Resolution of Nephrotic Syndrome Following Rituximab Therapy in a Patient Undergoing Immune Tolerance Induction

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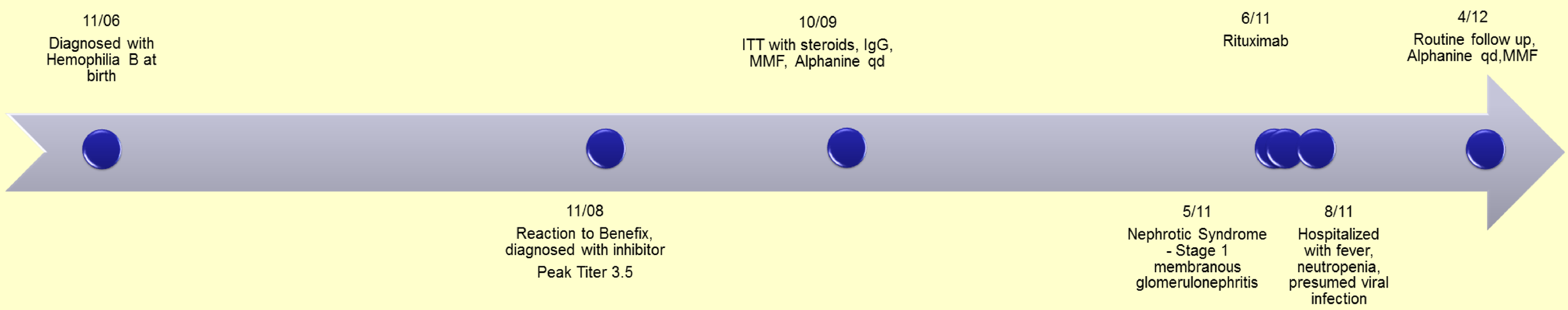
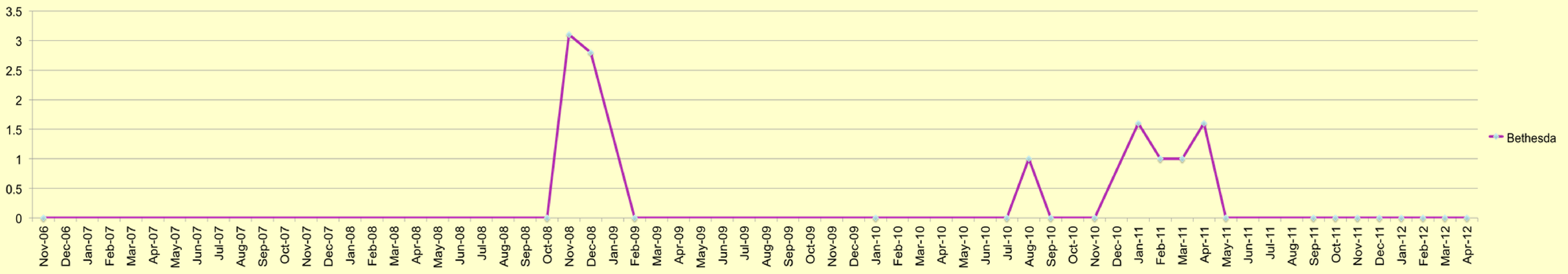
Introduction

Inhibitors develop in approximately 1.5-3% of hemophilia B patients. Immune tolerance induction (ITI) in these patients is often unsuccessful. Anaphylactic reactions and nephrotic syndrome are complications associated with inhibitors to factor IX.

Case Presentation

Our patient was diagnosed with severe Hemophilia B at birth, secondary to a family history of severe factor IX deficiency, with high titer inhibitors and anaphylaxis. Following 5 doses of on demand recombinant factor IX our patient developed anaphylactic reactions and was found to have an inhibitor (maximum titer 3.1BU). ITI was initiated using Alphanine (200 U/kg/day), as well as mycophenolate mofetil (MMF), immunoglobulin (IGG) and steroids. Treatment was well tolerated and his inhibitor and reactions to factor infusions resolved. With apparent successful ITI, the IGG and steroids were discontinued. Attempts to decrease his MMF and/or Alphanine resulted in small increases in inhibitor titer (1-2 BU) and recurrence of intermittent mild reactions to factor infusions. After 18 months of ITI, he developed proteinuria with a significant decrease in serum albumin. Renal biopsy revealed stage I membranous glomerulonephritis consistent with an immune complex mediated process. Following his biopsy, ITI was continued and rituximab was added. With the addition of rituximab he had prompt resolution of the nephrotic syndrome and renal function returned to baseline. He has been closely monitored for over 12 months without recurrence of his nephrotic syndrome.





Conclusion

Information on ITI in severe Hemophilia B patients is limited. When ITI is attempted response may be poor and the risk of nephrotic syndrome is a concern. With development of nephrotic syndrome, the standard of care has been to discontinue ITI due to concern for irreversible renal damage. This case highlights the importance of close monitoring for this complication and the potential for successful resolution of nephrotic syndrome and control of the inhibitor with more aggressive immune modulation.

References

Text

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