

Guillain-Barré syndrome as an extraintestinal manifestation of Crohn's disease

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Summary

A variety of extraintestinal manifestations, probably immune-mediated, may appear during relapses of Crohn's disease. We report the clinical observation of a 34-year-old woman who developed a Guillain-Barré syndrome, aphthous stomatitis and oligoarthritis during a relapse of Crohn's ileocolitis. This case suggests that the Guillain-Barré syndrome may be another extraintestinal manifestation of Crohn's disease.

Keywords: Crohn's disease, Guillain-Barré syndrome

Crohn's disease is a chronic inflammatory intestinal disorder of unknown aetiology which, in most cases, follows a relapsing and remitting course. It is well known that relapses may be accompanied by extraintestinal manifestations, including joint and skin symptoms, the pathogenesis of which is thought to be auto-immune.¹ We report a patient who developed a Guillain-Barré syndrome, aphthous oral ulcers, and peripheral arthritis during a relapse of Crohn's ileocolitis.

Case report

A 34-year-old woman was admitted to hospital with progressive weakness of her limbs for one day. On admission, she was afebrile, and general physical examination revealed aphthous oral ulcers, and arthritis involving two proximal intraphalangeal joints of the left hand, right hip, right knee, and left ankle. Neurological examination showed bilateral facial paresis, flaccid areflexic quadriplegia, and distal impairment of vibration sense. Perception of position, touch, pinprick, and temperature was normal. She developed bulbar paralysis and respiratory failure on the day after admission and had to be ventilated. Four years earlier she had been diagnosed as having Crohn's ileocolitis (based on radiological findings, colonoscopy, and biopsy). Since then she had had several relapses of Crohn's disease accompanied by aphthous stomatitis and asymmetric inflammatory polyarthritis involving the large joints of the lower extremities. For the last two months she had been treated with deflazacort (alternating 60 or 15 mg/day), and intramuscular injections of vitamin B12 (monthly). During the 10 days before admission she had had liquid diarrhoea with mucous (5–6

stools/day), abdominal pain, fever (38°C), loss of weight, and arthralgias in the left hand and lower limbs (Crohn's Disease Activity Index, 346).²

Laboratory values were as follows: leukocyte count $18.2 \times 10^9/l$; lymphocyte count $0.9 \times 10^9/l$; lymphocyte subpopulations: CD19 53%, CD3 41% (CD4/CD8 1.8); haematocrit 0.36; and erythrocyte sedimentation rate 38 mm/h. Cerebrospinal fluid (CSF) contained a protein level of 570 mg/l, normal glucose and no cells. An electrophysiological study performed on day 10 showed absent compound muscle action potentials. Extensive laboratory investigations, including stool cultures, porphyrins, serum and CSF protein electrophoresis, blood screen for connective tissue diseases, anti-GM₁ antibodies, HLA-B27, immunoglobulins, cryoglobulins, cold agglutinins, thyroid function tests, vitamin B12 and folic acid levels, HIV, hepatitis serology, and antibodies to viruses, *Mycoplasma pneumoniae*, *Campylobacter jejuni*, *Borrelia burgdorferi*, and *Salmonella typhosa*, as well as cranial and cervical magnetic resonance imaging (MRI), were normal or negative. The patient was treated with plasmapheresis (beginning on day 3; total plasma exchange, 18 l) and prednisone (1 mg/kg daily), but her condition did not improve, and developed distal muscle wasting. A repeat electrophysiological study performed six weeks after onset still showed inexcitable motor nerves, and electromyography revealed widespread signs of active denervation. At this time, CSF contained a protein level of 1300 mg/l. She developed fulminant bronchopneumonia, septicæmia and shock, and died three weeks later. Necropsy was refused.

Discussion

Although traditionally the Guillain-Barré syndrome has been defined as an inflammatory and demyelinating polyneuropathy, the existence of an axonal form of Guillain-Barré syndrome is now accepted.³ The present patient fulfilled clinical criteria for Guillain-Barré syndrome,⁴ and the electrophysiological findings (inexcitable motor nerves and marked evidence of muscle denervation) suggest an acute axonal form of Guillain-Barré syndrome. However, a primary demyelinating process cannot be totally excluded.⁵

On the other hand, although the pathogenesis of the Guillain-Barré syndrome remains unclear, considerable evidence favours

