Case Report

Successful Stem Cell Mobilization and CD34+ Cell Collection in a Poor Mobilizer: A Case Report Utilizing a Combination of Recombinant Growth Colony Stimulating Factor, Recombinant Human Growth Factor, and Plerixafor

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Abstract

Diffuse large B-cell lymphoma is the most prevalent form of non-Hodgkin's lymphoma that is usually treated with chemoimmunotherapy. If the disease proves refractory or recurrent, the primary treatment approach involves high-dose chemotherapy with bone marrow transplantation. The collection of peripheral blood stem cells before transplantation plays a vital role in the treatment process, necessitating the mobilization of blood stem cells from the bone marrow to the peripheral blood. Despite using standard methods such as granulocyte colony-stimulating factor (G-CSF), chemotherapy, and plerixafor, some patients cannot collect an optimal count of CD34+ cells for transplantation. Managing these patients with poor mobilization poses significant challenges. In this article, we present a case of a poor mobilizer patient who achieved prosperous mobilization by using recombinant human G-CSF, recombinant human growth hormone, and plerixafor.

Keywords: *Bone marrow cell transplantation, hematopoietic stem cell mobilization, human growth hormone, non-hodgkin's lymphoma, plerixafor*

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Introduction

Diffuse large B-cell lymphoma (DLBCL), the most common form of non-Hodgkin's lymphoma (NHL), accounted for 30% of cases.[1] Treatment with a combination of rituximab plus cyclophosphamide, doxorubicin, vincristine, and prednisone R-CHOP regimen chemotherapy leads to complete remission (CR) in approximately 50%–70% of patients.[2] In cases of relapsed or refractory DLBCL, autologous stem cell transplantation (ASCT) with high-dose chemotherapy is an established procedure that significantly improves disease-free survival.[3] Peripheral blood stem cells (PBSC) are the preferred source for transplantation, necessitating the mobilization of stem cells from the bone marrow into the peripheral blood. The minimum required count of PBSC for ASCT is 2 × 106 CD34+ cells per kilogram of body weight.[4] Mobilization strategies typically involve the use of cytokines alone or in combination with chemotherapeutic agents.[5] Common mobilizing agents include filgrastim, sargramostim, pegfilgrastim, and lenograstim.[6] Unfortunately, around 40% of patients do not achieve the desired count of CD34+ cells using granulocyte colony-stimulating factor (G-CSF) alone.

Plerixafor, a reversible inhibitor of CXCR4 involved in cell migration, has emerged as an innovative option for enhancing the mobilization of a larger quantity of PBSC.[7] Poor mobilization is generally defined as the inability to reach a minimum of 2 × 106 CD34+ cells per kilogram of body weight.[4] In certain cases, standard approaches such as G-CSF, chemotherapy, and plerixafor may still fail to collect an optimal count of stem cells

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for transplantation. This poses a challenge in treating these patients since successful transplantation requires adequate healthy stem cells.

In the mentioned article, a specific case is presented wherein the addition of recombinant human growth hormone (rhGH) to G-CSF and plerixafor has been found to enhance mobilization in poor mobilizers. rhGH has been addressed to significantly increase the effect of colony formation in myeloid and erythroid progenitors in nonclinical studies.[8]

Case Report

In January 2021, a 44-year-old female was diagnosed with NHL-DLBCL (activated B-cell) stage II, specifically in the right axillary and neck regions. She has no medical history or any particular disease in her relatives. She underwent six cycles of standard R-CHOP chemotherapy, which consists of rituximab, cyclophosphamide, daunorubicin hydrochloride, vincristine, and prednisone. The first treatment plan resulted in CR. However, 2 months later, she experienced a local recurrence with extensive involvement of the right breast, which was confirmed through a biopsy. The recurrence was classified as stage II bulky, with no evidence of bone marrow or central nervous system involvement.

To address the recurrence, the patient received salvage chemotherapy with the combination chemotherapy regimen including rituximab, ifosfamide, carboplatin, and etoposide (R-ICE regimen). In addition, intrathecal chemotherapy (methotrexate and cytarabine) was administered on the 1st day of each treatment cycle. A complete metabolic response was confirmed through a whole-body fluorodeoxyglucose positron emission tomography-computed tomography scan at the end of the treatment.

After completing radiotherapy to the axilla and right breast in January 2022, the patient was admitted to the hospital for ASCT. However, during the mobilization process using G-CSF 10 μg/kg/day for 4 days and plerixafor 240 μg/kg added the night before each apheresis started on the 5th day,[7] the peripheral blood CD34+ cell counts were <10 × 10^6/L, which was considered insufficient to initiate apheresis.

