Case Report

Isolated Testicular Relapse of Acute Myeloid Leukemia (AML) after Allogeneic Stem Cell Transplantation (ASCT): A Case Report

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Abstract

Allogenic Stem Cell Transplant (ASCT) is thought to be curative for patients with acute leukemia. Extramedullary relapse after ASCT is a cause for concern, as it usually precedes bone marrow relapse and can result in treatment failure and high mortality rates. The testis is an immune-privileged site, and relapse at this site is rare in AML. Here, we present a case of AML in a patient who had achieved complete remission and undergone ASCT, and who presented with testicular pain a year later. He was diagnosed with testicular relapse and subsequently with involvement of the cerebrospinal fluid (CSF), while his peripheral blood and bone marrow were negative for blasts and free from disease.

Keywords:

Acute myeloid leukemia, Testis, Cerebrospinal fluid, Relapse, Allogenic Stem Cell Transplan

Introduction

Isolated testicular recurrence of acute myeloid leukemia after allogenic stem cell transplantation is rare and is cause for concern, as it may herald relapse of the disease and treatment failure, as the testis is an immune-privileged site. Here, we present a case of a 35-year-old male patient with extramedullary relapse of acute myeloid leukemia post allogenic stem cell transplantation.

Case Report

A 35-year-old male patient presented with fever and weakness to the outpatient department in June 2022. His initial peripheral

blood examination was suggestive of Acute Leukemia with 30% blasts and a total count of 4000/cumm. His hemoglobin was 7 gm/dl. After a bone marrow work-up, he was diagnosed with AML. He was started on chemotherapy with Daunorubicin and Cytosar. Other than a few minor issues, he tolerated the therapy well. On day 14, his bone marrow was cleared of blasts. On day 21, he recovered from cytopenia. After 3+7 completed induction, he developed drug-induced transaminitis and fatty liver disease. He tested positive for Covid-19 and was admitted to the isolation ward. Appropriate treatment was given, and he recovered. He was consolidated with HIDAC, and he went into complete remission.

He was planned for bone marrow transplant. Cytogenetic study was done and showed a normal karyotype. NGS panel, NPM, and FLT3 were negative. HLA typing was done, and a matching donor was found in his sibling (10/10). Allogenic bone marrow transplant was done on 10.11.22. There was no Graft versus Host Disease (GVHD) on discharge, but a few months later, he developed delayed GVHD. In November 2023, he presented with testicular pain. A mass was felt, and FNAC (Fine Needle Aspiration Cytology) was done. FNAC showed immature myeloid cells and some blasts [Figure 1]. PET-CT (Positron Emission Tomography-Computed Tomography) showed 18-fluorodeoxyglucose (FDG) avid enhancing lesion in the prostate, penis, and bilateral epididymis, suggestive of relapsed malignant disease. There was no evidence of active malignant disease in the rest of the body. Concurrent peripheral blood and bone marrow work-up showed no blast population. Subsequently, CSF (Cerebrospinal Fluid) showed blasts [Figure 2].

He was admitted and underwent treatment in the hospital and went into remission. Subsequently, he is being treated in the outpatient department to the present time.

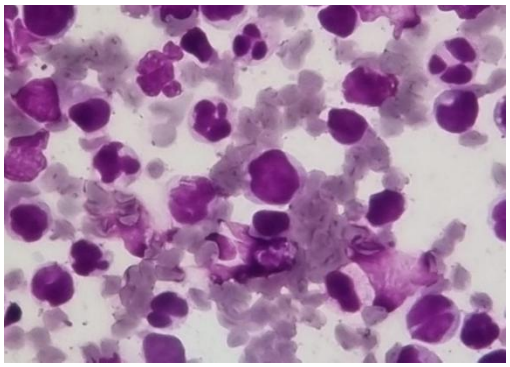

Figure 1: FNAC from Testicular Swelling (X 1000).

