

Case Report

A Lateral Neck Myeloid Sarcoma Presenting as Acute Otitis Externa

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Myeloid sarcoma (MS) is a solid extra-medullary tumor of immature myeloid cells which could occur before, during or after remission of acute leukemia at any site on the body. Owing to variation in differential diagnosis, pathologic evaluation and immunohistochemical staining are essential for definitive diagnosis. Rarely, MS has been shown as an isolated extramedullary relapse (iEMR) after allogeneic stem cell transplantation (allo-SCT), which often does not necessarily result in bone marrow involvement. It seems that despite chemotherapy and graft-versus-leukemia (GVL) effects on bone marrow, leukemic cells could remain alive in the extra-medullary region. However, in order to achieve longer survival, timely diagnosis as well as combined systemic, local, and cellular therapeutic modalities should be considered in any patient with iEMR after allo-SCT.

We report a left lateral neck isolated MS presented as acute otitis externa in a patient with prior allo-SCT due to acute myeloid leukemia (AML). Therefore, MS should be considered in patients with any history of acute leukemia even if the patient presents with signs and symptoms of an infectious disease.

Keywords: Myeloid sarcoma, Otitis externa, Temporal bone

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Introduction

Myeloid sarcoma (MS) or chloroma, because of green color production owing to the intracellular myeloperoxidase (MPO) enzyme, is characterized by the extra-medullary mass formation of myeloblasts or immature myeloid cells commonly in soft tissues, bones, testes, and gastrointestinal tract. It is slightly higher in males and occurs at any age in any tissue.

MS frequently is seen during acute leukemia especially acute myeloid leukemia (AML); however, it may be detected after allogeneic stem cell transplantation (allo-SCT) as an initial presentation of relapse, or it may precede infiltration of leukemic cells into the bone marrow or blood before appearance of leukemia, called isolated or primary MS.

Chloroma after allo-SCT may present as an isolated disease or concomitant BM relapse. It has been hypothesized that this rare phenomenon may be consequence of a decreased graft-versus-leukemia (GVL) impact on extra medullary tissues and occurs in less than 1% of patients within 4-56 months after SCT.¹

Clinical presentations of MS, in the head and neck region including the temporal bone, can be jaw pain, tongue lesion with bleeding, sinus pain and pressure, acute mastoiditis, ear fullness, otalgia and retro-auricular swelling which were reported previously.²

On light microscopic examination, MS can be

misinterpreted as Burkitt's or diffuse large B-cell lymphoma (DLBCL) or even as a non-hematopoietic tumor. Therefore, owing to no specific signs and symptoms as well as the broad differential diagnosis, immunohistochemistry staining on highly suspicious samples for MS could be very useful.³

We describe a large MS presenting as an acute otitis externa, involving the left side of the neck in a known case of AML after allo-SCT and bone marrow remission.

Case Report

On February 2017, a 30-year-old man presented with severe left earache and otorrhea. On examination, a left protruding auricle was noted (Figure 1). The ear canal was tender and filled with pus. Owing to a posterior erythematous bulging, the tympanic membrane was not visible. He remembered left-side ear fullness and mild otalgia from 6 months earlier, which was worsening during the last week. However, despite appropriate treatment for acute otitis externa and improvement of symptoms, the marked bulging of the canal remained unchanged. Further investigation revealed he had been diagnosed with AML French-American-British (FAB) subtype M1 three years ago, and underwent allo-SCT from his brother three months later. He had neither history of Graft Versus Host Disease nor relapse after the transplantation and was taking immunosuppression regimen at presentation. The last complete blood count (CBC)



Figure 1. Left Auricular Protuberance in a Patient With Acute Myeloid Leukemia Which Underwent Allogeneic Hematopoietic Stem Cell Transplantation 3 Years Ago.

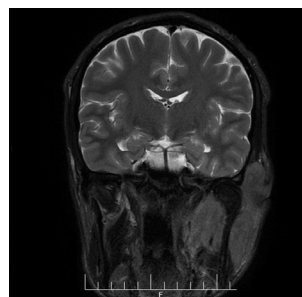


Figure 2. A Large Well-Defined Mass Presents Inferior to the Left Mastoid Apex and Extends to Left Mandibular Angle. The left parotid gland is embedded within the lesion on T2-weighted MR imaging (coronal view).

showed: WBC, 5800/ μ L, hemoglobin (HGB), 16.9 g/dL, and platelet (PLT), 175 000/ μ L. Pure-tone audiogram revealed a 30 dB left-side conductive hearing loss. Magnetic resonance imaging (MRI) of the brain demonstrated a large infiltrative mass lesion inferior to the mastoid apex. The lesion extended from left side of the skull base to left mandibular angle and subtemporal fossa. The left parotid gland was embedded within the lesion. Left mastoid air cells were filled with fluid. The left facial nerve was encased. No intracranial extension was seen (Figure 2).

Surprisingly, morphologic examination and immunohistochemical (IHC) staining of lesion biopsy were positive for CD99, TdT, MPO, CD3, and CD34 which were compatible with MS.

Bone marrow aspiration biopsies revealed about 50% cellularity containing a polymorphic population of hematopoietic cells. Megakaryocytes were also seen (Figure 3). Immunophenotyping of bone marrow aspirate by flow cytometry on the blast granulocytic area indicated 2% blast and 87% mature myeloid cells in various stages, and the result showed remission in this patient. Cytogenetic analysis revealed normal male karyotype with 46, XY. Analysis of short tandem repeats (STR) on whole blood showed 95% donor chimerism.

