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LONG-TERM LENALIDOMIDE MAINTENANCE IN MULTIPLE MYELONA: EFFICACY AND MENAGEMENT OR RARE SIDE EFFECTS – A CASE REPORT

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Abstract

The clonal growth of plasma cells in the bone marrow causes multiple myeloma (MM), a complicated blood cancer. This can lead to complications and myeloma-associated organ damage. Lenalidomide, an immunomodulatory drug, has made MM much more effective, especially in maintenance therapy after autologous stem cell treatment transplantation (ASCT). This case report describes a female patient with immunoglobulin G (IgG) type multiple myeloma who has been receiving ongoing therapy since her initial diagnosis.

After receiving a diagnosis of multiple myeloma in 2015, the 51-year-old female underwent VTD regimen (Velcade,Thalidomide,and Dexamethason) four cycles, an autologous stem cell transplant (ASCT), and two years of Velcade maintenance and bisphosphonate therapy for 6 months, which led to a complete remission.

After 3 months of free therapy in 2018, the disease relapsed, prompting a switch to the VRD regimen (Velcade, Revlimid, and Dexamethasone), which resulted in a full response after four cycles. Subsequently, she experienced severe gastrointestinal manifestations, such as diarrhea, which were unresponsive to supportive care and basic anti-diarrheal medication. Consequently, we initiated treatment with colesevelam. In 2019, she underwent a second ASCT and recovered successfully. Serum electrophoresis and a PET/CT scan in 2023 identified active tonsils and lymph nodes but no new tumors. The patient is still in remission, undergoing maintenance therapy with Lenalidomide, and receiving regular monitoring.

This case study highlights the complex problems of managing multiple myeloma, emphasizing the importance of individualized treatment regimens that include supportive care measures to mitigate side effects. Recent clinical studies indicate that colesevelam, a bile acid binder, efficiently reduces gastrointestinal symptoms associated with lenalidomide medication, thereby improving patient quality of life.

By managing medication-related side effects like diarrhea and life-threatening complications like electrolyte imbalance, healthcare practitioners can help patients adhere to long-term treatment regimens, eventually improving clinical results and sustaining lenalidomide's therapeutic advantages. This paper emphasizes the need for a comprehensive strategy for managing multiple myeloma, including pharmaceutical and supportive therapy to promote patient well-being.

Keywords: Multiple Myeloma, Lenalidomide, Maintenance therapy, Colesevelam, Diarrhea, Autologous stem cell transplantation

Introduction

Lenalidomide, a derivative of thalidomide, is classified as an immunomodulatory medication (IMiD). IMiDs have significantly improved the survival outcomes of individuals with multiple myeloma. Lenalidomide, in particular, is now considered the standard of therapy in the newly diagnosed scenario, the maintenance setting following an autologous stem cell transplant, and the relapsed/refractory setting. [1]

Multiple myeloma is a malignancy of plasma cells in the bone marrow that frequently causes bone damage and marrow failure. Individuals over 65 years old with a family history of multiple myeloma and a history of monoclonal gammopathy of unclear significance are more likely to develop multiple

myeloma than those without these characteristics. Bone pain, renal dysfunction, bone loss, decreased immunity, and anemia are some of the most prevalent consequences of multiple myeloma. [2] We diagnosed our patient with multiple myeloma, with initial extramedulary presentation, at the very young age of 51, which is earlier than the average onset, as most cases occur in persons over 65.

Lenalidomide, a second-generation immunomodulatory drug, effectively treats multiple myeloma (MM). This medicine treats multiple myeloma by altering the levels of vascular endothelial growth factor, interleukin-6, cytochrome c, caspase-8, immunological modulation, and direct cell killing. Combining lenalidomide with additional drugs, such as dexamethasone, bortezomib, ixazomib, carfilzomib, and daratumumab, can significantly improve MM. [3]

The aim of this case study is to demonstrate the complex management of multiple myeloma in a patient receiving long-term maintenance with lenalidomide medication, highlighting the significance of customized treatment options and ongoing monitoring. It aims to highlight lenalidomide's therapeutic advantages in maintaining remission and managing disease recurrence, as well as the difficulties presented by treatment-related side effects, notably gastrointestinal disorders such as diarrhea.

The purpose of this research is to show that colesevelam is beneficial in treating lenalidomide-induced diarrhea and enhances the patient's quality of life and treatment adherence. Furthermore, it emphasizes the importance of a comprehensive strategy that includes supportive care and continuous follow-up to improve patient outcomes in the setting of hematological malignancies.

