Ulcerative Colitis and Motor Neurone Disease: Causal or Coincidental?

S Rajendra, Z A Kadir, N Karim, Z Zain

ABSTRACT

Neurological involvement associated with inflammatory bowel disease is well established though rarely reported in the literature. The coexistence of motor neurone disease with ulcerative colitis has never been previously documented.

The case of a 53-year-old Indian male with distal ulcerative colitis who, two and a half years later, developed dysarthria, dysphagia, a wasted fasciculating tongue and palatal palsy characteristic of bulbar type motor neurone disease is described. Topical and oral steroids together with azathioprine and mesalazine suppositories controlled the bowel symptoms but did not improve the neurological deficit. Subsequently, the antiglutamate agent riluzole improved the mobility of his tongue.

The close temporal relationship and relative infrequency of both these conditions in a Malaysian population along with the recognised association between ulcerative colitis and other neurological conditions deserve careful consideration as to whether a common denominator is involved. Documentation of coexistence of both disorders in a single patient is important in case similar associations are reported in future.

Keywords: ulcerative colitis, motor neurone disease, neurological complication, free radicals

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INTRODUCTION

The association of neurological disorders with enteric disease is uncommon but well recognised. Up to 3% of patients with inflammatory bowel disease (IBD) have neurological involvement[1,2]. Thromboembolic phenomena, myelopathy, myopathy, myositis, multiple sclerosis and various neuropathies have been described in association with inflammatory bowel disease but to date there is no documentation of the coexistence of motor neurone disease and ulcerative colitis[1-10]. We report a patient with recto-sigmoid ulcerative colitis complicated by bulbar type motor neurone disease.

CASE REPORT

A 53-year-old Indian male was in good health till October 1995 when he presented to a surgeon in another hospital with recurrent bouts of loose bloody stool with mucus and abdominal pain. A diagnosis of rectosigmoid ulcerative colitis was established by colonoscopy and histopathological examination. Symptoms partially resolved with oral steroids and 5-aminosalicyclic acid. Two years later, he presented to this hospital with difficult to control colitis, a weak tongue with an inability to articulate, slurring of speech, difficulty chewing and drooling of saliva.

Clinically, he was pale and neurological examination showed dysarthria, dysphonia, a wasted fasciculating immobile tongue, palatal palsy and an exaggerated jaw jerk. Muscle wasting and fasciculations of upper and lower limbs were present. Muscle tone was increased and tendon reflexes brisk. Superficial reflexes were normal and plantar responses flexor. Muscle power was normal as was sensation, gait and bladder and bowel function. Haemoglobin concentration was 11.8 g/dl, erythrocyte sedimentation rate 24, and serum ferritin, folate and vitamin B12 were within normal limits. Fasting glucose, renal profile, liver function tests, calcium, PT, PTT and thyroid function assays were all normal. Antinuclear antibody, rheumatoid factor, ANCA, VDRL, HTLV & HIV 1/ 2 titers, serum protein electrophoresis and urine for Bence Jones protein were all negative.

Serum complement levels i.e. C3 and C4 were normal at 1.88 g/L and 0.41 g/L respectively as was creatinine kinase concentration at 109 U/L. Acetyl choline receptor and anti-ganglioside antibodies (anti-GM1) were not detected. No ova or parasites were present in stool and culture for salmonella, shigella, campylobacter and other common pathogens was negative. Colonoscopy revealed severe recto-sigmoid ulceration with pseudopolyp formation. Histology of colonic biopsies showed an increase in basal lymphocytes and plasma cells together with

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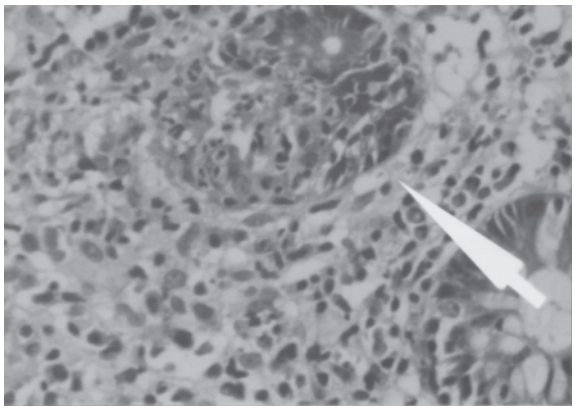

Fig. 1 Colonic biopsy from patient showing cryptitis (arrow) with an increase in plasma cells in the lamina propria; original magnification x 40.

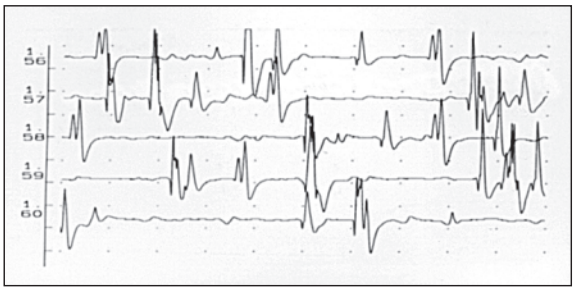

Fig. 2 Electromyograph of the right extensor digitorum muscle showing complex units with fibrillation and fasciculations.

