-14% [9]. It has been known that extramedullary relapses can involve the soft tissue of the head and neck, bone, skin and central system. However, they have reported to involve other sites such as the breast, nasopharynx, paranasal sinusoids, bladder, stomach, intestines, testis, perineum, pleural and peritoneal cavity [10]. Granulocytic sarcomas of the breast and stomach are uncommon neoplasms. Especially, The relapse with GS after bone marrow transplantation is extremely rare without bone marrow involvement. The pathogenesis of GS after alloSCT still unexplained. The potential mechanism of GS without leukemic marrow involvement is that the graft versus leukemia (GVL) effect is particularly more potent in the bone marrow, but is thinner in the extramedullary sites. DLI could eradicate marrow remnant of tumor cells, but could not be effective in the extramedullary relapses [11]. However, DLI was suggested that the GVL effect developed from chronic GVHD is effective avoiding bone marrow relapse, but is not effective in extramedullary relapses.

The prognosis of patients with GS is extremely poor and the majority of patients died to disease within a short time. Management of GS after alloSCT is extremely difficult. There is no consensus on the treatment of GS as there have not been many randomized prospective trials. Previously, treatments for granulocytic sarcoma have included surgical, local radiotherapy and chemotherapy. However, allogeneic stem cell transplantation could be effective treatment for GS. Although local therapy can offer long-term survival, most patients develop systemic relapse. Systemic or combined therapy should be considered in patients with good performance status [12].

However, DLI could be effect that showed in the literature and planed a second transplant in repeated relapse [13,14]. Our case was well tolerated systemic chemotherapy, later we

planned DLI in the our patient because of good performance. The combine therapy modalities can be more toxic in patient that have made allo SCT, so we can be careful.

Table 1: The cases of granulocytic sarcoma of the breast.

Author, Year	Age of patient (years)	Side of presentation	Clinical follow up
Eshghabadi et al ¹⁵ , 1986	45	R	Alive, at 64 months
Pettinato et al ¹⁶ , 1988	56	L	Alive, at 11 months
Jung et al ¹⁷ , 1998	28	R	Dead, at 30 months
Breccia et al ¹⁸ , 2000	71	L	Alive, at 19 months
Quintas- Cardoma et al ⁴ , 2003	31	R	Alive, at 37 months
Shea et al ¹⁹ , 2004	55	B	Alive, at 24 months
Valbuena et al ²⁰ , 2005 (2 case)	31 60	R R	Alive, at 96 months Alive, at 96 months
D'Costa et al ²¹ , 2007	45	L	AML after 6 months
Azim et al ⁷ , 2008	52	L	Alive, at 12 months
Chavez et al ²² , 2009	29	R	Dead, at 16 months
Gündüz et al ²³ , 2012	30	R	Dead, at 17 months
Kim et al ⁶ , 2013(2 case)	39 48	R B	Dead, at 2 months Dead, at 24 months
Nalva et al ¹ , 2015	33	B	Alive, at 12 months
Huang et al ²⁴ , 2015	58	L	Alive, at 4 months
Vieira et al ²⁵ , 2017	45	B	Not evaluated
The present case, 2018	57	R	Alive, at 3 months

We found 18 patients (**Table 1**) with granulocytic sarcoma of following AML that have breast involvement in the literature. The age of presentation ranged from 28-71 years with a mean age of 45 years. The duration time of follow-up ranged from 2 to 96 months. Patients usually present with a mass. Our case presented 57 years old with a palpable mass in the right breast. Later, the abdominal pain and vomiting that had persisted for 1 month added to the patient's complaints. The results of gastroscopy was found GS in stomach. Our case presented with unusual localizations (stomach and breast). The only 6.5% of myeloid sarcomas derive from the gastrointestinal tract [26]. These patients usually present with nonspecific symptoms including abdominal pain, vomiting or bleeding without bone marrow involvement ,that the same as in our case. The median time from SCT to GS relapse has been reported as 10 to

17 months [12, 27, 28]. However, our case was 57 year-old, and this time was 16 months after allo SCT. Mammographic studies have shown that the lesions can have both regular and irregular borders and are non-calcified. However, GS is difficult to distinguish from other types of tumor using mammography or breast ultrasonography. In the present case; mammography showed a single, irregular, poorly defined mass that was 2,5x3,5x4 cm in diameter, without calcification on the right breast. Hema-toxylin and eosin staining can reveal a range of changes in morphology, causing the common misdiagnosis of GS. To approve the final diagnosis of GS, the immunohistochemical detection of MPO positive cells is useful. However, A panel of immunohistochemical markers comprising of MPO, CD34, CD43, CD117 and CD68 is positive in the majority of cases and 75% of cases are immunopositive for CD45 (20,22).

The results of immunohistochemistry were positive for CD34, lysozyme, MPO, CD117, CD33 in pathology preparations of the breast and the results of the gastroscopic biopsy showed diffuse neoplastic infiltration that the tumor cells expressed CD43, CD117, CD33, CD34 and MPO in our patient.

In conclusion, it is difficult to make a clinical decision for the treatment of GS. The prognosis of patients who develop EM relapse after allo SCT remains poor. Immunophenotyping after biopsy is essential for differential diagnosis.

Conclusion

In conclusion, GS is malignant neoplasm of myeloid origin that could be in any area of the body. GS derived from the breast and stomach is relatively rare and tends to be misdiagnosed. The prognosis of granulocytic sarcoma remains poor. The patients with granulocytic sarcoma should be carefully evaluated with clinical and immunohistochemical results. However, it is necessary to perform a diagnostic search of any kind of mass that develops during the follow-up in patient with leukemia.

Ethics declarations

Conflicts of interest: None.

Consent for publication: The authors state that an informed and written consent was obtained from the patient prior to the publication.

Ethical approval: The authors declare that the article follows the Helsinki declaration guidelines and the manuscript has not been submitted to any other journal.

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