SOHO ANNUAL MEETING 2024

Navigating the Nexus: Lenalidomide associated TTP

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INTRODUCTION

Thrombotic thrombocytopenic purpura (TTP) is a life-threatening thrombotic microangiopathy marked by thrombocytopenia, microangiopathic hemolytic anemia, and microvascular thrombosis with multiorgan failure. Commonly due hereditary or acquired ADAMTS13 deficiency, its association with lenalidomide, is notably rare.
We present a case of a 56-year-old male with a history of multiple myeloma, in remission on lenalidomide who developed TTP.

CASE PRESENTATION

We report a case of a 56-year-old male with a history of IgG lambda multiple myeloma, who underwent autologous stem cell transplant and has been on lenalidomide 10mg daily for 5 years. He presented with jaundice, palpitations, and paraesthesia in his extremities, remained stable with otherwise unremarkable physical exam. Laboratory findings revealed hemoglobin of 7 dL, Platelets 3 x 10^3/µL, bilirubin 5 mg/dL, creatinine /g1.03 mg/dL, haptoglobin <8 mg/dl, LDH 498 U/L, and schistocytes on peripheral smear concerning for microangiopathic hemolytic anemia. Critically low ADAMTS13 activity with detectable anti- ADAMTS13 antibodies confirmed the diagnosis. Bone marrow biopsy during his hospitalization showed normocellular marrow with increased atypical immature B cells that could represent an evolving myeloid disorder or simply a reactive/inflammatory state.

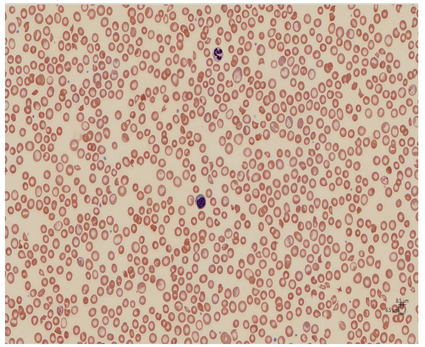
Management and Outcome

Lenalidomide was discontinued. The patient was treated with plasma exchange, high-dose steroids followed by rituximab.

Due to concerns of plasma exchange affecting the efficacy of the rituximab, caplacizumab was initiated. This regimen led to clinical and haematological improvement, with the hemoglobin and platelet levels returning close to normal ranges.

DISCUSSION

Thrombotic Thrombocytopenic Purpura (TTP) is a life-threatening condition with a mortality rate of up to 90% if left untreated. Characterized by microangiopathic hemolytic anemia, thrombocytopenia, and microvascular thrombosis, TTP is driven by a deficiency or dysfunction of the ADAMTS13 enzyme, which can be congenital or more commonly acquired, often due to autoantibodies against ADAMTS13. Lenalidomide, a critical component of multiple myeloma (MM) maintenance therapy, has been associated with rare cases of immune-mediated thrombotic microangiopathy (TMA), including TTP.



Peripheral blood smear with schistocytes

In this case, a MM patient developed TTP with critically low ADAMTS13 activity (<0.03 IU/mL) and detectable inhibitors following lenalidomide treatment. Notably, the patient had no prior history of autoimmune disorders, but a literature review suggests that such disorders might increase the risk of lenalidomide-induced TTP. Reports indicate a potential connection between autoimmune backgrounds and the development of anti-ADAMTS13 antibodies. Despite lenalidomide's rapid renal clearance, thrombocytopenia persisted in our patient, necessitating continued plasma exchange, rituximab, caplacizumab, and prednisone. The therapeutic regimen led to significant hematologic improvement.

CONCLUSION

Evidence is growing in support of an underlying pathophysiology behind lenalidomide and TTP. Providers should be aware of this rare but serious risk and be more vigilant in patients with rheumatological disorders. Prompt recognition and comprehensive treatment are crucial to improving patient outcomes in such cases.

REFERENCES

ACKNOWLEDGEMENTS

Dikélélé Elessa – author of similar case series

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