Clinical Commentary: Late-onset neutropenia and neurological relapse during long-term rituximab therapy in MOG-antibody spectrum disorder

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Rituximab is an anti-CD20 chimeric monoclonal antibody that depletes B-cells. Although initially developed as a treatment for haematological malignancies, rituximab is now frequently used in patients with autoimmune disorders, including inflammatory disorders of the central nervous system (CNS) associated with aquaporin-4 (AQP4)[1] and myelin oligodendrocyte glycoprotein (MOG) antibodies[2], and multiple sclerosis[3].

Biotti et al describe two patients with relapsing MOG-antibody associated disease who were treated with rituximab and developed late-onset neutropenia – a recognised complication of rituximab seen in both patients with cancer and autoimmune disease.[4] Both patients presented with fever and grade 4 neutropenia (absolute neutrophil count < <0.5 x 10^9/L) several months after the last cycle of rituximab, requiring treatment with antibiotics and granulocyte-colony stimulating factor (G-CSF). Neutropenia recurred in one patient three months later, requiring further treatment with G-CSF. MRI-confirmed relapses occurred in both patients during episodes of neutropenia, despite adequate B-cell depletion with undetectable CD19 lymphocyte counts. One patient continued treatment with rituximab after resolution of the neutropenia, and the other patient was started on tocilizumab.

The cases presented highlight two important clinical issues. Firstly, neurologists treating patients with neuroinflammatory disorders with B-cell depleting agents need to be aware of late-onset neutropenia. Although this complication is less common in the setting of autoimmune diseases than in patients with haematological malignancies[4], severe (grade 3/4) neutropenia can occur and increases the risk of infections. Febrile neutropenia is a medical emergency requiring urgent treatment with antibiotics and possibly G-CSF. Whether patients with late-onset neutropenia should continue treatment with rituximab is unclear. It may be possible to re-treat safely[4], although enhanced full blood count monitoring should be considered. Secondly, these cases add to other recent reports of ongoing relapses in MOG-

antibody disease patients treated with rituximab[2]. Whether treatment failure in this setting is due to existing antibody-producing cells in the CNS despite peripheral B cell depletion, B-cell independent pathobiological mechanisms important in the pathogenesis of MOG-antibody associated diseases, or both is unclear. A better understanding of the neuroimmunologicial basis of MOG-antibody associated disease is required to develop more targeted treatment strategies.

References

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