Abstract
A female patient with a three year history of Crohn's disease of the colon developed myasthenia gravis. Despite diversion of the faecal stream by an ileostomy, and total colectomy, the patient had continuing problems with perineal and perianal abscesses and fistulas. Her myasthenia gravis became unresponsive to anti-cholinergics so a thymectomy was performed. The perineal and perianal disease improved subsequently. This case supports the theory that functional disturbances of the thymus may have a role in the pathogenesis of inflammatory bowel disease.


An association between myasthenia gravis and Crohn's disease has been reported previously in only one patient. We describe a female patient who developed both these conditions, the treatment of which was unsatisfactory until a thymectomy was performed. Thymectomy has previously been reported to be of benefit in ulcerative colitis, but it is possible that it may also have a beneficial effect in Crohn's disease.

Case report
The patient first attended the Royal Liverpool University Hospital in 1985 when she was 21 years old, worked as a clerk, and smoked eight cigarettes per day. She had presented to another hospital two years previously with abdominal pain, weight loss, diarrhoea, and anaemia, when a diagnosis of Crohn’s disease was made. Despite treatment with prednisolone and sulphasalazine she continued to have diarrhoea, weight loss, and malaise, and so was referred here. She had been amenorrhoeic for six months before her first attendance at this hospital.

On examination she was pale and unwell. There was an ill defined mass in the right iliac fossa and multiple anal skin tags. Investigations showed anaemia (haemoglobin 7 g/dl) and thrombocytopenia (670 x 10^9/l) with low serum iron, a raised erythrocyte sedimentation rate (65 mm in first hour) and hypoalbuminaemia (28 g/l). A small bowel enema was normal, but colonoscopy showed extensive patches of severe inflammation, deep ulcers, pseudopolyps, and bleeding with sparing of the rectum, splenic and hepatic flexures, and caecum. Biopsies showed heavy inflammation with loss of architecture and a few granulomata. She was treated with elemental diet (E 028, Scientific Hospital Supplies, Liverpool) and blood transfusion, as well as further prednisolone and sulphasalazine.

For the next 18 months her colitis remained controlled, albeit on regular courses of prednisolone. In late 1986, she developed diplopia and unilateral ptosis induced by fatigue; a positive tension test and the presence of antibodies to acetyl choline receptor (AChR) in the serum confirmed a diagnosis of myasthenia gravis. The symptoms responded to treatment with pyridostigmine, but the side effects of pain and diarrhoea complicated her management. At this time she also developed episcleritis and erythema nodosum.

In 1987 her colitis became poorly controlled and a subtotal colectomy and ileorectal anastomosis were performed. Histological examination of the resected colon confirmed Crohn’s colitis with patchy full thickness inflammation and multiple granulomata. Subsequently pelvic abscesses, perineal fistulas, and persisting diarrhoea necessitated excision of the rectum and formation of a permanent ileostomy in October 1989, but the perineal problems failed to resolve. Between October 1989 and August 1991 multiple courses of antibiotics were given, and 12 separate operations to open perineal sinuses and abscesses were performed, but improvements were short lived. Additionally, her myasthenia became difficult to control, and in August 1991 a thymectomy was performed. Histological examination showed (normal) atrophic thymus tissue. Her myasthenia subsequently responded and pyridostigmine was withdrawn. One further operation was done in October 1991, at which a perineal sinus was explored and re-opened. The patient has had no further problems from perineal disease during the subsequent 17 months to date. She continues to suffer from episcleritis and has also been found to have an ovarian cyst, but there is no clinical, radiological, or laboratory evidence of active Crohn’s disease.

Discussion
Whether there is a true association between Crohn’s disease and myasthenia gravis is unclear. At the time of our patient’s presentation a survey of published works did not show any cases with both conditions, but subsequently a single case has been reported, suggesting that any association is likely to be weak. One review has addressed the coexistence of autoimmune diseases in patients with inflammatory bowel disease, but although patients with ulcerative colitis had an increased prevalence of autoimmune disorders over controls, those with Crohn’s disease did not. Whether myasthenia gravis was specifically sought in that study is not stated, but the fact that it was not mentioned suggests that none of the patients who were reviewed suffered from it.

There is clear evidence that myasthenia gravis
Crohn's disease and myasthenia gravis: a possible role for thymectomy

is an immune mediated disease. Circulating antibodies to the AChR are found in patients with myasthenia gravis, T lymphocyte function is abnormal, and the thymus is enlarged, with prominent germinal centres and Hassall's corpuscles. In addition, there is an established association with autoimmune thymotoxicosis.

In inflammatory bowel disease there has been no convincing and reproducible abnormality in studies of peripheral blood counts of T and B cells, and the ratios of CD4+/CD8+ T cells are also normal. Tsuchiya et al, however, have described an association between thymic abnormalities and inflammatory bowel disease. The normal age involution of the thymus does not occur in patients with myasthenia gravis or ulcerative colitis, and the T cells obtained from the thymus of patients with myasthenia gravis and ulcerative colitis have reduced ratios of suppressor (CD8+) to helper (CD4+) T cells when compared with T cells obtained from patients having elective cardiac surgery. Only two patients with Crohn's disease were studied, however, and CD4+/CD8+ ratios were found to be normal. Similar studies of T cells from inflamed mucosa of patients with Crohn's disease and ulcerative colitis have not showed any significant changes from controls. Nevertheless, available evidence suggests that the tissue damage in both ulcerative colitis and Crohn's disease is mediated by immune mechanisms, and it is possible that our patient's perineal disease improved as a result of thymectomy. Indeed, an uncontrolled trial of thymectomy in patients with ulcerative colitis resistant to conventional treatment has been reported to increase duration of remission.

As far as we are aware, treatment with thymectomy has not been reported in Crohn's disease, although drugs that change the immune response are the mainstay of treatment for both Crohn's disease and ulcerative colitis. Interestingly, James reported remission of Crohn's colitis in a patient who developed HIV associated immunodeficiency, suggesting that CD4+ T lymphocytes may be important in the pathogenesis of Crohn's disease. We believe that this report, considered with other evidence, suggests that the potential of thymectomy as a treatment for inflammatory bowel disease should be investigated further.