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Case Report

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Can bispecific antibody therapies for multiple myeloma be a risk factor for the development of secondary haemotopoietic malignancy? A case report

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ABSTRACT

With the introduction of many new treatments in multiple myeloma and the effective use of autologous stem cell transplantation, significant prolongation of overall survival has been achieved. Despite this, there is still no cure for this disease. Relapsed/refractory conditions seen after multiple treatments have brought the use of new agents to the agenda. Elranatamab is a humanized bispecific antibody used in relapsed or refractory multiple myeloma which targets B-cell maturation antigen on myeloma cells and CD3 on T cells . With this mechanism, elranatamab could activate T cells to induce cytotoxic T-cell response against myeloma cells. Although we have an idea and experience about the short-term adverse effect profile and management, our ideas about the long-term adverse effect and safety profile are not yet clear due to the fact that it is a very new agent. We described an unexpected hematologic event during the use of elranatamab in the following case.

Keywords: Multiple myeloma, bispecific antibodies, haemotopoietic malignancy

INTRODUCTION

With the introduction of many new treatments in multiple myeloma and the effective use of autologous stem cell transplantation, significant prolongation of overall survival has been achieved. Despite the introduction of novel agents, there is still no cure for this disease. Relapsed/refractory conditions seen after multiple treatments have brought the use of new agents to the agenda. Elranatamab, a humanized bispecific antibody utilized in the treatment of relapsed or refractory multiple myeloma, functions by targeting B-cell maturation antigen (BCMA) on myeloma cells and CD3 on T cells, thereby eliciting a cytotoxic T-cell response against myeloma cells.[1] Despite our familiarity with the short-term adverse effect profile and management strategies associated with its use, the long-term adverse effects and safety profile of elranatamab remain uncertain due to its recent introduction as a therapeutic agent. Herein, we present a case detailing an unexpected hematologic event observed during elranatamab therapy, emphasizing the importance of ongoing surveillance and comprehensive understanding of its safety profile in clinical practice.

CASE

Born in 1947, female patient received radiotherapy (RT) for solitary plasmacytoma in the posterior right costal region in 2008.

In 2011, the patient received radiotherapy for a symptomatic plasmacytoma in the left thigh. Subsequent follow-up revealed a bone marrow biopsy compatible with lambda light chain predominant myeloma. The patient underwent four cycles of VAD (vincristine, adriamycin, and dexamethasone) but declined autologous Hematopoietic Stem Cell Transplantation (AHSCT). She was treated with thalidomide monotherapy for three years until 2017, when she experienced recurrence with bone plasmacytomas and associated fractures in 2017 and 2018.

During further follow-up, due to progressive myeloma, the patient was treated with VCD (bortezomib, cyclophosphamide, and dexamethasone) combination. Subsequent follow-up positron emission tomography-computed tomography (PET-CT) scans revealed new lytic lesions in the skeletal system, prompting treatment with ixazomib, cyclophosphamide, and dexamethasone. Daratumumab, bortezomib, and dexamethasone therapy was initiated following routine myeloma laboratory analyses that indicated a biochemical recurrence. The patient had progressed in 2023 and could have an access to elranatamab with the early compassionate access program.

Following six cycles of elranatamab treatment, the patient's PET-CT scan and myeloma laboratory analyses indicated

complete remission. To assess the occurrence of anemia, a bone marrow aspiration and biopsy were performed after ten cycles of elranatamab treatment. The trephine biopsy revealed diffuse dyshematopoiesis and a hypercellular bone marrow with an increase in reticulin fibers. Young-blastic morphologic cell increase with patchy-interstitial distribution was reported. The patient exhibited a moderately increased ratio of CD34 (+) precursor cells (10%-15%) and CD117 (+) precursor cells (10%-20%). Given these findings, along with the presence of excessive blasts characteristic of myelodysplastic syndrome and transformation to acute myeloid leukemia (MDS related AML), a therapeutic regimen consisting of azacitidine and venetoclax was initiated, taking into account the patient's age and performance status.

DISCUSSION

We conducted a comprehensive evaluation of a patient who developed AML during bispecific antibody therapy for relapsed/refractory myeloma. Despite the patient's history of multiple prior RT treatments, a recognized risk factor for AML development, it is of particular interest that leukemia emerged following completion of ten cycles of elranatamab treatment, coinciding with a period of controlled myeloma. Hematologic AEs related with elranatamab use were frequent anemia (68%; grades 3/4: 43%) and neutropenia (62%; grades 3/4 : 51%) are the most common ones and it's known that these effects are generally manageable with dose reductions or interruptions.[2] BCMA expression has also been identified in AML. Some studies show that BCMA mRNA expression was higher in complete remission versus no response patients.[3]

CONCLUSION

Our case underscores the necessity for a prolonged follow-up period and increased clinical experience to elucidate the potential impact of bispecific antibody therapies like elranatamab on the pathogenesis of AML in the context of myeloma treatment. The emergence of AML in our patient, despite successful control of myeloma, highlights the complexity of disease interactions and the need for vigilant monitoring during novel therapeutic interventions. Further investigation into the long-term effects of such therapies is essential for optimizing treatment strategies and minimizing adverse outcomes in patients with relapsed/refractory myeloma.

ETHICAL DECLARATIONS

Informed Consent

The patient signed the informed consent form.

Referee Evaluation Process

Externally peer-reviewed.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Financial Disclosure

The authors declared that this study has received no financial support.

Author Contributions

All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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