Multiple Sclerosis with Ulcerative Colitis- Chance association or cause and effect?

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Abstract

A 35 year old female presented with loose bloody stools, abdominal pain, weight loss and parasthesia of the lower limbs and lower abdomen. Flexible sigmoidoscopy and rectal biopsy showed features of ulcerative colitis. MR scan of brain and spine revealed multiple plaques of demyelination in keeping with multiple sclerosis. The association between inflammatory bowel disease and multiple sclerosis is discussed.

Case History

A 35 year old female presented with a three month history of loose bloody stools with mucus. She was opening her bowels 20 times daily, had colicky abdominal pain and weight loss of one stone. The diarrhoea had improved with two courses of steroids from her GP. She had a past history of proctitis diagnosed in 1999, hemorrhoids and a borderline glucose tolerance test. Her mother had ulcerative colitis. She had been an ex-smoker for some years, lived with her husband and children and worked as a care assistant in a nursing home.

When she stood to walk to the examination couch she mentioned a one week history of parasthesia of the legs and lower abdomen, with poor balance, impaired manual dexterity, and difficulty initiating micturition. She recalled previous similar episodes affecting patches on the arms and chest.

On examination light touch and pin-prick sensation were altered with a sensory level at T10 on the left and T4 on the right. Proprioception was impaired in the lower limbs and gait was unsteady although Rhomberg's test was negative. Clonus and Lhermitte's sign were not present. The abdomen was soft and non tender with no masses.

Initial investigations including full blood count, electrolytes and liver function tests were normal. CRP was 52 mg/L and ESR 10 mm/hr. Endomyseal antibody and syphilis serology were negative. Abdominal x-ray was normal. She was admitted and treated with intravenous hydrocortisone, prednisolone enemas and azathioprine, and anticoagulated with enoxaparin. Flexible sigmoidoscopy showed marked inflammatory changes to the mid sigmoid colon and above (figure 1).

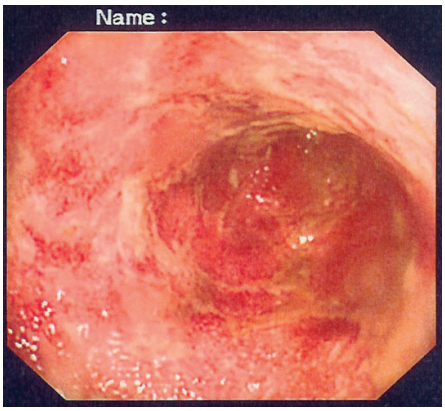

Figure 1: *Sigmoidoscopic appearance of sigmoid colon showing erythema, oedema, scarring atrophy and shallow ulceration.*

Histology of the rectal biopsy showed chronic moderately active inflammation with cryptitis, crypt abscess formation, and moderate crypt distortion and atrophy consistent with ulcerative colitis. An MR scan of brain and spine revealed numerous areas of demyelination in the periventricular white matter and at T1 in the cord (figures 2 and 3). A lumbar puncture was performed. The CSF was clear and colourless with a glucose of 7.1 mmol/L, protein 0.29 g/L, WCC 3 x106/L, RCC 112 x106/L, culture no growth. She was seen by the neurologists who

confirmed the diagnosis of multiple sclerosis and offered her treatment with β interferon which she declined. She developed hepatitis secondary to treatment with azathioprine which was stopped, but otherwise did well with both colitis and multiple sclerosis going into remission.

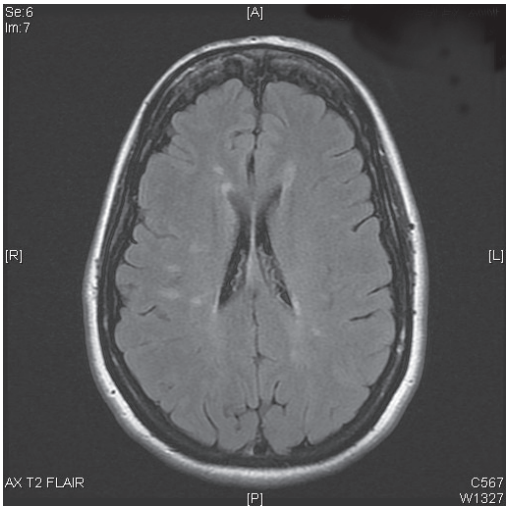

Figure 2. *MR brain showing numerous areas of high signal in the periventricular white matter, some in a classical pericallosal distribution, consistent with demyelination in the clinical context.*