Case Presentation

A 54-year-old female patient, has been receiving therapy for immunoglobulin G (IgG) type multiple myeloma since April 2015. She has a family history of breast cancer but no major personal health history.

A pathohistological study of a biopsy from a destructive tumor in the vertebral body at the Th9 level led to the diagnosis of multiple myeloma. The treatment began with four rounds of VTD chemotherapy (Velcade , Thalidomide, and Dexamethasone), followed by 16 Gy of radiation. By October 2015, the patient had achieved full remission, prompting an autologous stem cell transplant (ASCT) with cryopreserved hematopoietic stem cells. We put her on Velcade maintenance medication for two years after the transplant, with regular monitoring for recurrence.

In September 2018, the patient showed signs of an illness recurrence. We switched her therapy to the VRD regimen (Velcade, Revlimid (Lenalidomide), Dexamethasone) in response to the recurrence. After four cycles, she achieved a full response, as evidenced by laboratory testing and clinical evaluation.

From January 22 to February 20, 2019, the patient underwent hospitalization due to overall weakness, malaise, and less frequent loose stools. The patient had gastrointestinal problems, including diarrhea, most likely as a result of her chemotherapy regimen. She got supportive treatment, including anti-diarrheal medicine.

On March 15, 2019, she had a second ASCT after conditioning chemotherapy with 250 mg Melphalan. The post-transplant recovery was easy, with engraftment achieved by day +10.

We performed regular imaging scans to monitor for disease recurrence. A whole-body MRI on April 20, 2022, revealed no focal lesions and normal findings in the brain, cerebellum, and subarachnoid regions. The left shoulder's subacromial bursa showed fluid buildup, but the skeletal system showed no signs of metabolic activity.

A cervical spine MRI indicated a disc herniation at the C5/6 level but no new lesions related to her myeloma. As part of additional laboratory tests, we performed serum protein electrophoresis on March 7, 2023, and the results were as follows: Total protein: 73.2 g/L (reference range: 60.3–72.8 g/L), albumin: 59.0% (reference range: 43.2–56.0 g/L), and gamma globulin: 15.3% (reference range: 6.2–15.4 g/L). The findings showed the presence of paraprotein in the gamma zone, necessitating further immunofixation investigation.

On May 8, 2023, immunofixation revealed a slightly positive IgG-Lambda paraprotein. We recommended repeating the test in three months to monitor her myeloma status continuously.

During this time period, a PET/CT scan revealed enhanced metabolic activity in the enlarged palatine tonsils (SUVmax 7.3) and metabolically active lymphatic tissue in the left cervical area (SUVmax 4.8). Importantly, there was no evidence of metabolically active localized lesions in the lungs or abdomen.

The current clinical and laboratory findings likely classify our patient as R-ISS Stage II (moderate risk) for multiple myeloma. The patient's serum albumin levels were normal, and there were no signs of kidney damage or high-risk chromosomal abnormalities. However, the presence of a slightly positive IgG-Lambda paraprotein showed that the myeloma is still active.

Furthermore, imaging revealed no focal lesions, but the patient suffered a compression fracture, suggesting a higher disease load. In the absence of significant risk factors, such as higher β2-microglobulin levels or high-risk chromosomal abnormalities, Stage II appears to be the most acceptable classification at this point. Continuous monitoring and further testing, such as β2-microglobulin and genetic assessments, are necessary to improve her prognosis and inform treatment options.

As of the most recent follow-up, the patient is still in remission, with continuous maintenance that includes routine anti-infective prophylaxis and monitoring for late effects of medication.

We have encouraged her to maintain a suitable hygiene and food regimen, and we have scheduled frequent check-ups for her. This example exemplifies the complexity of managing multiple myeloma, emphasizing the importance of personalized treatment protocols, continuous monitoring, and supportive care to manage side effects, particularly gastrointestinal disorders like diarrhea. The patient's journey emphasizes the importance of a holistic care strategy in the treatment of hematologic malignancies.

Discussion

Researchers found that colesevelam, a bile acid binder, dramatically reduced gastrointestinal symptoms in a study to assess the efficacy of treating lenalidomide-induced diarrhea in multiple myeloma patients. The study included 25 individuals who had grade 1 or greater diarrhea while using lenalidomide maintenance treatment.

