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A Case of Elranatamab Induced Primary Adrenal Insufficiency

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BACKGROUND

Relapsed/refractory multiple myeloma (RRMM) remains a significant therapeutic challenge, particularly in patients exposed to proteasome inhibitors, immunomodulatory agents, and anti-CD38 monoclonal antibodies. B-cell maturation antigen (BCMA)–targeted bispecific antibodies have emerged as an effective treatment option in this setting.

Elranatamab, a BCMA×CD3 bispecific antibody, has demonstrated overall response rates of ~60% in heavily pretreated patients, with a manageable safety profile. However, these agents are associated with immune-mediated toxicities, including cytokine release syndrome (CRS), cytopenias, infections, and potentially rare endocrine complications.

RESULTS

A 42-year-old male with penta-refractory RRMM received elranatamab after six prior lines of therapy. The patient achieved a stringent complete response (sCR) after two cycles, despite aggressive disease features including lytic lesions and plasmacytomas.

During treatment:

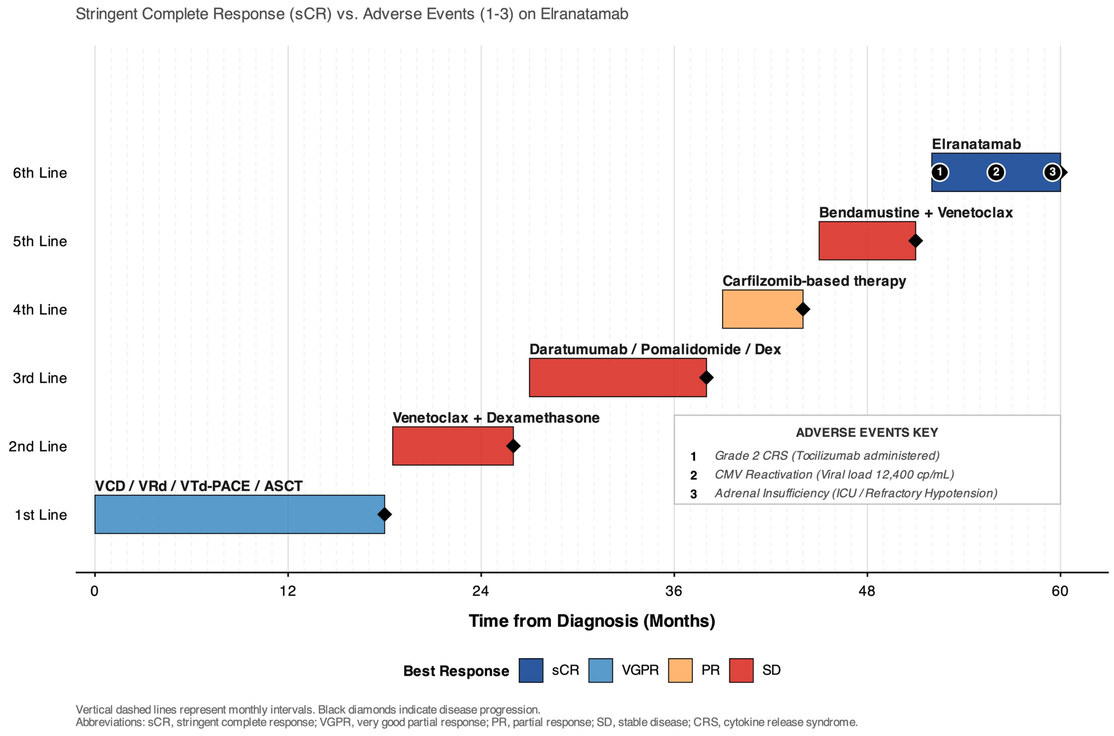
- Cycle 1: Grade 2 CRS occurred during step-up dosing and resolved with tocilizumab.
- Cycle 4: CMV reactivation developed, managed with appropriate antiviral strategies.
- Cycle 9: The patient presented with severe, refractory hypotension requiring ICU admission.