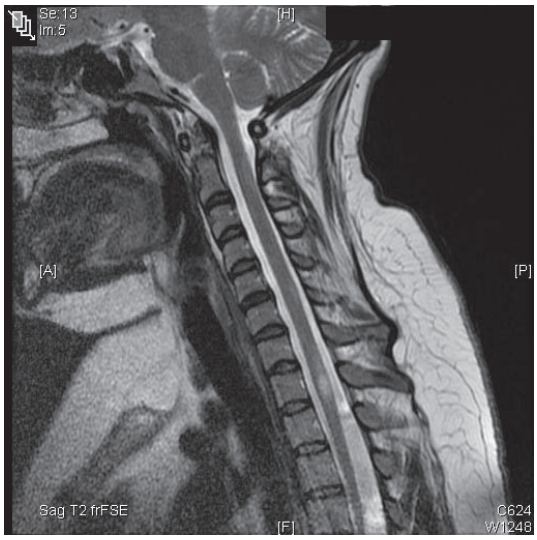

Figure 3. *MR Spine showing abnormally high T2 signal intensity within the cord at T1 level indicative of a demyelinating plaque.*

Discussion

A number of case reports since 1982 have described an association between inflammatory bowel disease (IBD) and multiple sclerosis (MS).[1-3] In a prospective cohort study by Edwards and Constantinescu patients with MS had a higher prevalence of IBD than the general population, whilst Kimura et al found the prevalence of MS at onset of IBD was 3.7 times that expected.[4,5] Other larger retrospective studies have found an increased risk of MS for those with ulcerative colitis (UC), but not with Crohn's disease.[6,7]

The cause of MS and IBD is largely unknown, although both are chronic immune mediated diseases thought to involve T Helper type 1 cell mediated autoimmunity.[4,8] The disease processes are likely to be complex and concordance studies in monozygotic twins show that besides genetics, environmental factors contribute to the development of MS and IBD.[9] UC and MS might share a common etiological factor, such as common pathogens; they might share common exacerbating factors such as stress; and patients might have a common autoimmune or genetic predisposition.[6,7] One study showed familial aggregation of MS and IBD occurred nine times more often than would be expected by chance.[10]

Although not relevant in our case, treatment of IBD may itself precipitate MS. The data sheets for anti-TNFα therapies Infliximab, Etanercept and Adalimumab, used in the treatment of IBD, warn of the development of MS and demyelination. One randomized placebo-controlled trial of an anti-TNF agent to treat MS was discontinued when it was observed that the anti-TNFα treated patients were having more exacerbations than the placebo treated patients.[11] However, the controlled clinical trials with anti-TNF medications have not established whether there is a causal association between the drug and MS, or if the association is chance,

given the increased risk for demyelination in IBD patients independent of treatment.[11] To add to the confusion there is one case report of a patient developing UC when Interferon β1a was used to treat her relapsing-remitting MS.[12] In an attempt to clarify the impact of anti-TNFα Gupta et al conducted a large retrospective study of patients between 1988-1997, a time period before anti-TNFα was on the market.[11] In a cohort of 8 million patients from the GP research database they too found a positive association between IBD and demyelinating disease.[11]

In conclusion we present a 35 year old female with ulcerative colitis and multiple sclerosis. We suggest the two conditions are linked and that the association is not due to chance.

Other neurological conditions including stroke and venous sinus thrombosis are also associated with IBD, these occurring because of IBD patients' pro-thrombotic state. Chronic polyneuropathy, cerebral vasculitis and IBD associated amyloid of the nervous system have also been described, and neurological signs and symptoms may occur in association with IBD related nutritional deficiencies.[13] Clinicians must be prepared for unusual neurological symptoms in patients with IBD. Given concerns that anti-TNF in the treatment of IBD could itself cause demyelination, further work is needed to tease out the interaction of genetic and environmental factors in IBD and MS so clinicians can properly inform patients of the risks of treatment.

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