After 12 weeks of colesevelam medication, 88% of patients reported a decrease in diarrhea intensity, with 68% experiencing full remission. The study also showed that colesevelam did not interact with lenalidomide's pharmacokinetics, preserving the medication's therapeutic advantages. Patient-reported outcomes showed significant improvements in gastrointestinal symptoms and overall quality of life after colesevelam treatment, with few side events recorded.

These data demonstrate that colesevelam is an effective therapy for lenalidomide-related diarrhea, allowing patients to continue their medication while improving their quality of life. This study is especially important for situations where gastrointestinal side effects complicate continuous treatment. [4]

Another study observed 22 people with multiple myeloma who were getting continuous lenalidomide maintenance therapy. They were interviewed at a specialized cancer clinic in London for a study that looked at their qualitative experiences. Four main themes came out of the interviews.

The findings revealed patients' varying perceptions of lenalidomide's function, with many expressing thankfulness for the medication as a way to ease relapse anxieties and restore a feeling of normalcy in their lives. However, the study found substantial disparities in side effects across age groups, with younger patients reporting tolerable symptoms and older patients with comorbidities experiencing a larger symptom load, which occasionally led to treatment cessation. [5]

The effectiveness and safety of lenalidomide in treating multiple myeloma (MM) were studied by looking at all the data from seven randomized controlled trials, which included 2,357 patients. The results showed that treatments with lenalidomide had much higher overall response rates and progression-free survival rates than treatments without lenalidomide, especially in MM patients who had relapsed or failed previous treatments.

Notably, whereas lenalidomide maintenance treatment after autologous stem cell transplantation (ASCT) increased progression-free survival, it did not significantly improve overall survival. These results show that lenalidomide has the potential to be an important part of MM therapy. They also show that more research is needed to look into safety issues, especially the chance of side effects and secondary primary cancers. [6]

Adverse reactions associated with lenalidomide include myelosuppression (primarily neutropenia but also thrombocytopenia), gastrointestinal issues, skin eruptions, atrial fibrillation, asthenia, decreased peripheral blood stem cell yield during stem cell collection, venous thromboembolism, and secondary malignancies in long time treatment. [7] In addition to experiencing

reduced movement, our patient also developed neuropathy, which is a common adverse effect of the medications prescribed to them.

An analog of thalidomide, lenalidomide is an immunomodulatory drug that has strong anticancer and antiangiogenic properties that affect the growth of new blood vessels, inflammation, and the immune system. Following oral administration, it readily absorbs, has a half-life of 3 hours, and excretes 67% unchanged in urine; people with renal impairment require dose changes.

Lenalidomide, available in various capsule strengths, has been associated with negative outcomes like deep venous thrombosis, severe myelosuppression, and potential birth abnormalities, rendering it unsuitable for use during pregnancy. It can interact with other medications, most notably boosting digoxin levels and increasing the thrombogenic effects of dexamethasone. Clinical practice uses lenalidomide to treat multiple myeloma, especially when combined with dexamethasone, and has demonstrated effectiveness in treating chronic lymphocytic leukemia and myelodysplastic syndromes with 5q deletions. [8]

Research conducted to investigate the influence of lenalidomide on thrombotic events in newly diagnosed multiple myeloma (NDMM) patients revealed crucial data about its effects on venous thrombosis and coagulation markers. A cohort of patients on a VRD regimen extensively used thromboprophylactic treatments, yet thrombotic events persisted.These findings emphasize the need to carefully select thromboprophylactic treatments for MM patients. [9]

A further analysis investigated DVT in lenalidomide-treated newly diagnosed multiple myeloma (MM) patients. They discovered an 8% thromboembolic risk. Inflammation and abnormal fibrin structure have long been known to produce thromboembolic events in MM. MM had lower thrombosis rates than other cancers, but thalidomide raised awareness of venous thromboembolism. These results make thromboprophylaxis even more important and show that aspirin may lower the risk of thrombotic events while on lenalidomide, which calls for more research. [10]

In another study examined thromboembolic events in newly diagnosed multiple myeloma patients using VRD from January 2013 to June 2021. Eight patients had TEs, including 7 DVTs and 1 PE. Two patients did not receive thromboprophylaxis due to low platelet counts, while the other six were on aspirin, warfarin, and rivaroxaban.The study revealed lenalidomide substantially altered coagulation markers.

