Rituximab for the management of Factor VIII Deficiency in a Patient Requiring Surgical Intervention

Jessica Tan and Sarah Fotheringham
Department of Pharmacy Eastern Health

Objective: To report on the use of rituximab as a single agent for management of acquired haemophilia, secondary to Factor VIII deficiency, in a patient requiring pacemaker insertion.

Presentation: An 86 year old European female presented following multiple syncopal episodes due to slow atrial fibrillation. Cardiology opinion deemed pacemaker insertion was required. Factor VIII deficiency puts the patient at risk of significant bleeding during pacemaker insertion. Options were sought to prevent bleeding prior to pacemaker insertion.

Past medical history:
- Atrial fibrillation
- Hypertension
- Meningioma
- bilateral small vessel cerebral ischaemia
- renal impairment; and
- acquired haemophilia due to antibodies to factor VIII.

Acquired Haemophilia:
Factor VIII deficiency may be caused by inhibitors directed against the clotting factors. This leads to acquired haemophilia and may result in major bleeding episodes and is associated with significant morbidity. Around 18% of cases of acquired haemophilia are thought to be secondary to autoimmune disorders.

The aim of treatment of acquired haemophilia is to eliminate Factor VIII autoantibodies which act as inhibitors of the clotting factor. Many of the current treatment options, which include immunosuppressants such as cyclophosphamide or prednisolone, comes with a wide array of undesirable adverse effects. Moreover, it is often a slow process and requires a prolonged treatment period.

Rituximab is an anti-CD20 monoclonal antibody that depletes B cells to eradicate Factor VIII inhibitors. Several case studies of rituximab 375mg/m² (for 4 doses) being used either as monotherapy or part of a combination therapy for the treatment of haemophilia have been reported. Repeat treatments with rituximab for relapsed patients have also been shown to result in remission.

Interventions, case progress and outcomes:
Although treatment with rituximab is costly, the use of haemolytic agents in the treatment of bleeding episodes may result in much higher expenses. In 2008, the average cost of resolution of a single bleeding episode requiring hospitalisation can be as much as $US32,150² (~$AUD42,000, at November 2016 exchange rates) as opposed to rituximab therapy for inhibitor eradication which would have a cost associated of approximately $AUD 15,000 ². Haematology opinion was sought to identify opportunities to mitigate risk of haemorrhage in preparation for pacemaker insertion.

Rituximab recommended the monoclonal antibody rituximab based on case reports²,³ of activity against Factor VIII antibodies and the potential for a longer duration of action compared to epotacog alfa (NovoSeven™). A non-formulary approval was sought and pharmacy performed a literature review. Published case series, including reports of rituximab leading to cure to acquired antibodies to factor VIII, provided supportive evidence for this indication²,³,⁴. The request for rituximab was approved.

A dose of 680mg was calculated using 375mg/m² and administered once each week for four weeks. After four doses, the patient’s factor VIII levels (113%) were within normal range (60-150%) and pacemaker insertion occurred without surgical complication.

Six months following rituximab therapy and pacemaker insertion, activated partial thromboplastin time (APTT) remained within normal range (35; 24-40).

Haematology review is planned for December 2016 to review long term benefit of rituximab.

Conclusions:
Rituximab was successfully used to prevent significant bleeding during PPM insertion for a patient with acquired haemophilia due to factor VIII deficiency.

References:

Contact Details:
For more information please contact Jessica Tan on jessica.tan@easternhealth.org.au

www.easternhealth.org.au