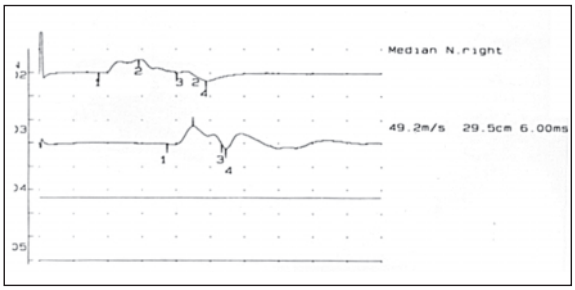

Fig. 3 Nerve conduction study of right median nerve revealing a markedly reduced motor unit potential amplitude with a normal conduction velocity.

architectural crypt distortion, cryptitis and focal crypt abscesses which was consistent with a diagnosis of ulcerative colitis (Fig 1). Lumbar puncture revealed colourless cerebrospinal fluid, normal cell count, a protein concentration of 0.35 mg/dl and no oligoclonal bands. Visual evoked potentials and MRI (with gadolinium enhancement) of the brain were within normal limits. MRI of the cervical spine showed narrowing of the intervertebral foramina at C5/6 and C6/7 but clinically, there was no evidence for cervical radiculopathy or myelopathy. Electrophysiological evaluation revealed complex units with frequent fibrillation and fasciculations and evidence of denervation with preserved motor conduction velocity (Figs. 2 and 3).

A diagnosis of predominantly bulbar type motor neurone disease was made.

Topical and oral steroids together with azathioprine (2 mg/kg) and mesalazine suppositories (500 mg bd) induced a remission of his colitis within three months but the neurological deficit progressively worsened. Subsequently, riluzole (100 mg daily) a drug which presynaptically inhibits the release of glutamic acid in the central nervous system was commenced and the patient reported that his tongue was more mobile. He defaulted treatment for 18 months before seeking medical attention again recently, whence he displayed extreme emotional lability, was only able to utter incomprehensible words and had significantly more muscle wasting of both upper and lower limbs. He had been self-medicating with prednisolone 10 mg po daily to keep his colitis at bay.

DISCUSSION

Various neurological complications have been reported in association with ulcerative colitis; albeit in a sporadic fashion. These include thromboembolic disease causing cerebrovascular disorders, neuropathy (usually as an acute or chronic inflammatory demyelinating polyneuropathy) which occurs mostly in ulcerative colitis and myopathies and myelopathies which are more characteristic of Crohn's disease[1-7]. There is a concurrence of multiple sclerosis and inflammatory bowel disease both within families and within individuals[8-10].

To the best of our knowledge, this is the first report of motor neurone disease complicating ulcerative colitis. This link may be coincidental, related to the basic disease or to its complications or treatment. Complications and extraintestinal manifestations may precede or follow the diagnosis of IBD and may occur with exacerbations of bowel symptoms or independently[11]. The pathogenesis of neurological complications in inflammatory bowel disease is largely unknown though coagulation abnormalities, vasculitis, factor V Leiden mutation, circulating immune complexes, autoimmunity, and an infective aetiology (e.g. *Campylobacter jejuni* infection causing an acute inflammatory demyelinating polyradiculoneuropathy) have been implicated[1,12-16]. The prevalence of autoimmune disorders is three times greater than expected in patients with ulcerative colitis[17]. In this patient, the absence of autoantibodies and the failure of immunosuppressive therapy to halt the progression of neurological deficit argue against an autoimmune hypothesis. An underlying vasculitis is unlikely, in view of a normal ESR and continued neurological deterioration despite steroid and azathioprine therapy.

Similarly, normal complement levels in this patient make circulating immune complexes an unlikely aetiological factor. Furthermore, no iatrogenic cause(s) or infective agent was identified; nor was a definable metabolic or nutritional deficiency documented in this patient.

Abnormalities of cell-mediated and humoral immunity, of regulatory pathways, and inflammatory mechanisms have been demonstrated in IBD and are related to various extraintestinal manifestations[18-20]. Excess formation of free radicals resulting in tissue damage has been documented in both motor neuron disease and ulcerative colitis. Mutations in the gene on chromosome 21 encoding the enzyme Cu/Zn superoxide dismutase is present in 20% of familial cases of motor neurone disease and 2% of all cases[21]. The enzyme detoxifies the superoxide anion by catalytic conversion to hydrogen peroxide which is then removed by other free radicals. Aberrant function of the mutant enzyme could result in accumulation of free radicals and resulting damage to lipids, intracellular proteins and DNA. Reactive oxygen metabolites are generated in high amounts in patients with inflammatory bowel disease[22,23]. Reduced levels of antioxidant enzymes (superoxide dismutase, catalase and glutathione) and metallothionen (both endogenous copper and zinc containing proteins involved in radical scavenging), have been detected in inflamed mucosa from patients with inflammatory bowel disease compared to non-inflammed mucosa and controls[24-26]. This imbalance will render the mucosa more susceptible to oxidative damage resulting in inflammation.

The reasonably close temporal relationship between the two disorders and the relative infrequency of both conditions in a Malaysian population, along with previously published neurological complications of inflammatory bowel disease, may suggest a common denominator. Documentation of coexistence of both disorders in a single patient is warranted in case similar associations are reported in future.

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