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Accepted 2 February 1995

Criteria for diagnosis of Guillain-Barré syndrome	Associations of Guillain-Barré syndrome
<p><i>Features required for diagnosis</i></p> <ul style="list-style-type: none"> • progressive motor weakness of more than one limb • areflexia, universal or distal with definite hyporeflexia of the biceps and knee jerks <p><i>Features strongly supportive of the diagnosis</i></p> <ul style="list-style-type: none"> • clinical features (ranked in order of importance) <ul style="list-style-type: none"> – progression: symptoms and signs of motor weakness develop rapidly but cease to progress by four weeks into the illness – relative symmetry – mild sensory symptoms or signs – cranial nerve involvement (particularly facial weakness) – recovery: usually begins 2–4 weeks after progression stops – autonomic dysfunction – absence of fever at the onset of neuritic symptoms • CSF features: after the first week of symptoms, CSF protein is elevated or may rise on serial lumbar punctures; 10 or fewer mononuclear leukocytes/mm³ CSF. • electrodiagnostic features: motor nerve conduction block or slowing (conduction velocity below 60% of normal) at some point during illness (not all nerves are affected). 	<ul style="list-style-type: none"> • viral infections: influenza virus, Herpes virus, hepatitis, HIV and AIDS, and other viruses • bacterial infections: <i>Campylobacter jejuni</i>, <i>Mycoplasma pneumoniae</i>, <i>Borrelia burgdorferi</i> (Lyme disease), and other bacteria • vaccination • sarcoidosis • systemic lupus erythematosus • lymphoma (particularly Hodgkin's disease) • solid tumours (particularly lung cancer) • endocrine disorders: hyperthyroidism, hypothyroidism, Hashimoto's thyroiditis, Grave's disease, Cushing's syndrome, Addison's disease • pregnancy • surgery and spinal epidural anaesthesia
Box 1	Box 2
	<p>Crohn's disease: extraintestinal manifestations associated with intestinal disease activity</p> <ul style="list-style-type: none"> • oligoarticular arthritis • aphthous stomatitis, erythema nodosum • uveitis, iritis, episcleritis • Guillain-Barré syndrome (present report)
	Box 3

an immunological basis, implicating both cellular and humoral responses.⁶ It is unknown whether the pathogenesis of the axonal form of Guillain-Barré syndrome is different from the more common cases in which demyelination is predominant, but it seems that *Campylobacter* enteritis could play a role.⁷ In the present patient, however, there was no evidence of *Campylobacter* infection, and the antibody-mediated immune response seemed to be the main pathogenetic factor (CD19, 53%; CD3, 41%). In this sense, a depression of T-suppressor cells caused by corticosteroid therapy might have had a promoting effect on the development of the Guillain-Barré syndrome.⁸ Guillain-Barré syndrome has been linked to a remarkable diversity of disorders,

including ulcerative colitis.⁹ There is also a report of Miller Fisher syndrome (a clinical variant of Guillain-Barré syndrome) and Crohn's disease.¹⁰ However, as far as we know this is the first case of Guillain-Barré syndrome to be reported during a relapse of inflammatory bowel disease. Although we cannot rule out a coincidental association, the presence of other extraintestinal manifestations (aphthous oral ulcers and peripheral arthritis) that clearly correlate with the activity of the underlying bowel disease¹ supports a common pathogenetic mechanism. In this sense, Guillain-Barré syndrome could be included in the list of extraintestinal manifestation of Crohn's disease.

1 Glickman RM. Inflammatory bowel disease: ulcerative colitis and Crohn's disease. In: Isselbacher KJ, Braunwald E, Wilson JD, Martin JB, Fauci AS, Kasper DL, eds. *Harrison's principles of internal medicine*, 13th edn. New York: McGraw-Hill, 1994; pp 1403–17.

2 Best WR, Beckett JM, Singleton JW, Kern F Jr. Development of a Crohn's disease activity index: National Cooperative Crohn's Disease Study. *Gastroenterology* 1976; **70**: 439–44.

3 Feasby TE, Gilbert JJ, Brown WF, et al. An acute axonal form of Guillain-Barré polyneuropathy. *Brain* 1986; **109**: 1115–26.

4 Asbury AK. Diagnostic considerations in Guillain-Barré syndrome. *Ann Neurol* 1981; **9** (suppl): 1–5.

5 Hall SM, Hughes RAC, Atkinson PF, McColl I, Gale A. Motor nerve biopsy in severe Guillain-Barré syndrome. *Ann Neurol* 1992; **31**: 441–4.

6 Winer JB, Gray IA, Gregson NA, et al. A prospective study of acute idiopathic neuropathy. III Immunological studies. *J Neurol Neurosurg Psychiatry* 1988; **51**: 619–25.

7 Yuki N, Yoshino H, Sato S, Miyatake T. Acute axonal polyneuropathy associated with anti-GM₁ antibodies following *Campylobacter* enteritis. *Neurology* 1990; **40**: 1900–2.

8 Steiner I, Wirguin I, Abramsky O. Appearance of Guillain-Barré syndrome in patients during corticosteroid treatment. *J Neurol* 1986; **233**: 221–3.

9 Zimmerman J, Steiner I, Gavish D, Argov Z. Guillain-Barré syndrome: a possible extraintestinal manifestation of ulcerative colitis. *J Clin Gastroenterol* 1985; **7**: 301–3.

10 Viñals M, Anciones B, Cruz Martínez A, Barreiro P. Síndrome de Miller-Fisher recidivante asociado a neuritis braquial. *Neurología* 1989; **4**: 61–5.