**Non fatal PML after rituximab in a patient with GPA**

Granulomatosis polyangiitis (GPA) and microscopic polyangiitis (MPA) are ANCA–related vasculitides characterized by inflammation of small- to medium-sized vessels. Until recently, induction therapy consisted of high dose corticosteroids and cyclophosphamide, followed by maintenance therapy with azathioprine or methotrexate. Rituximab is an anti-CD20 B-cell–targeted therapy, which in 2011 was FDA-approved for induction of disease remission in patients with GPA and MPA. It is now being used increasingly for both induction and maintenance, and may be more effective as an induction agent in relapsing patients and those with PR3-ANCA..

Progressive multifocal leukoencephalopathy (PML) is a rare but often fatal demyelinating disease of the central nervous system, resulting from the infection of glial cells by the John Cunningham polyomavirus (JCV). Although JCV is highly prevalent in the general population, PML is extremely rare in immunocompetent individuals. However, patients treated with immunosuppressive or immunomodulatory therapy are at higher risk, with the highest incidence associated with use of Natalizumab. Cases of PML have been reported in patients treated with Rituximab for autoimmune disease. To date there are two reported cases of patients developing PML after treatment with Rituximab for GPA.

We present a third case of a patient who developed PML after receiving Rituximab for treatment of GPA. This patient presented at the age of 68 with a 3-month history of fevers, night sweats and weight loss. He also reported cough and breathlessness, intermittent jaw claudication and generalised arthralgia. Initial investigations revealed high CRP and ESR, microcytic anaemia and hypoalbuminaemia with a positive PR3-ANCA. Urinalysis was strongly positive for blood, and his ACR was raised at 43mg/mmol, although his eGFR was preserved at 72. He then developed a common peroneal nerve mononeuropathy and commenced treatment with high dose steroids and 6 pulses of IV Cyclophosphamide (10mg/kg). His neuropathy progressed in the context of a persistently elevated CRP and he received 2 x 1g Rituximab. As inflammatory markers were still elevated 4 weeks later, azathioprine was added at 75mg daily. Over the next 4 weeks. his inflammatory markers normalised and neuropathy improved - 3 months later he was considered to be in remission. However, 4 months after this he presented with a 4-week history of progressive dysarthria, with cerebellar signs on examination. MRI demonstrated cerebellar changes highly suspicious for progressive multifocal leukoencephalopathy, and JC virus was detected in CSF. Azathioprine were stopped. 9 months later, he remains B cell deplete, although lymphocyte counts have improved. There has been some improvement in coordination, although mobility and speech continue to be impaired.

This case adds to the literature on the risk of PML in patients treated with Rituximab for GPA. Although this is a rare complication of treatment, it must be considered in the differential for patients treated with Rituximab who present with new neurological symptoms.

Reference

1. Brunetta et al, ASN 2015