After one cycle of lenalidomide, prothrombin and thrombin times changed significantly. No significant effect on platelet function was seen. These data imply that lenalidomide may induce venous thrombosis through coagulation pathway changes rather than platelet impacts. The study suggests that anticoagulant medicines may be better than antiplatelet treatments for thrombus prevention in multiple myeloma patients. [11]

Conclusion

In conclusion, this case report emphasizes the importance of lenalidomide in the long-term management of multiple myeloma by demonstrating its efficacy in sustaining remission and addressing disease recurrence.

The use of colesevelam as a supportive medication offers an achievable approach to reducing treatment-related side effects, particularly diarrhea and its life-threatening complications like electrolyte imbalance and cardiovascular complications, which can have a major influence on patient quality of life.

Continuous monitoring and a targeted care approach are required to maximize results and improve the overall well-being of individuals with multiple myeloma. This instance shows the importance of a holistic strategy for handling complicated hematological diseases.

References

1. Holstein SA, Suman VJ, McCarthy PL. Update on the role of lenalidomide in patients with multiple myeloma. Therapeutic Advances in Hematology [Internet]. 2018 May 26 [cited 2024 Oct 20];9(7):175–90. Available from: https://journals.sagepub.com/doi/pdf/10.1177/2040620718775629
2. Raedler LA. Revlimid (Lenalidomide) Now FDA Approved as First-Line Therapy for Patients with Multiple Myeloma. American Health & Drug Benefits [Internet]. 2016 Mar [cited 2024 Oct 20];9(Spec Feature):140. Available from: https://pmc.ncbi.nlm.nih.gov/articles/PMC5013840/
3. Zhang CW, Wang YN, Ge XL. Lenalidomide use in multiple myeloma (Review). Molecular and Clinical Oncology. 2023 Nov 28;20(1).
4. Hultcrantz M, Hassoun H, Korde N, MacLachlan K, Mailankody S, Patel D, et al. Colesevelam for lenalidomide associated diarrhea in patients with multiple myeloma. Blood Cancer Journal. 2024 Sep 19;14(1).
5. Buck C, Francisco Brenes Castillo, Bettio E, Land J, McCourt O, Poole H, et al. The impact of continuous lenalidomide maintenance treatment on people living with multiple myeloma—a single-centre, qualitative service evaluation study. Supportive Care in Cancer [Internet]. 2024 Jul 1 [cited 2024 Aug 28];32(7). Available from: https://link.springer.com/article/10.1007/s00520-024-08663-4#citeas
6. Qiao SK, Guo XN, Ren JH, Ren HY. Efficacy and Safety of Lenalidomide in the Treatment of Multiple Myeloma. Chinese Medical Journal. 2015 May;128(9):1215–22.
7. Imbesi S, Allegra A, Calapai G, Musolino C, Gangemi S. Cutaneous adverse reactions to lenalidomide. Allergologia et Immunopathologia [Internet]. 2015 Jan [cited 2024 Oct 20];43(1):88–91. Available from: https://www.sciencedirect.com/science/article/pii/S0301054613002322
8. Hoffman R, J E, Silberstein LE, Heslop HE, Weitz JI, Anastasi J, et al. Hematology : basic principles and practice. 7th ed. Philadelphia, Pa: Elsevier; 2018.
9. Li P, Xu B, Xu J, Xu Y, Wang Y, Chen C, et al. Lenalidomide Promotes Thrombosis Formation, but Does Not Affect Platelet Activation in Multiple Myeloma. International journal of molecular sciences [Internet]. 2023 Sep 14 [cited 2024 May 9];24(18):14097–7. Available from: https://pmc.ncbi.nlm.nih.gov/articles/PMC10532040/
10. Menon SP, Rajkumar SV, Lacy M, Falco P, Palumbo A. Thromboembolic events with lenalidomide-based therapy for multiple myeloma. Cancer [Internet]. 2008 [cited 2020 Jul 1];112(7):1522–8. Available from: https://pmc.ncbi.nlm.nih.gov/articles/PMC2614405/
11. Li P, Xu B, Xu J, Wang Y, Xu Y, Chen C, et al. The Mechanism Underlying Lenalidomide-Induced Thrombosis Susceptibility. Blood [Internet]. 2023 Nov 28 [cited 2024 Feb 15];142(Supplement 1):6505–5. Available from: https://ashpublications.org/blood/article/142/Supplement%201/6505/505495/The-Mechanism-Underlying-Lenalidomide-Induced