Case Report

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Hemi-paraplegia and hemi-anaesthesia in the inflammatory bowel disease clinic

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Case description

In this case report, we present a rare case of central nervous system demyelination secondary to infliximab therapy.

A 47-year-old gentleman with a 15-year history of left sided ulcerative colitis presented to the gastroenterology clinic with a 1-month history of bloody diarrhoea associated with a significantly elevated faecal calprotectin. A trial of oral and rectal mesalazine as well as oral steroids proved ineffective. He had previously been intolerant to both Azathioprine and 6-mercaptopurine. Decision was made to escalate his treatment to methotrexate and infliximab 5 mg/kg (originator). He was managed in the outpatient setting and did not require hospitalization.

First infliximab infusion was given on 14 May 2020. Second and third infusion were given two and six weeks after respectively. One week prior to the third infusion, he began to develop tingling and numbness down the right side of his body and he felt his right foot was more sensitive to changes in temperature. His Methotrexate was stopped but it was decided to proceed with giving the third infusion of infliximab. In the following two weeks he then developed weakness in the left leg and reported urinary hesitancy.

He was reviewed in the ambulatory unit by the neurologist twelve days following the start of his neurological symptoms. On clinical examination, cranial nerves were intact. He had good muscle bulk and no focal wasting. Tone was normal bilaterally, but power was mildly reduced on the left, 4/5 in wrist, digits, hip flexion and knee extension. Reflexes were present bilaterally, but the supinator, knee and ankle reflexes were brisk on the left. Coordination was intact. There was reduced proprioception and temperature sensation on the right side, with a sensory level just below the clavicle, whilst touch, vibration and two-point discrimination were preserved bilaterally. Plantars were downgoing bilaterally.

An urgent MRI of the spine was subsequently arranged which revealed a right sided intramedullary cord lesion at C4 with some focal eccentric enhancement (Figure 1).

A subsequent MRI of his head revealed white matter plaques in the cerebral hemisphere and corpus callosum (Figure 2). The post contrast sequences (not shown) showed no features of active demyelination.

CSF analysis was positive for IgG oligoclonal bands. Serum oligoclonal band testing revealed no abnormalities. These findings supported a diagnosis of Brown-Sequard syndrome secondary to a cord lesion due to multiple sclerosis (MS). The diagnosis of MS was based on evidence of widespread inflammation in the brain and the spinal cord in addition to positive oligoclonal bands in the CSF, which can be used as criteria for dissemination in time (2017 revised McDonald criteria).[1]

His infliximab was discontinued after his third infusion with no deterioration to his colitis and his neurology gradually started to improve two weeks later. He had a further flare of his MS a few months later manifesting as diplopia. Repeat MRI showed signal change involving the right deep parietal lobe that was more conspicuous than before probably representing some disease progression. Following discussion in the neuroinflammatory MDT it was decided that given the significant inflammatory activity he should be started on Natalizumab. Although this is not a licensed treatment for ulcerative colitis, being an anti-integrin, it was thought that it may also have the added benefit of reducing the risk of colitis flare. His first Natalizumab infusion was eight months after his last infliximab infusion.

Discussion

Anti-TNF drugs are an established therapeutic option in treatment of a number of inflammatory conditions including inflammatory bowel disease. Although these drugs can prove very effective, they can be associated with potentially serious adverse effects. One rare but potentially serious side effect is demyelinating disease.

A large French study, carried out between 2005 and 2008, identified 33 patients who developed demyelinating

Figure 1. Sagittal T2 and coronal T1 post contrast sequences show an expansile lesion at the level of C4 with a focal area of enhancement in the left lateral cord, in keeping with active demyelination.