After the previous unsuccessful attempts at mobilizing an optimal count of stem cells for transplantation, the patient was discharged and readmitted 2 weeks later for another attempt. This time, mobilization was carried out using a combination of rhGH at a dose of 100 μg/kg/day (up to a maximum daily dose of 6 mg) and G-CSF at a dose of 10 μg/kg/day, both administered subcutaneously for 5 days.[9] On the 5th day of mobilization, the peripheral blood CD34+ cell count reached 10 × 10^6/L. In addition, a subcutaneous injection of plerixafor (20 mg) was administered. After 11 h, the peripheral blood CD34+ cell count increased to 17 × 10^6/L. Apheresis was then performed, collecting 2.6 × 106/kg CD34+ cells, which met the required threshold for transplantation. The conditioning chemotherapy regimen for the transplant consisted of carmustine, etoposide, cytarabine, and melphalan. As shown in Table 1, the patient experienced successful engraftment of neutrophils on day 10 and platelets on day 12. Throughout the patient's stay, no significant complications were encountered.

It has now been 1 year since the transplant, and there have been no indications of recurrence. This positive outcome suggests that the transplantation procedure effectively achieved disease control. Regular follow-up and monitoring will continue to assess the patient's long-term progress.

Discussion

In the case of our patient, prior radiotherapy was identified as the only known risk factor for failed mobilization. However, there may be other unidentified causes contributing to the unsuccessful mobilization. It is worth noting that even in healthy donors without apparent risk factors, approximately 5% fail to mobilize with conventional regimens.[10]

New strategies for stem cell mobilization have been explored to improve the success rate. These include the use of plerixafor alone or in combination with chemotherapy for mobilization.[11] The combination of plerixafor and G-CSF, with or without chemotherapy, has been shown to reduce the rate of mobilization failure from 12% to 4%.[12]

A study by Carlo-Stella *et al*. showed that a combination of rhG-CSF and rhGH resulted in successful CD34+ cell collection and transplantation in 11 out of 16 patients.[9]

Mobilization failure after plerixafor remains a challenge, and a standardized approach for managing this situation has yet to be established. Further research and clinical studies are needed to explore and optimize strategies for successful stem cell mobilization in such cases. rhGH has been shown to act on hematopoietic progenitors by directly binding to specific membrane receptors or indirectly by stimulating the production of insulin-like growth factor I (IGF-I) or interacting with hematopoietic cytokines.[13] However, the specific mechanism through which rhGH enhances the ability of stem cells to mobilize in patients with heavily pretreated relapsed or refractory cancers remains a subject of hypothesis.

Table 1: Laboratory test results through the patient's hospital stay

Hospitalization day (*n*)	1	2	3	4	5	6	7	8	9	10	11	12
White blood cells (per µL)	20,000	20,000	22,300	41,300	1700	200	100	600	2000	5000	5600	6300
Platelets (per µL)	148,000	94,000	102,000	107,000	85,000	42,000	17,000	13,000	19,000	20,000	23,000	27,000
Fasting blood glucose (mg/dL)	160	110	120	99	81	96	89	83	87	95	102	98

One of the main concerns with rhGH therapy is the potential for acute and delayed complications. Short-term side effects include sodium and water retention, while long-term side effects may include reduced insulin sensitivity. Common mild side effects of rhGH therapy include peripheral edema, arthralgias, paresthesias, myalgias, carpal tunnel syndrome, and joint stiffness. Most of these side effects either resolve on their own or can be managed by adjusting the dosage of the drug.[14] In the case of your patient, no acute side effects were reported.

Regarding our patient, this is the first report of mobilization using a combination of rhGH, rhG-CSF, and plerixafor in a poorly mobilized individual. However, prospective studies are necessary to establish the effectiveness and safety of this combination therapy. Further research and clinical trials are required to elucidate the optimal use of rhGH in stem cell mobilization and to better understand its potential benefits and risks in this context.

It can be concluded that stem cell mobilization can be a challenging process, particularly in patients with prior radiotherapy or other risk factors. Conventional mobilization regimens, such as G-CSF alone, may not consistently achieve an optimal count of CD34+ cells to transplantation. rhGH has been investigated for its potential to enhance stem cell mobilization by acting on hematopoietic progenitors directly or indirectly through the stimulation of IGF-I production or interaction with hematopoietic cytokines. However, the use of rhGH is not without concerns. While alternative strategies, including rhGH, show promise in improving stem cell mobilization, further research, prospective studies, and clinical trials are needed to establish their effectiveness, optimal dosing, and long-term safety profiles.

The authors confirm that they have obtained the necessary patient consent forms. The patient has consented to publish her clinical information in the journal while understanding that her name will remain confidential.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given her consent for her images and other clinical information to be reported in the journal. The patient understands that name and initials will not be published and due efforts will be made to conceal identity, but anonymity cannot be guaranteed.

Authors' Contribution

M. Karimifar, A. Darakhshandeh, and A. Moghaddas contributed to the conception and design of the case report. M. Kazemi Najafabadi, and A. Moghaddas performed the literature review. A. Darakhshandeh, and M. Karimifar managed the patients and performed data extraction. All authors contributed equally to the analysis and interpretation of the data. All authors provided substantial contributions to the final version of the manuscript and approved it for publication.

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Conflicts of interest

There are no conflicts of interest.

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