Rituximab as the monotherapy management of Multiple Sclerosis and Ankylosing Spondylitis: A case report

Anna Mejia (Le)
Clinical Pharmacist, Department of Pharmacy Eastern Health

Objective

To describe the management of severe relapsing-remitting multiple sclerosis (MS) using rituximab in a patient with ankylosing spondylitis (AS).

Background

AS is a chronic inflammatory disease that predominantly affects the axial skeleton (*figure 1).* Rituximab is a monoclonal antibody, which selectively targets and depletes B lymphocytes and is used to treat several autoimmune diseases. B cell depletion occurs via several pathways, including complement mediated cell lysis, growth arrest, and B cell apoptosis (*figure 3*).[1] Efficacy of rituximab in AS patients has been examined in several reports and has shown to be an effective therapy.[2] Rituximab has therefore been suggested as an alternate treatment in patients who fail to respond or are intolerant of other therapies.[1,2]

MS is an inflammatory demyelinating disease of the central nervous system (*figure 2).* It is one of the main causes of acquired neurologic disability in young adults.[3] There is increasing evidence that B lymphocytes are involved in the pathogenesis of MS, in conjunction with various external factors.[4] There has been case reports of new onset demyelinating disease that developed in association with the use of Etanercept.[5]

A phase 1, open-label, multicentre study and a randomised double-blind placebo controlled study investigated the use of rituximab in the management of MS which showed reduced inflammatory brain lesions and clinical relapses at varying lengths of time.[6, 7]

Figure 1: Pathophysiology of Ankylosing spondylitis

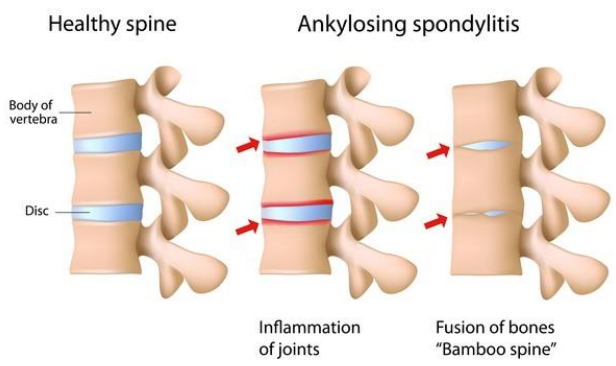
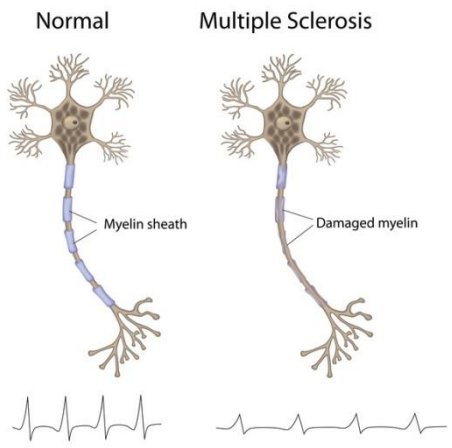


