Paraplegia as Manifestation of an Isolated Central Nervous System Relapse Following Allogeneic Hematopoietic Stem Cell Transplantation in a Woman with Acute Myelogenous Leukemia

Bi-Hui Yang[1], Yan Zhu[2], Juan Du[1], Yu-Lin Zhang[1], Sha Li[1], Lin Liu[1], Xiao-Hua Luo[1]

[1]Department of Hematology, First Affiliated Hospital of Chongqing Medical University, Chongqing 400016, China
[2]Department of Hematology, Southwest Hospital, Third Military Medical University, Chongqing 400038, China

To the Editor: Allogeneic hematopoietic stem cell transplantation (allo-HSCT) is a curative therapy for patients with acute myelogenous leukemia (AML) due to the intensive conditioning chemoradiotherapy and the effect of graft-versus-leukemia (GVL). An isolated extramedullary (EM) relapse of acute leukemia (AL) is a rare occurrence observed more commonly after allo-HSCT rather than following conventional chemotherapy alone.[1] The prognosis of patients with EM relapse is less favorable than bone marrow (BM) relapse, and there are no standard therapies.

In March 2013, a 42-year-old woman was diagnosed with acute myelomonocytic leukemia (AML-M5) and had white blood cell (WBC) count of 130.3 × 10^9/L. There was no central nervous system (CNS) leukemia documented at diagnosis. She had breast cancer 2 years ago and received a mastectomy of the left breast, followed by adjuvant chemotherapy and radiotherapy. There was no evidence of breast cancer relapse at follow-up.

In June 2013, the patient received human leukocyte antigen (HLA)-identical sibling HSCT with a conditioning regimen of busulfan and cyclophosphamide. Follow-up of immune reconstitution and minimal residual disease (MRD) is shown in Figure 1a. The BM aspirate collected 2 months after the allo-HSCT showed increased AML blasts (10.00%) and Wilms' tumor 1 (*WT1*)/Abelson murine leukemia viral oncogene homolog (*ABL*) transcript (0.03%). As a result, the prednisone and cyclosporine doses were decreased to induce GVL. A reexamination of BM after 1 week showed no abnormal immature cells. In October 2013, the patient was diagnosed with extensive chronic graft-versus-host disease (GVHD) and under-controlled using immunosuppressor. In March 2014, an analysis of cerebrospinal fluid (CSF) showed increased protein content (0.49 g/L), megakaryocyte number (10.0 × 10^6/L), and 3% myeloblasts despite repeated intrathecal injections for prophylaxis of CNS leukemia. MRI of the head revealed no leukemia infiltration, and the BM remained in complete remission. The patient received 7 intrathecal injections, and the CSF tests showed no leukemia infiltration. On April 25, 2014, the patient presented with bilateral lower limb fatigue and numbness, developed lower limb hypoesthesia, and fecal incontinence after 4 days. The neurological examination indicated decreased bilateral lower limb muscle powers, absent bilateral patellar tendon reflex, and positive pathology reflex on the right side. The hypoesthesia and paralysis progressed to the level of the fourth ribs and developed into paraplegia quickly. MRI of the whole spinal cord revealed slightly long T1 and long T2 signal lesions at vertebral level T5–T12. The lesions involved the bilateral lateral and posterior funiculi and showed unobvious increased by enhanced MRI [Figure 1b]. The patient developed a severe pulmonary infection and died shortly after central respiratory failure.

GVL has a significant role in the prevention of relapse after allo-HSCT. Allo-transplanted patients suffering from GVHD have a significantly reduced incidence of BM relapses attributed to the coexistent GVL effect. However, the rate of CNS relapse is independent of GVHD.[2] Our patient had early evidence of recurrence in the BM after allo-HSCT based on MRD monitoring, and immunosuppression was intentionally reduced to induce GVL. The patient had a continuous remission in the BM but suffered from a CNS relapse. The result could be explained by the effects of GVL because the CNS might be less effectively targeted than medullary sites. It is extremely rare for CNS leukemia to cause cranial nerve impairment, primarily including facial nerves, oculomotor, or trigeminal nerves. It was reported that spinal cord compression is a rare complication of myeloid leukemia and is always associated with granulocytic sarcomas.[3] In our case, the possible causes of

Address for correspondence: Dr. Xiao-Hua Luo, Department of Hematology, The First Affiliated Hospital of Chongqing Medical University, 1 Youyi Road, Yuzhong District, Chongqing 400016, China
E-Mail: xiaohua.luo@gmail.com

Access this article online

Quick Response Code:

Website: www.cmj.org

DOI: 10.4103/0366-6999.189922

Received: 06-04-2016 **Edited by:** Xin Chen
How to cite this article: Yang BH, Zhu Y, Du J, Zhang YL, Li S, Liu L, Luo XH. Paraplegia as Manifestation of an Isolated Central Nervous System Relapse Following Allogeneic Hematopoietic Stem Cell Transplantation in a Woman with Acute Myelogenous Leukemia. Chin Med J 2016;129:2260-1.