Extensive evaluation excluded septic, cardiogenic, and other common causes of shock. Endocrine work-up revealed:

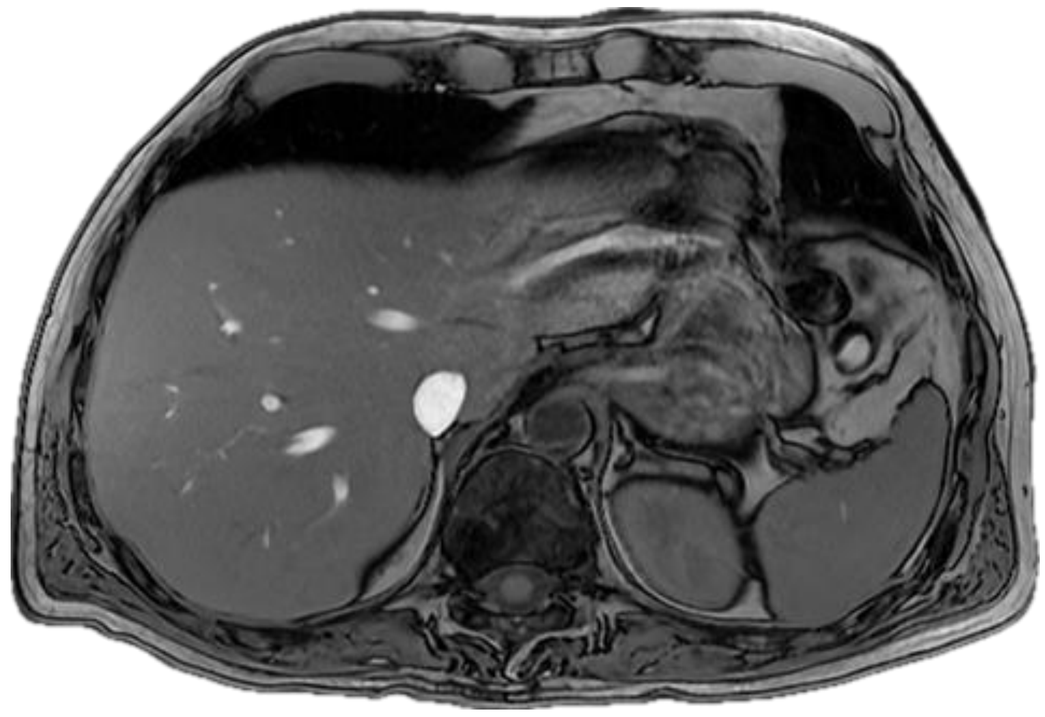
- Low cortisol (3.1 µg/dL)
- Elevated ACTH (530 pg/mL)

Adrenal MRI demonstrated marked bilateral adrenal atrophy. These findings supported a diagnosis of primary adrenal insufficiency, likely immune-mediated. Hemodynamic stability was achieved only after initiation of high-dose corticosteroids, with rapid clinical improvement and discontinuation of inotropic support within 48 hours. Elranatamab was discontinued, and the patient was maintained on physiologic hydrocortisone replacement. Notably, the patient sustained sCR despite treatment cessation.

Figure 1. Longitudinal Clinical Course and Treatment Response



Vertical dashed lines represent monthly intervals. Black diamonds indicate disease progression.
Abbreviations: sCR, stringent complete response; VGPR, very good partial response; PR, partial response; SD, stable disease; CRS, cytokine release syndrome.



CONCLUSION

This case highlights a rare but potentially life-threatening complication of elranatamab therapy—primary adrenal insufficiency, likely due to immune-mediated adrenalitis.

Clinicians should consider adrenal insufficiency in patients receiving bispecific antibodies who present with unexplained hypotension, especially when unresponsive to fluids and vasopressors. Early endocrine evaluation and prompt corticosteroid treatment are critical and may be life-saving.

As BCMA-targeted therapies become more widely used, awareness of atypical immune-related toxicities is essential to optimize patient outcomes while preserving durable responses.

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