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Breast Location for *De Novo* Extramedullary Myeloid Sarcoma

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Abstract

Background: Myeloid Sarcoma (MS) is a rare hematologic cancer, which can occur as a breast mass to be distinguished from other non-hematopoietic tumors.

Case Presentation: This report describe the unusual clinical history of a young woman diagnosed with MS. Radiotherapy/surgery alone may be inadequate, while chemotherapy and hematopoietic stem cell transplantation demonstrated to improve the prognosis for the isolated extramedullary localization.

Conclusion: Performing a needle biopsy in order to exclude the diagnosis of a primitive breast disease is irreplaceable.

Keywords: Breast mass; Myeloid sarcoma; *De Novo*

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Abbreviations

MS: Myeloid Sarcoma; AML: Acute Myeloid Leukemia; AlloHSCT: Allogeneic Hematopoietic Stem Cell Transplantation; MRI: Magnetic Nuclear Imaging

Background

Myeloid Sarcoma (MS), also known as granulocytic sarcoma or chloroma, is a rare hematologic cancer. It is characterized by proliferation of immature myeloid cells in one or more extramedullary tissues. MS has been reported in 2.5% to 9.1% of patients with Acute Myeloid Leukemia (AML). It can arise simultaneously (de novo AML related MS), following (secondary MS) or preceding (de novo extramedullary MS) the onset of bone marrow involvement [1,2]. More rarely MS could also be detected in the setting of myelodysplastic or myeloproliferative tumour. The most common involved location are soft tissues, skin, bones, periosteum, central nervous system and lymph nodes, but many other sites are described in multiple reports [3]. The diagnosis of MS required a tissue biopsy with immunohistochemical stains, fluorescence in situ hybridization and molecular analysis. The pathological differential diagnosis of MS is non-Hodgkin lymphoma, lymphoblastic leukemia, blastic plasmacytoid dendritic cell neoplasm and non-hematopoietic tumour [1,4].

Bone marrow biopsy and imaging to define the extension of tissue involvement are the other diagnostic and staging workup examinations.

The prognosis of MS is poor, both in the novo and in secondary subtypes, with a 5-year survival rate of 20% to 30%. Systemic chemotherapy is recommended also for isolated extramedullary form. Allogeneic Hematopoietic Stem Cell Transplantation (AlloHSCT) should be considered in every patient when it is practicable [2,5,6].

Case Presentation

A 24-year-old female presented a huge solid mass at the outer and central quadrants of the

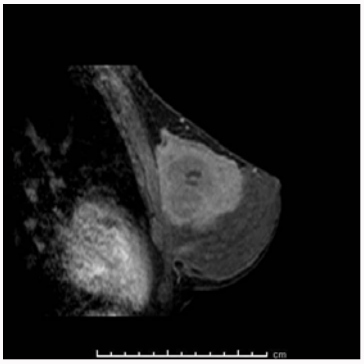

Figure 1: Sagittal contrast enhanced MRI of the left breast shows an irregular marginated heterogeneously high enhancing mass, in the upper and central quadrants.

left breast with sudden onset, apparently capsulated, 6 cm x 3 cm diameter, with a disomogeneous and vascularized structure at the ultrasound. Another mass, diameter 1.7 cm x 0.8 cm, was located at the inner quadrant. She had no history of breast cancer. Physical examination revealed petechiae at the lower limbs. MRI showed in the left breast, with prevalence in the upper quadrants, a mass of inhomogeneous enhancement, with diameters of 8.6 cm x 7.3 cm x 6.6 cm with disomogeneous content for the presence of central colliquated areas (Figure 1). Another lesion, diameter 2.4 cm, with the same features, was present at the lower quadrant. In the ipsilateral axilla there were two lymph nodes with thickened cortical of about 2 cm in diameter.

