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Case Report

Very Late Relapse of Plasma Cell Myeloma after Allogeneic Hematopoietic Stem Cell Transplantation

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Abstract

Very late (more than 10 years) relapse of plasma cell myeloma after allogeneic hematopoietic stem cell transplantation (allo-HSCT) is rare. The most common relapse pattern in such cases involves the bone marrow. Here, we report the case of a 51-year-old woman whose myeloma relapsed 15 years after allo-HSCT. She retained full donor chimerism, and the myeloma presented as soft tissue in the colonic wall. According to our review of the literature, this case presents the longest time to relapse after allo-HSCT. Patients with myeloma who undergo allo-HSCT should continue to receive regular follow-up even after 15 years.

Keywords: Allo-peripheral blood stem cell transplantation, late relapse, myeloma

Introduction

The recurrence of plasma cell neoplasms after treatment and complete remission for decades is relatively rare,[1] especially in patients who underwent allogeneic stem cell transplantation with full chimerism.[2] Here, we report the case of a patient with a very late (15 years) relapse of plasma cell myeloma after undergoing allogeneic peripheral blood stem cell transplantation (allo-PBSCT). To the best of our knowledge, this is the most delayed relapse of myeloma in a patient who underwent allo-PBSCT.

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Case Report

A 51-year-old woman was diagnosed with multiple myeloma with the presenting symptoms of bone pain and anemia in November 2001. She received a bone marrow examination which showed up to 15% plasma cells, and immune-fixation electrophoresis showed monoclonal immunoglobulin G (IgG) kappa gammopathy. She received thalidomide-based treatment followed by an allo-PBSCT from a male donor (the patient's

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younger brother) in February 2002. Her treatment regimen consisted of busulfan and cyclophosphamide. She experienced mild (grade 1–2) acute graft-versus-host disease after transplantation, and cyclosporine was stopped after 1 year. Thereafter, no maintenance dose of thalidomide was given. She received regular follow-up and remained disease-free for 15 years. Then, in November 2017, she experienced left-side abdominal pain and vomiting with no stool passage for several days. She went to a local community hospital for assessment, and an abdominal computed tomography scan revealed a transverse colon tumor with adjacent soft tissue involvement that was causing an obstruction [Figure 1]. A left hemicolectomy was performed because colon perforation was suspected, and the recurrence of plasma cell neoplasm as plasmacytoma was determined by pathology [Figure 2]. She was then transferred to our hospital for further management. On arrival, laboratory tests revealed albumin: globulin ratio of 0.67, albumin concentration of 2.9 g/dL, IgG concentration of 2943 mg/dL, and β2-microglobulin concentration of 7665 μg/L. Immunoelectrophoresis of her serum and urine revealed monoclonal IgG kappa (κ) gammopathy, which was compatible with the pattern 17 years ago. A bone marrow examination determined the presence of only 2% plasma cells, and flow cytometry analysis revealed the predominance of kappa light chains (60.5%). Her blood type remained the donor type, and a chromosomal study of the bone marrow biopsy revealed XY sex chromosomes in all tested cells, which represented that the patient was still in full chimerism. Bortezomib, thalidomide, and dexamethasone were prescribed as salvage treatment in December 2017; however, the disease progressed rapidly and she died of sepsis in March 2018.

Discussion

For plasma cell neoplasms, recurrence after decades in a disease-free condition is relatively rare.[1] Further, although autologous stem cell transplantation is currently more popular because of lower treatment-related mortality,[3] a myeloablative conditioning regimen followed by allogeneic hematopoietic stem cell transplantation (allo-HSCT) is thought to be a potentially curative option for plasma cell myeloma with a graft-versus-myeloma effect.[4] The primary goal is to eradicate the disease and rescue the patient with normal cells in the allogeneic graft. Complete remission rates of up to of 50%–60% have been reported with myeloablative conditioning. Obtaining complete remission is the most important factor predicting long-term survival. Allogeneic transplantation using myeloablative high-dose conditioning is still associated with a very high transplant-related mortality rate, and should only be considered in exceptional cases of high-risk or relapsed multiple myeloma, especially in younger patients. Furthermore, in a retrospective analysis by a German group, 76 of 155 patients experienced relapse in a median follow-up period of 45 months, and the patients who lost full donor chimerism exhibited a trend toward a shorter progression-free survival time ($P = 0.05$); although, the difference in overall survival was not statistically significantly ($P = 0.16$).[2] In their series, the authors also determined that the relapse pattern of most patients was extramedullary progression. A group from the City of Hope published a long-term follow-up study that investigated late relapses following reduced-intensity allogeneic transplantation in patients with multiple myeloma.[5] In their series, 6 of 38 patients experienced very late relapses, occurring 6.5–11.5 years after allogeneic transplant, and none of the relapses were extramedullary.