Figure 2: Pathophysiology of Multiple Sclerosis



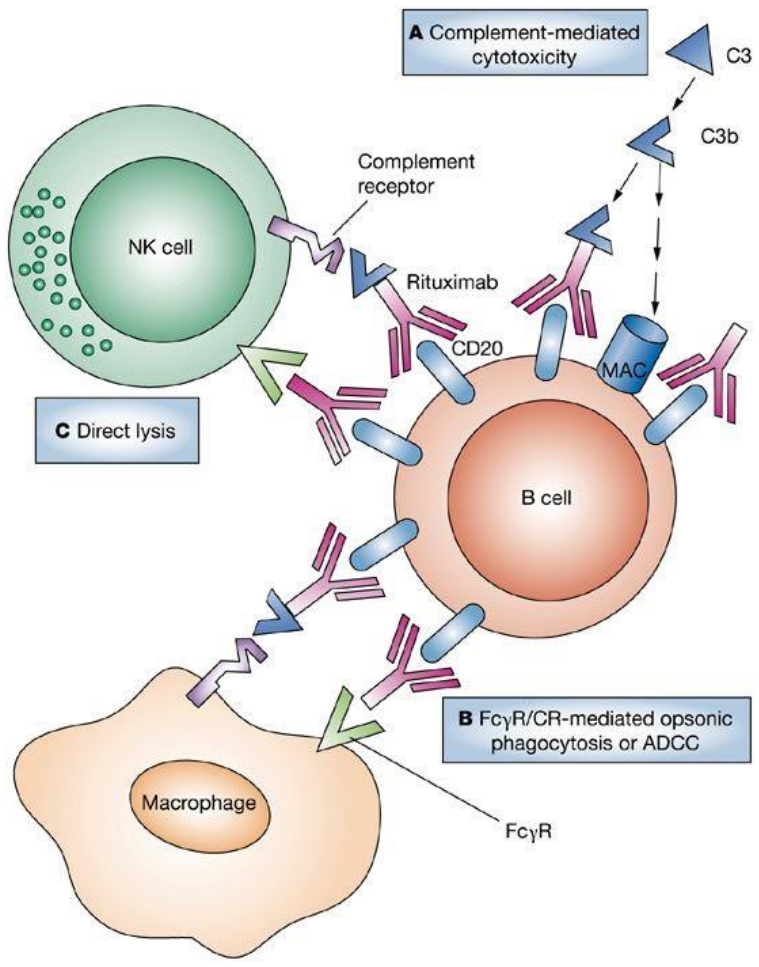
Clinical features

A 43-year-old Caucasian male was admitted to hospital in early 2017 due to progressive weakness, bladder dysfunction, limb neuropathy and balance concerns which were affecting his quality of life. The patient has a past medical history of AS *(table 1)* and developed MS secondary to etanercept. Etanercept was ceased and further TNF-alpha inhibitors were deemed contraindicated. He failed to respond adequately to methylprednisolone, methotrexate or dimethyl fumarate *(figure 4).*

Table 1: Past Medical History and Current Medications

Medication Name and Strength	Dose and Frequency	Indication
Methotrexate 10mg	One tablet orally once weekly on Mondays	MS and AS
Folic acid 5mg	One tablet orally daily (except Mondays)	Prevention of methotrexate adverse effects
Oxybutynin 5mg	Half (2.5mg) a tablet orally twice daily	Urinary incontinence secondary to MS
Diclofenac 25mg	One tablet orally daily	AS related pain
Temazepam 10mg	One tablet orally nocte PRN	Sleep
No other medical conditions **Allergies/ Adverse reactions:** TNF – alpha inhibitors (contraindicated – MS)		