An ultrasound guided needle biopsy of the largest breast mass was performed and histopathology showed a diagnosis of Myeloid Sarcoma. Histologically there was a proliferation of monomorphic little-medium size cells spread between residual ductal structures (Figure 2). The immunohistochemical analysis revealed that malignant cells were positive for myeloperoxidase, CD34, CD43 and CD68/KP1. Lymphoid (CD20/L26, CD79a, CD3, CD30/BERH2) and epithelial (cytokeratin) markers were negative. Peripheral blood analysis showed 46.000 leukocytes/mmc, haemoglobin level of 12,2 gr/dl, 85.000 platelets/mmc and 1244 U/L of lactate dehydrogenase. Bone marrow aspirate and biopsy, together with molecular and cytogenetic assay, were consistent with a diagnosis of AML–M4Eo with inversion [16] (p13,q22) resulting in fusion gene CBFbeta-MYH11. The study of cerebrospinal fluid was negative for localization of leukemia.

Induction chemotherapy was started with continuous infusion Cytarabine 100 mg/mq/days 1-10, Etoposide 50 mg/mq days 1-5 and Daunorubicin 50 mg/mq on days 1,3 and 5. The restaging showed a pattern of partial remission resulting from a bone marrow complete hematologic response associated with reduction of the breast mass (4.9 cm x 4.1 cm x 4 cm) on MRI. For the disease persistence in the extramedullary site, the patient was treated with a re-induction chemotherapy cycle consisted with Fludarabine 30 mg/mq days 1-5, Cytarabine 2000 mg/mq days 1-5, Idarubicin 10 mg/mq days 1-3 and Granulocyte colony stimulating factor from day -1 to day +5 obtaining a stable hematologic complete remission, decrease of minimal residual disease measured with quantitative real time PCR of chimeric transcript CBFbeta-MYH11 and further reduction of dimension of MS. After a subsequent cycle of Cytarabine 800 mg/mq every 12 hrs on days 1-3 and autologous peripheral blood stem cells harvest also the MRD became negative. Therefore HSCT using a

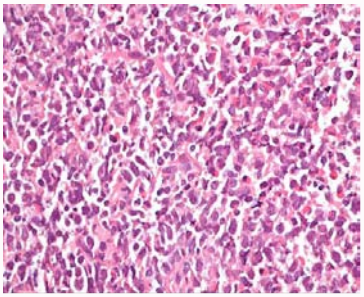

Figure 2: Medium-size myeloid tumor cells and inflammatory background with eosinophils. H&E 400x.

matched unrelated donor (MUD) 10/10 was performed. Sepsis from Klebsiella Pneumoniae was the only severe complication occurred during this long combined treatment. The patient doesn't develop any sign of Graft Versus Host Disease. Nowadays, 40 months after transplantation, persists a picture of complete hematologic and molecular remission associated with MRI breast pattern of complete response. Follow up with periodic response assessment performed with MRI of the breast and bone marrow aspirate for morphological and molecular tests will continue.

Discussion

The breast is an uncommon location for de novo extramedullary myeloid tumor. MS of the breast is more commonly observed in the context of a myeloid neoplasm originating from the bone marrow during its natural history (de novo AML related MS or secondary MS) [7]. The prevalence of mammary gland involvement is 6% in a recent retrospective survey including 48 MS patients [2]. Gynecomastia or isolated breast mass may be the presentation of this entity. Histologically differential diagnoses of breast lesion are low grade Non Hodgkin Lymphoma, lobular carcinoma, undifferentiated carcinoma, malignant melanoma and inflammation [8]. Mammography, MRI and ultrasonography are commonly used to study a breast lump but MS is often indistinguishable from other benign tumour or lymphoma [9]. Diagnosis must be done only through tissue biopsy and immunohistochemistry. The prognosis of the disease is dismal and systemic chemotherapy demonstrates a fundamental role to improve the prognosis even for the isolated extramedullary localization. Radiotherapy or surgeries alone are inadequate. Furthermore, numerous retrospective surveys support the role of allo HSCT in the management of this rare hematologic neoplasm [2,3,6,10].

Conclusion

Primary involvement of the breast is a rare event in lymphoproliferative diseases and can be confounded with a primitive invasive breast cancer. In this case report, the young age of the patient and the absence of risk factors for breast malignancies suggest to avoid a surgical approach in the diagnostic-therapeutic pathway. The authors underline the importance of performing a needle biopsy in order to exclude all possible diagnosis of a primitive breast disease.

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