In our patient, full donor chimerism was confirmed through a chromosome study, and the relapse pattern was extramedullary. Her disease relapsed very late (more than 15 years), and to the best of our knowledge is the longest relapse time reported to date. The relapse pattern of very late relapse patients remains unclear, but our case indicates that patients with very late relapse may have the same relapse pattern as those who experience relapse earlier. Another issue of interest is the origin of this recurrence. In our case, recurrent myeloma was impressed after the immunoelectrophoresis study revealed

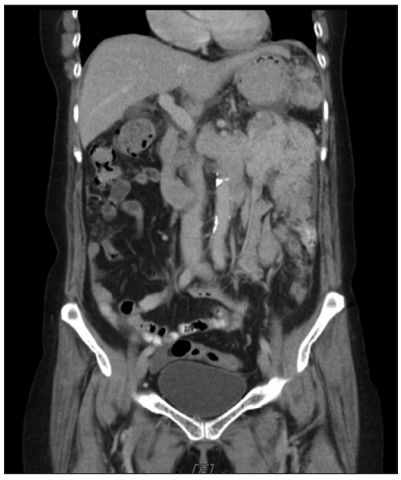

Figure 1: Abdominal computed tomography revealed a transverse colon tumour with adjacent soft tissue involvement

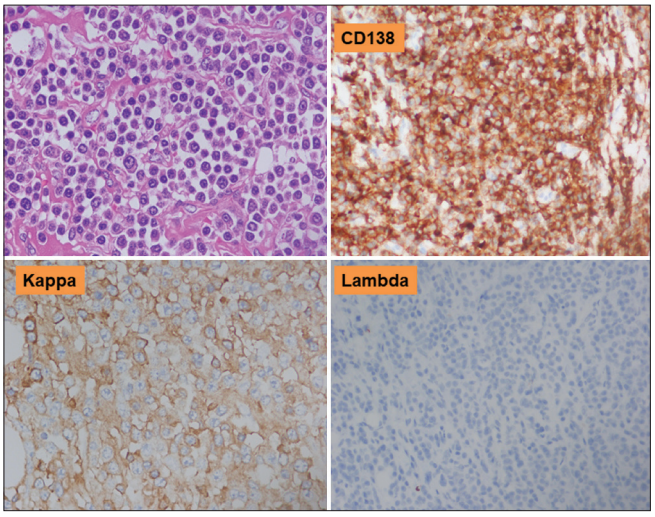

Figure 2: Soft tissue removed from the colon exhibited plasma cell infiltration with CD138 (+), Kappa light chain (+), and lambda (−)

monoclonal IgG gammopathy. However, the origin of this recurrence is unclear. Donor cell-derived hematological malignancies after allo-HSCT have been reported in some case reports.[6-8] In our case, the plasma cell neoplasm and monoclonal IgG gammopathy results initially impressed recurrence. In contrast, a bone marrow biopsy followed by a chromosome study showed 100% donor chimerism in our patient even after this episode. Donor cell-derived multiple myeloma and plasmacytoma was also considered. Further gene studies of the removed tumor could have provided an answer; however, the sample was not available after excision at the local community hospital, and a further gender examination was not available after the investigation.

Conclusion

The patient in this case presented with very late (15 years) recurrence under full chimerism after allo-PBSCT. Although a myeloablative conditioning regimen followed by allogeneic transplantation for patients with myeloma has still shown encouraging results, recurrence can still occur even after a very long time. Prospective studies are needed to clarify the benefits of the widespread use of novel agents as conditioning regimens, especially the newest drugs such as pomalidomide and carfilzomib. Annual follow-up for such cases is recommended even 10 years after transplantation. For myeloma patients receiving allo-HSCT, full donor chimerism should not be considered as the only indicator that the disease is in complete remission. An extramedullary relapse pattern should be considered in these cases, and any early symptoms such as an abnormal mass or tumor should be considered to be a relapse.

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Ethical statement and Declaration of patient consent

The study was reviewed and has been approved by the IRB of E-Da hospital (IRB No. 2019012).

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient gave her consent for her images and other clinical information to be reported in the journal. The patient (when she was still alive) and her family signed informed consent for further publication of this case report about this rare pathological cancer.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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