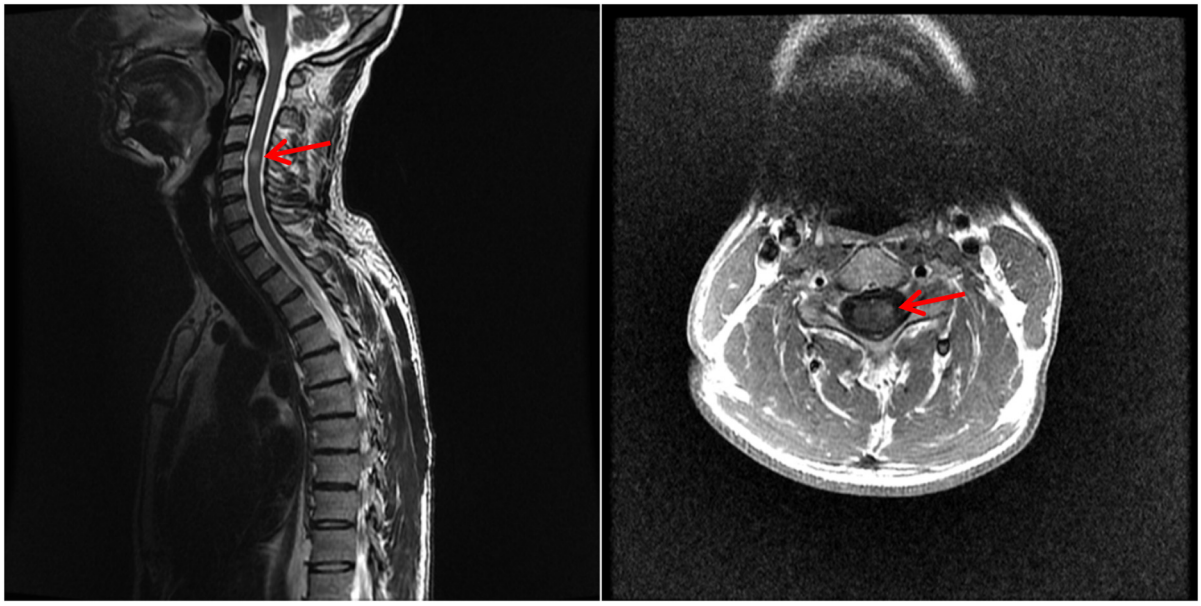
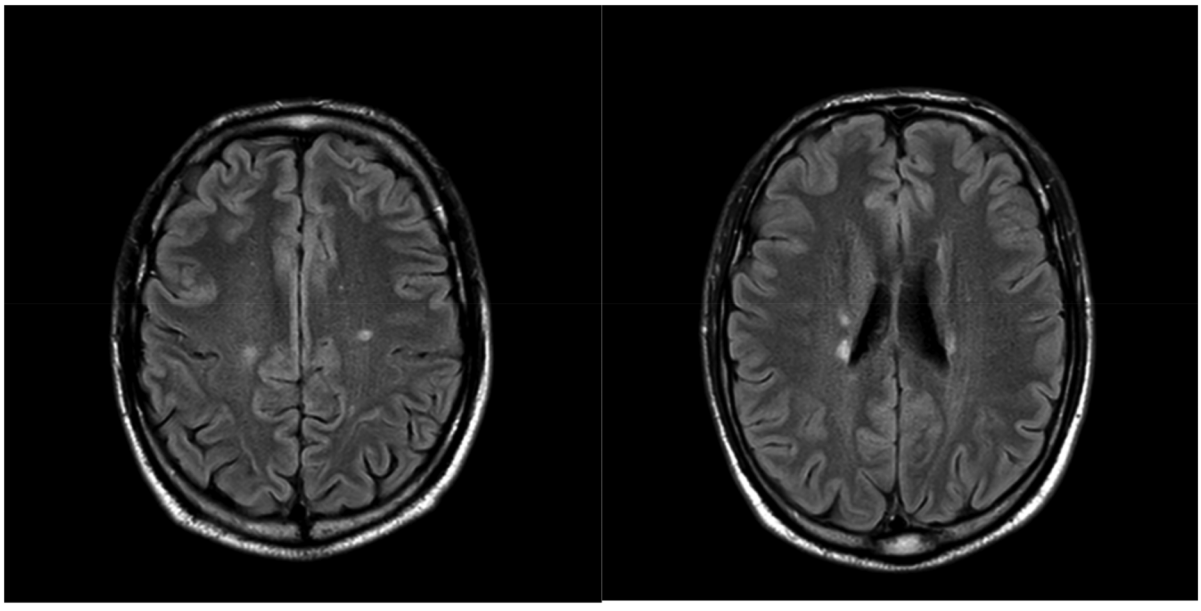


Figure 2. T2 FLAIR sequence showing periventricular and callosal lesions which are disseminated in space.



disorder during anti-TNF therapy with either infliximab (n = 15), etanercept (n = 12) or adalimumab (n = 6) with two patients having a positive rechallenge.[2] Several other studies have also shown an association between optic neuritis and demyelinating disease with the use of etanercept, infliximab and adalimumab.[3,4] In randomised controlled trials and postmarketing studies, the prevalence of demyelination with infliximab,

etanercept or adalimumab has been reported to range between 0.05 and 0.2%.[5]

Causal relationship between anti-TNF therapy and demyelinating disease remains unclear and questions have been raised as to whether demyelinating events in patients receiving anti-TNF therapy are the result of uncovering latent MS, onset of novel demyelinating event or merely an accidental coexistence of the two disorders.[6] Nevertheless, NICE guidelines suggest anti-TNF therapy should not be given when there is a clear history of demyelinating disease, may be best avoided if there is a possible history of demyelinating disease or a strong family history of demyelination and should be withdrawn if demyelination occurs.[7]

With regards to the more novel biologic agents used in IBD, there is currently no data to suggest an association between Vedolizumab or Ustekinumab and demyelinating disorders suggesting these may be preferential in patients with personal or family history of demyelinating disease.

Brown-Sequard syndrome is a rare entity resulting from hemisection injury of the spinal cord, often in the cervical cord region.[8,9] It is characterized by ipsilateral loss of motor function, vibration and proprioception below the level of the lesion secondary to damage to corticospinal tracts and contralateral loss of pain and temperature secondary to damage to the spinothalamic tracts. It is typically caused by traumatic spinal cord injury; however, there are also several non-traumatic causes. These include tumours, infections, disc herniation, autoimmune diseases and multiple sclerosis.[9]

MRI is the imaging of choice with CT scan performed in those unable to have an MRI. Imaging typically reveals a high T2 signal weighted lesion usually localised to one side of the spinal cord.[10]

A detailed history may identify patients at risk of demyelination with initiation of anti TNF therapy. However, if there is uncertainty it may be appropriate to arrange an MRI of brain and, if previous possible symptoms suggest, spinal cord before commencing the biologic treatment to detect lesions which could suggest pre-existing demyelination.

Written informed consent was obtained from the patient for the publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Declarations

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