

Infliximab for the Management of Treatment Resistant Central Nervous System Vasculitis: A Case Report

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BACKGROUND AND LITERATURE REVIEW

Central Nervous System (CNS) vasculitis is inflammation of blood vessel walls in the brain or spine due to overactivity of the immune system. The inflamed vessel wall can inhibit the flow of oxygen to the brain, leading to a loss of brain function. In some cases, CNS vasculitis is life-threatening.¹

Currently, there is a lack of evidence-based treatment. Treatment recommendations are largely based on case series and case reports. A retrospective audit by Vallet H et.al found infliximab reduced disease flare in 90% of 124 patients after 6 months.² Efficacy of infliximab in CNS vasculitis patients has been examined in several other reports and has shown to be an effective therapy. Infliximab has therefore been suggested as an alternate treatment in patients who fail to respond or are intolerant of other therapies.^{3,4,5}

Infliximab is a chimeric monoclonal antibody biologic that works by binding to and inactivating TNF- α , a chemical messenger which plays a significant role in promoting inflammation (figure 1).⁶

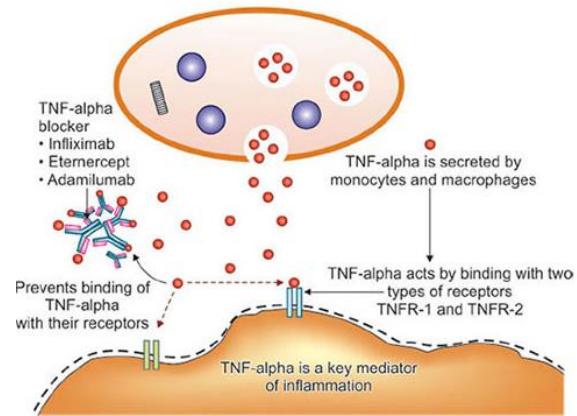


Figure 1: Mechanism of action of infliximab

McCoy, M. (2017). Mode of Action of TNF inhibitors. Journal of Neuroinflammation

DIAGNOSIS

TREATMENT DECISION

TREATMENT OUTCOME

NOVEMBER 2017

- 45-year-old Caucasian male presented with headaches, paraesthesia and weakness
- Stopped working in construction (previously healthy and had no previous medical history)
- Prednisolone, pantoprazole, pregabalin and baclofen commenced for symptomatic treatment

JANUARY – JUNE 2018

- Exclusion of an underlying infective cause; treated for an undifferentiated CNS inflammatory disorder
- Oral steroids, intravenous (IV) immunoglobulin and IV rituximab (2 doses) trialed with minimal improvement however, there was a partial response to high dose IV methylprednisolone and plasma exchange
- Developed depression and postural hypotension
- Duloxetine, fludrocortisone and midodrine commenced

OCTOBER – NOVEMBER 2018

- Diagnosis of CNS vasculitis confirmed by brain biopsy
- MRI of brain and spinal cord detected multiple inflammatory lesions characterised by T2 hyper intense lesions with variable gadolinium enhancement
- Trialed and failed IV cyclophosphamide (5 cycles)

FEBRUARY 2019

- Reviewed in clinic post deterioration of his treatment resistant CNS vasculitis and found to have severe autonomic failure secondary to brainstem involvement
- Cerebrospinal fluid (CSF) from lumbar puncture showed elevated protein and moderate lymphocytosis (lymphocytes $17 \times 10^6/L$ (reference $< 6 \times 10^6/L$))
- Wheelchair-bound, urinary/faecal incontinent, dysphagic (requiring PEG feeds)

- Ongoing paraesthesia, spasms, and neuropathic pain
- Patient admitted to hospital

MARCH 2019

- Non-formulary infliximab requested by the neurology team
- Extensive literature review by the medication evaluation team
- Application for compassionate access completed by the treating neurologist
- Application for non-formulary infliximab approved
- Patient education by neurology pharmacist
- Infliximab 5mg/kg IV was administered at 0, 2, 6 weeks and to be continued 6-weekly thereafter, with goal to lengthen duration between doses once symptoms stabilise

APRIL – JUNE 2019

- MRI at 6 weeks post infliximab showed no further progression of disease
- At week 11, there were improvements in neuropathic pain, urinary/bowel incontinence, mobility and dysphagia (now able to tolerate oral intake)
- Postural hypotensive medications were ceased

JULY – SEPTEMBER 2019

- Repeat lumbar puncture in July shows normalisation of CSF lymphocytosis (lymphocytes $5 \times 10^6/L$ (reference $< 6 \times 10^6/L$))
- Most recent MRI in September shows resolution of inflammation and cord swelling with no gadolinium enhancement
- Prednisolone ceased
- Patient able to walk small distances with assistance
- Ongoing non-formulary infliximab and compassion stock requested by neurology with plan to reduce frequency of infusions to 10-weekly

CONCLUSION

Infliximab treatment resulted in resolution of the acute inflammation in previously refractory disease. Ongoing review will determine its long-term efficacy and safety for this patient.

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