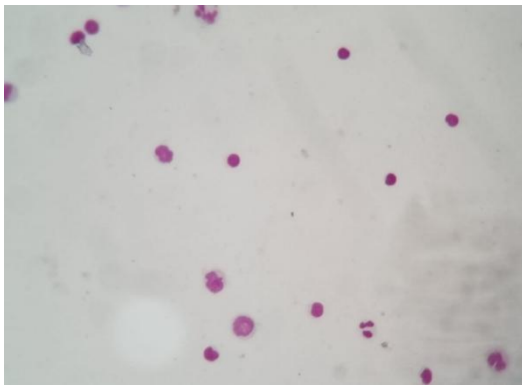

Figure 2: CSF (X 400)

Discussion

Allogenic stem cell transplant (ASCT) has been regarded as a potentially curative treatment in patients with acute leukemia, both myeloid and lymphoid. Disease relapse can cause the patient to suffer a loss of physical and mental well-being. It is concerning for the physician, as it can lead to treatment failure and mortality. Bone marrow relapse (BMR) is more common than isolated extramedullary relapse (iEMR) or mixed bone marrow and extramedullary relapse. Some studies show a rate of 41% for BMR and 3.9% to 5.8% for iEMR [1, 2]. BMR is found to occur earlier than iEMR. In their study of acute leukemia patients, both AML and lymphoblastic leukemia (ALL), Shem-Tov et al. found the relapse in bone marrow to occur at about 3.6 months versus 10.1 months for extramedullary relapse [1]. Gursel Gunes et al., in their study of acute leukemia and accelerated/blastic phase of chronic myeloid leukemia, found it to be at about 5.8 months for BMR and 10.73 months for extramedullary relapse [2]. Harris et al. found that the 5-year cumulative incidence of isolated extramedullary relapse to be 9%, and isolated bone marrow relapse to be 29%, with a median duration for relapse at 112 days for bone marrow and 348 days for extramedullary sites [3]. Shaffer et al. reported their patient to have relapsed about 2 months after a complete response to therapy [4]. Dang et al. described the testicular relapse in their patients at about 2 years after remission [5]. In comparative analysis of extramedullary relapse, some studies have found an increased incidence in acute lymphoblastic leukemia than in acute myeloid leukemia [2]. The sites commonly affected in extramedullary relapse are skin, soft tissue, central nervous system, bone, lymph nodes, and visceral sites [1, 2, 3].

Isolated testicular relapse in AML in adults is rare, occurring in about 1–2% of patients with bone marrow relapse [4], and only a few case reports are available for comparative analysis. Shaffer et al. reported the case of a 29-year-old male with AML who had isolated testicular relapse after 120 days of diagnosis. He had complete remission and had a previous CNS relapse which was treated successfully. After the testicular relapse, he had a bone marrow relapse and later died of fungal sepsis [4]. Grier et al. described an 18-year-old patient who had isolated testicular relapse at 86 months from his diagnosis. He subsequently had central nervous system relapse after 9 months [6]. Yildirim et al. described an 18-year-old patient of AML who had a relapse, thereafter, after remission, had an allogenic bone marrow transplant. He had isolated testicular relapse 18 months after the bone marrow transplant. Our patient had relapsed within a year of BMT. Two months later, he had a bone marrow relapse and, following consolidation, he expired [7]. Lucas Santos et al. reported a 23-year-old patient of AML who had BMT and later had a graft versus host disease at 100 days and, 5 years later, developed an isolated testicular relapse in a cryptorchid testis [8]. Mojtaba et al. described a 45-year-old patient of AML who had complete remission and, 6.5 years later, developed isolated bilateral testicular relapse with granulocytic sarcoma. He was treated with radiotherapy followed by chemotherapy and achieved complete remission [9].