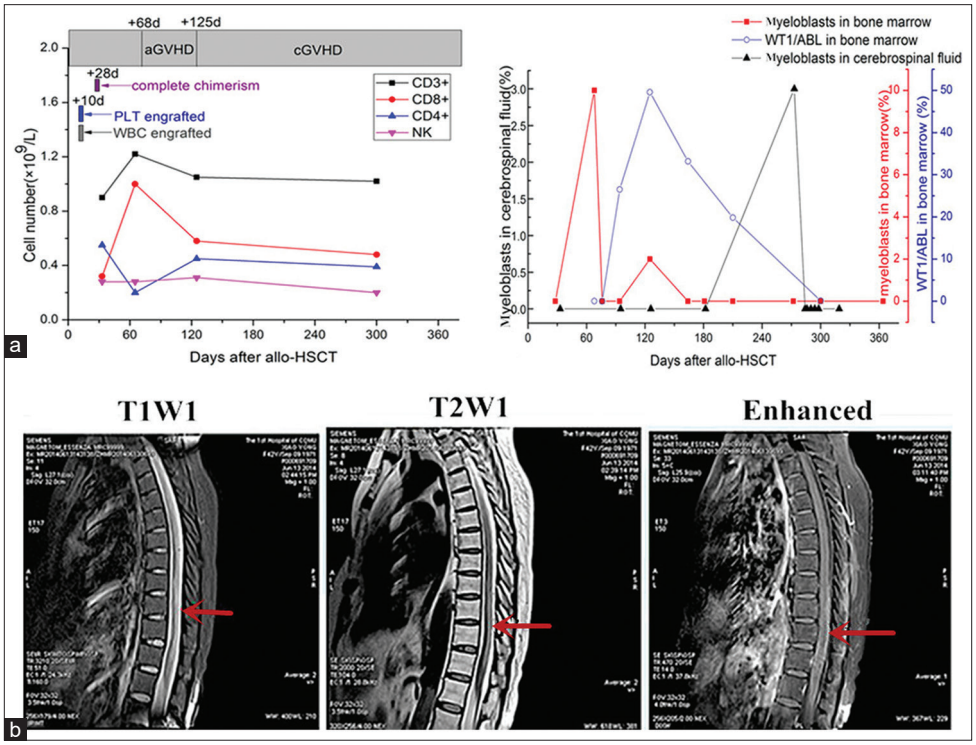

Figure 1: (a) Follow-up of immune reconstitution and minimal residual disease. (b) MRI scan of the spinal cord showing abnormal signal between the T5–T12 after allo-HSCT. GVHD: Graft-versus-host disease; CD: Cluster of differentiation; NK: Natural killer; PLT: Platelet; WBC: White blood cell; allo-HSCT: Allogeneic hematopoietic stem cell transplantation; WT1/ABL: Wilms' tumor 1/Abelson murine leukemia viral oncogene homolog.

abnormal MRI signals were sequelae of radiotherapy for breast cancer, opportunistic infections, complications associated with intrathecal injections, and extremely rare GVHD in the CNS.[4,5] Our patient was diagnosed with AML-M5 and had higher WBC counts at the first diagnosis, which predicted a high risk of CNS disease. The patient later presented with lower limb weakness and numbness developing into paraplegia that was followed by rapid deterioration and death. Importantly, the patient showed abnormal myeloblasts in the CSF after HSCT. Therefore, the abnormal MRI signals due to spinal cord compression were likely caused by CNS leukemic infiltration. Regrettably, there was no autopsy conducted to obtain pathological proof.

In conclusion, this rare case suggested that the GVL effect might not be uniformly effective throughout the body, and leukemic stem cells might be "protected" in the CNS. The unexplained paraplegia may be considered a potential sign of CNS involvement, and CSF evaluations should always be performed for early diagnosis.

Acknowledgments

We would like to thank Dr. Fei Xiao for his excellent assistance with this manuscript.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Shimizu H, Saitoh T, Hatsumi N, Takada S, Handa H, Jimbo T, *et al.* Prevalence of extramedullary relapses is higher after allogeneic stem cell transplantation than after chemotherapy in adult patients with acute myeloid leukemia. Leuk Res 2013;37:1477-81. doi: 10.1016/j.leukres.2013.08.017.
2. Davies JK, Taussig DC, Oakervee H, Davies AJ, Agrawal SG, Gribben JG, *et al.* Long-term follow-up after reduced-intensity conditioning allogeneic transplantation for acute myeloid leukemia/myelodysplastic syndrome: Late CNS relapses despite graft-versus-host disease. J Clin Oncol 2006;24:e23-5. doi: 10.1200/JCO.2006.05.7281.
3. Landis DM, Aboulafia DM. Granulocytic sarcoma: An unusual complication of aleukemic myeloid leukemia causing spinal cord compression. A case report and literature review. Leuk Lymphoma 2003;44:1753-60. doi: 10.1080/1042819031000104051.
4. Fukuno K, Tomonari A, Takahashi S, Ooi J, Takasugi K, Tsukada N, *et al.* Varicella-zoster virus encephalitis in a patient undergoing unrelated cord blood transplantation for myelodysplastic syndrome-overt leukemia. Int J Hematol 2006;84:79-82. doi: 10.1532/IJH97.06044.
5. Joseph PJ, Reyes MR. Dorsal column myelopathy following intrathecal chemotherapy for acute lymphoblastic leukemia. J Spinal Cord Med 2014;37:107-13. doi: 10.1179/2045772312Y.0000000081.