Figure 3: Mechanism of action of Rituximab



Taylor RP *et al. Nat Clin Pract Rheumatol. 2007; 3(2):86 - 95*

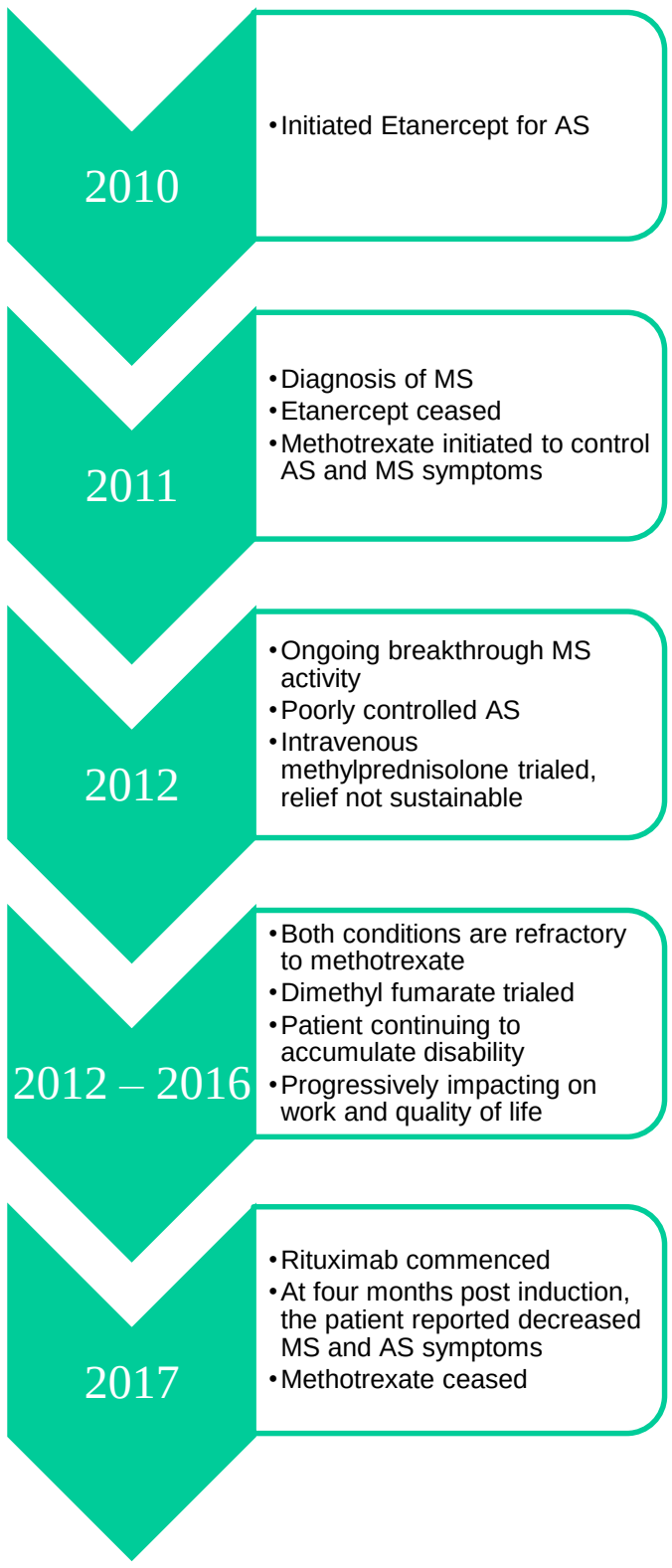
Interventions, case progress and outcomes

For simplicity and to minimise the risk of adverse effects, monotherapy for both indications (MS and AS) was desirable. The patient's high JC virus level contraindicated the use of natalizumab[8] and alternative agents for MS such as fingolimod and teriflunomide would not have been effective in managing his AS. In collaboration with the rheumatology team, it was decided to commence rituximab for the management of both conditions.

Rituximab therapy involved induction with 1g intravenously on days 0 and 14 followed by 6 monthly maintenance therapy.

Over the following nine months, symptoms for both conditions decreased, there were no adverse effects reported and methotrexate was reduced to 5mg weekly and subsequently ceased *(figure 4).*

Figure 4: Timeline of events



Conclusion

Rituximab induction was successful in managing symptoms of MS and AS. There is great potential for it to be used in a similar setting. However, long term efficacy and safety of rituximab in this context remains unknown. Therefore, more research in this area would be beneficial.

References

1) Smith JA. Update on ankylosing spondylitis: Current concepts in pathogenesis. Curr Allergy Asthma Rep. 2015;15(1):489.

2) Rodriguez-Escalera C, Fernández-Nebro A. The use of rituximab to treat a patient with ankylosing spondylitis and hepatitis B. Rheumatology. 2008;47(11):1732–33.

3) Atlas: Country resources for neurological disorders 2004. Geneva, World Health Organization, 2004.

4) Duddy M, Niino M, Adatia F, et al. Distinct effector cytokine profiles of memory and naïve human B cell subsets and implication in multiple sclerosis. J Immunol 2007; 178: 6092 – 9.

5) Desai SB, Furst DE. Problems encountered during anti-tumor necrosis factor therapy. Best practice & Research Rheumatology. 2006; 20 (4): 757 – 790.

6) Hauser SL, Arnold DL, Fox RJ, et al. B – Cell Depletion with Rituximab in Relapsing- Remitting Multiple Sclerosis. N Engl J Med 2008; 358: 676 – 88.

7) Bar-Or A, Arnold D, Shafer S, et al. Rituximab in Relapsing-Remitting Multiple Sclerosis: A 72- Week, Open-Label, Phase 1 Trial. Ann Neurol 2008; 63: 395 – 400.

8) Kappos L, Bates D, Edan G, et al. Natalizumab treatment for multiple sclerosis: updated recommendations for patient selection and monitoring. Lancet Neurol 2011; 10: 745 – 58.

Contact details

For more information please contact Anna Mejia (Le) on anna.le@easternhealth.org.au