In their univariate analysis, Gursel Gunes et al. found sex, extramedullary involvement at the time of diagnosis, conditioning regimen used, and chronic GVHD affected the extramedullary relapse rate. In our case, the patient did have a GVHD, but he had relapse. Their multivariate analysis showed all the above, except sex, were independent risk factors [2]. Shem-Tov et al. found the diagnosis of ALL, advanced disease at transplant, prior extramedullary disease, and poor cytogenetics as risk factors [1]. Our patient was NGS negative and classified as intermediate risk. Harris et al. found that previously reported factors like CD56 and T-cell markers expression, and reduced intensity conditioning were not associated with increased risk in their study [3]. Methods like inducing cGVHD and local radiation boosts are used to prevent relapse. Quaranta et al. found that a testicular boost resulted in a very low incidence of primary failure in the testicles, but the risk is not altogether eliminated. Their study was done on a mixed population of ALL and AML with testicular recurrence [10]. Dang et al. reported that the cases they reported had chronic

GVHD but still had testicular relapse. Chronic GVHD may not be effective in immunoprotected sites like the CNS and testis [5].

Our case had an isolated testicular relapse, followed by CNS relapse. He subsequently went into persistent CNS relapse and is on chemotherapy with scrotal radiation, and is on OPD follow-up treatment.

Conclusion

Testicular relapse in adults, after remission and allogenic stem cell transplant, is very rare. Not many studies with different data sets are available. Chronic graft-versus-host disease and myeloablative conditioning may protect patients from systemic relapse but have a low potential for protection against testicular relapse. The systemic barrier in the testis, resulting in leukemic cells being protected at these sites from systemic chemotherapy and escaping from the attack of donor lymphocytes, is thought to be responsible for the relapse [7]. A testicular boost may be protective but can result in gonadal failure. Testosterone replacement may be considered in these cases [11].

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References

1. Shem-Tov N, Yerushalmi R, Fein JA, Danylesko I, Shimoni A. Isolated extramedullary relapse of acute leukemia after allogeneic stem cell transplantation: different kinetics and better prognosis than systemic relapse. Biol Blood Marrow Transplant. 2017;23(7):1087–94.
2. Gunes G, Goker H, Demiroglu H, Aksu S, Haznedar R. Extramedullary relapses of acute leukemias after allogeneic hematopoietic stem cell transplantation: clinical features, cumulative incidence, and risk factors. Bone Marrow Transplant. 2019;54(4):595–600.
3. Harris AC, Kitko CL, Couriel DR, Braun TM, Choi SW, Magenau J, et al. Extramedullary relapse of acute myeloid leukemia following allogeneic hematopoietic stem cell transplantation: incidence, risk factors and outcomes. Haematologica. 2013;98(2):179–84.
4. Shafer DW, Burris HA, O'Rourke TJ. Testicular relapse in adult acute myelogenous leukemia. Cancer. 1992;70(6):1541–4.
5. Dang BN, De Oliveira SN, Bowles L, Moore TB. Isolated testicular recurrence of AML in patients with chronic GVHD >1 year following allogeneic stem cell transplant. J Pediatr Hematol Oncol. 2017;39:e423–5.
6. Grier DD, Eskew A, White T, McLean TW. An unusual case of acute myeloid leukemia: late isolated testicular relapse followed by isolated central nervous system relapse. Pediatr Blood Cancer. 2010;55(6):1231–3.
7. Yildirim I, Uçkan D, Cetin M, Tuncer M, Tezcan I. Isolated testicular and bone relapse in children with acute myeloblastic leukemia and chronic graft versus host disease after allogeneic BMT. Turk J Pediatr. 2007;49:206–9.
8. Patto de LS, Figueiredo BC, Campos GAB, Machado RL, Ribeiro RC, Silva SS. Recurrence of acute myeloid leukemia in cryptorchid testis: case report. Einstein (Sao Paulo). 2014;12(1):109–11.
9. Ghadiany M, Attarian H, Hajifathali A, Khosravi A, Molanaee S. Relapse of acute myeloid leukemia as isolated bilateral testicular granulocytic sarcoma in an adult. Urol J. 2008;5(2):132–4.
10. Quaranta BP, Halperin EC, Kurtzberg J, Clough R, Martin PL. The incidence of testicular recurrence in boys with acute leukemia treated with total body and testicular irradiation and stem cell transplantation. Cancer. 2004;101(4):845–50.
11. Amendola BE, Hutchinson R, Grossman HB, Amendola MA. Isolated testicular leukemic relapse response to radiation therapy. Urology. 1987;30(3):240–3.