Rituximab as a Therapeutic Agent for Steroid Refractory Warm Autoimmune Hemolytic Anemia in the Setting of EBV-Post Transplant Lymphoproliferative Disorder

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Introduction

- Autoimmune hemolytic anemia (AIHA) is characterized by autoantibodies against red blood cells. Most cases (65-70%) are of the warm subtype
- Very rarely, it can be a complication in patients who have undergone solid organ transplant, and tends to present early after transplant (within the 1st year)
- ~ 50% of these can be attributed to the use of immunosuppression, infections such as EBV, medications or post-transplant lymphoproliferative disorder (PTLD).
- We describe a case of steroid refractory AIHA treated with Rituximab in a patient with EBV-positive PTLD

	Warm AIHA	Cold AIHA
Mechanism	IgG and complement mediated	IgM and complement mediated
Causes	Lymphoproliferative disorder Autoimmune disorders (ie SLE) EBV, HIV, HepC	Lymphoproliferative disorder Mycoplasma, EBV
Coombs test	Coombs positive for IgG +/- C3	Coombs positive for C3 only

Case Presentation

- A 70-year-old F with PMH of renal transplant on Tacrolimus, polymorphic EBV-positive PTLD diagnosed via left axillary lymph node biopsy presented to the hospital with increasing malaise and lightheadedness
- Labwork was significant for a Hb of 3.3 g/dL. Hemolysis labs were positive with LDH 763 U/L, haptoglobin <10 mg/dL, absolute reticulocyte counts 0.186 m/mcL
- Coombs test was positive with direct antiglobulin test IgG 4+ and direct antiglobulin test C3 1+ consistent with Warm AIHA. EBV DNA polymerase chain reaction (PCR) was positive.
- CTAP showed lymphadenopathy near the upper pole of the right transplanted kidney and the small bowel mesentery.
- She was initiated on methylprednisolone 1mg/kg and prednisone 60 mg daily. After 8 days of treatment, her hemolysis did not improve as shown in Figure 1 and 2.
- Given refractoriness to steroids and concerns for worsening immunosuppression in the setting of PTLD from steroids, she was started on Rituximab IV 375 mg/m^2 weekly for a total of 4 weeks. She subsequently received consolidation Rituximab thereafter 375 mg/m2 every 21 days for 4 cycles.
- She showed good clinical response with improvement of her symptoms and resolution of hemolysis.

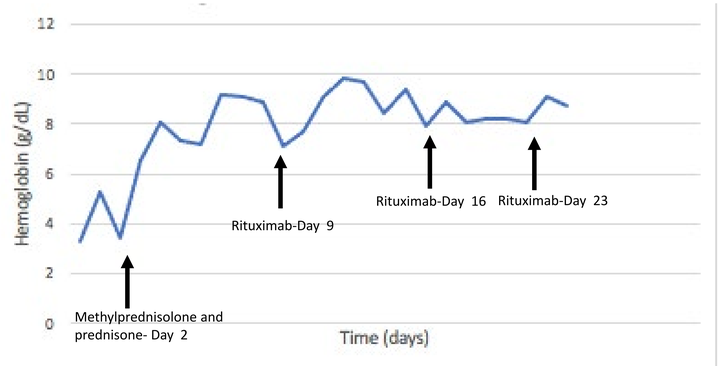

Figure 1: Hemoglobin trend with treatment for AIHA

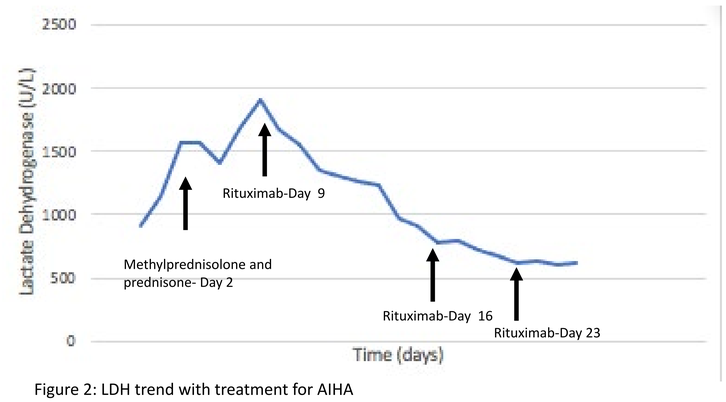

Figure 2: LDH trend with treatment for AIHA

Discussion/Conclusion

- The case is a rare example of association of warm AIHA in patient with EBV PTLD, 10 years after kidney transplant.
- 1st line therapy for warm AIHA includes corticosteroids, usually prednisone, until Hb and hemolysis improves which is usually seen during the 2nd-3rd week of therapy. Second line treatment includes Rituximab, a monoclonal antibody directed against CD20 on B cells
- Our case highlights the importance of considering alternate treatments to steroids such as Rituximab in this patient population, given concerns of worsening PTLD with steroid induced immunosuppression. Additionally, Rituximab having therapeutic benefit for PTLD may make this a favorable alternate.

References

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