The patient underwent chemotherapy regimen with cytarabine (Alexan, Bio Pharma, Multan, Pakistan) and interferon- α (PDferon-B, Pooresh Darou, Tehran, Iran) for one month combined with local radiotherapy for 15 sessions. The lesion size decreased and he is still alive 15 months after diagnosis without any complications. We obtained written informed consent from the patient.

Discussion

As Maddox mentioned, periauricular bulging and chronic otalgia suggest a malignant involvement of temporal bone; however, our patient did not have facial nerve paresis.⁴ Early diagnosis is critical for timely treatment and could improve outcome of any malignancy. Therefore, despite the rarity of temporal bone involvement, MS should be considered in a patient with a history of AML. Temporal lymphoma or sarcoma and cholesteatoma involving the external canal could mimic MS; however, an absence of keratinized debris on examination and positive tumor markers for CD3, CD43, and MPO on IHC staining could distinguish MS. Imaging

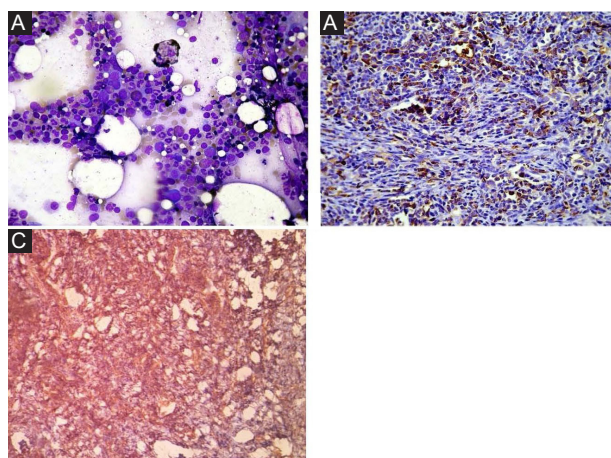


Figure 3. Bone Marrow Aspiration Smear Showed 50% Cellularity Including Sufficient Megakaryocytes, Normal Ratio of Myeloid to Erythroid Cells, and no Blast. Wright staining \times 400 (A); the tumor cells show positive MPO (B), and CD34 (C) staining 400X..

modalities are helpful for determining tumor extension and to differentiate abscess or hemorrhage. MRI findings are not specific in MS and usually comprise a well-demarcated mass which is iso/hypo intense on T1 and mildly hyperintense on T2 weighted images with gadolinium enhancement.^{5,6}

Isolated extramedullary relapse (iEMR), including MS after allo-SCT, is a rare phenomenon and often precedes systemic relapse. In a recent series reported by Shem-Tov et al, the incidence rate of iEMR was 5.8% at 59 months median follow-up of 556 patients with acute leukemia after allo-SCT. The risk factors associated for iEMR were diagnosis of AML, intermediate and advanced disease at transplant time, poor cytogenetics, previous extramedullary disease (EMD), and younger age. In addition, the overall survival (OS) after the first relapse, including bone marrow relapse (BMR), was 11.1%, and iEMR was the only major independent post allo-SCT factor for better survival. Although patients with a first EMR were at risk to develop recurrent EMRs, BMR does not occur in most transplanted patients compared with non-transplanted patients. It is of note that EMR nearly always heralds systemic relapse.⁷

Several local and systemic treatment strategies have been

purposed for EMD including MS. Almond et al emphasized systemic chemotherapy like cytarabine; fludarabine, cytarabine, idarubicin and G-CSF (FLAG), or idarubicin and cytarabine as a cornerstone of treatment even in isolated MS and some evidence suggests that cytarabine might play an important role in this condition. Since bone marrow involvement in patients with EMR after allo-SCT was less common in the recent series, and systemic toxicity increases with multidrug chemotherapy, we used only cytarabine plus IFN- α in regards to an antiproliferative effect and extension of patient survival with chronic myeloid leukemia receiving IFN- α , as the systemic therapy in this patient.^{8,9}

Local treatments including radiotherapy or surgery do not influence OS or progression to acute leukemia; however, they could be used for rapid debulking resulting in symptom improvements and prevention of extramedullary progression. Some promising results have been seen in immune therapies using a humanized anti-CD33 monoclonal antibody in tumors positive for CD33, or immune checkpoint blocking agents such as ipilimumab. In addition, cellular therapy, either donor lymphocyte infusion or second transplant, should be considered in case of EMR after allo-SCT.⁷ Finally, in contrast to temporal bone MS case series reported by Chang et al, our patient's longer survival, at least in part, might be due to the better outcome in the setting of iEMR after allo-SCT.¹⁰ In conclusion, to the best of our knowledge, acute otitis externa presentation of MS has not been described yet. Clinical practitioners should be aware of MS in patients with a history of acute leukemia even if the patient presents with signs and symptoms of an infectious disease. Despite a possible better prognosis in iEMR after allo-SCT, a combination of systemic, local and immune therapy as well as cellular therapy may provide longer survival.

Conflicts of Interest

Authors have no conflict of interest.

Ethical Statement

An informed consent was obtained from the patient and the patient name was kept concealed.

Authors' Contributions

RM and KM designed and edited the manuscript. HS and AA did data collection and manuscript writing. AA prepared final version of the manuscript.

Acknowledgments

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