*Lesson of the week***Antibody negative coeliac disease presenting in elderly people—an easily missed diagnosis**

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Epidemiological studies screening cohorts of healthy volunteers in the United States of America, the United Kingdom, and other European countries have determined that the prevalence of adult coeliac disease in the general population is in the magnitude of 1 per 100 to 200.¹⁻⁴

The diagnosing of coeliac disease is often delayed,³⁻⁷ perhaps owing to a failure to recognise the protean manifestations of this disease in both primary and secondary care.⁵⁻⁹ Coeliac disease used to be perceived as involving gastrointestinal symptoms suggestive of malabsorption, but this manner of presentation is now described as the classic (typical) form.⁴ Patients with coeliac disease may have the silent or atypical form (no gastrointestinal symptoms), and the condition may present insidiously—for example, with iron deficiency anaemia, osteoporosis, cryptogenic hypertransaminasaemia, or neurological symptoms.⁵⁻¹⁰ The increasing recognition of coeliac disease is attributed to the use of new serological assays that have a high sensitivity and specificity.⁴ Antibody testing, however, is not the absolute method of diagnosis. We present a case of an elderly man presenting with coeliac disease in whom the condition would not have been recognised without a second duodenal biopsy.

Case report

In May 2003 a 79 year old man with longstanding dyspepsia presented to his general practitioner with worsening indigestion, tiredness, and rapid weight loss. Blood tests arranged by the doctor showed a macrocytic anaemia with low concentrations of vitamin B-12 and folate. The patient subsequently had a negative result on endomysial antibody testing. A gastroscopy in June 2003 did not show any macroscopic abnormalities, and routine quadrantic duodenal biopsies were histologically normal. Over the following three months the patient's condition deteriorated. He developed anorexia, with a documented weight loss of 15 kg. For the first time, the patient started to complain of lower gastrointestinal symptoms. Although he did not have an increased frequency in defecation, he noted that the stool had become foul smelling, and he described abdominal bloating and increased flatus. When the patient was seen in a gastroenterology clinic his immunoglobulin concentrations, IgG and IgA gliadin antibodies, endomysial antibodies, and tissue transglutaminase activity were checked. In addition, an urgent colonoscopy yielded a macroscopically normal result. Routine terminal ileal and colonic biopsies were all normal. His blood tests were reviewed: results for endomysial antibodies and IgA gliadin were now positive; IgG gliadin was negative;

Endoscopic features of coeliac disease with scalloping and mosaic appearance of small bowel

and transglutaminase activity was 237 (normal range 0-10 units per millilitre). Repeat gastroscopy showed macroscopic features consistent with coeliac disease (figure) and duodenal biopsies showed total villous atrophy. The patient was breathless, had a haemoglobin concentration of 82 g/l, had developed ankle oedema, and had an albumin concentration of 30 (normal range 35-48) g/l. In view of this, in February 2004 he was started on both a gluten-free diet and 30 mg of prednisolone daily. He was also transfused with 2 units of packed cells. Video capsule endoscopy showed virtual pan-atrophy of the small bowel but no evidence of lymphoma.

By August 2004 the patient no longer required prednisolone and subsequently gained 8 kg. He now had few gastrointestinal symptoms, and because of this improvement, he was committed to the gluten-free diet. Results on testing for IgG and IgA gliadin antibodies and endomysial antibodies were negative. Repeat duodenal biopsy showed an almost complete histological resolution except for intraepithelial lymphocytes.

Discussion

Coeliac disease is still incorrectly perceived as being both an uncommon disease and a disease of childhood or infancy. Most cases are adult, however, and occur in people aged 40-60 years.¹⁻⁵ Patients in this age group may present with coeliac disease in an atypical manner. However, if an elderly patient presents with symptoms and signs suggesting malabsorption, coeliac disease should be part of the differential diagnosis.

Editorial by Watson and p 773

Consider duodenal biopsy for elderly patients with overt malabsorption, even if coeliac antibody profile is negative

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In our case, the family doctor had already considered this possibility and arranged a gastroscopy as well as checking the patient's endomysial antibodies. Why were both these investigations negative? Our understanding of coeliac disease has been that histological changes are patchy and more prominent in the proximal small bowel rather than distally; this is thought to be related to the higher gluten load proximally.^{4 11} However, reports have been published of villous atrophy being initially missed on duodenal biopsy and only subsequently recognised if repeat small bowel biopsies are obtained.^{4 11} Cases of small bowel villous atrophy evolving over a period of time have also been documented. Initially, all that may be seen on biopsy could be an increase in intraepithelial lymphocytes and in particular an increase in the ratio of gamma to delta T cells (in the presence of positive antibodies).^{12 13} In our case, both duodenal biopsy specimens were reviewed blindly by an independent gastrointestinal histopathologist. Despite this second assessment, there were still no subtle features of coeliac disease on the initial biopsy.

Although endomysial antibody testing is highly specific (in excess of 90%), this antibody has been reported as being negative in lesser grades of villous atrophy (for example, partial or subtotal villous atrophy).^{4 14} Although uncommon, antibody negative coeliac disease is also well described.^{4 15} We repeated the antibody titre (at a dilution of 1 in 20) on the original sample and it was still negative. A recently described alternative explanation is that of masking of endomysial antibody by IgA smooth muscle actin autoantibodies (J Dunne et al, 11th coeliac international symposium, Belfast, 2004). Irrespective of the mechanisms, in clinical terms both these results were initially negative, and we were able to make the diagnosis only when the patient presented with a "coeliac crisis" (the most severe form of coeliac disease, presenting with overt malabsorption).⁴ Our case is highly unusual because the patient initially had both a negative antibody profile and a normal duodenal biopsy. Perhaps at the earliest stage of presentation the patient had not developed all the immunological features of coeliac disease; this would be supported by the fact that macroscopic abnormalities were only noted at the time of the second endoscopy and video capsule endoscopy. If we had not reconsidered the possibility of coeliac disease (and repeat testing) then we would not have been able to diagnose the condition or treat it appropriately.

Coeliac crisis is a rare condition, usually described as presenting with marked malabsorption and a good response to a gluten-free diet and steroids.⁴ With the arrival of serology testing for coeliac disease, fewer cases have been described in the literature.

Doctors in both primary and secondary care should always consider the possibility of coeliac disease even in elderly people. Negative serology should not necessarily reassure the clinician. In the presence of a clinically deteriorating patient a duodenal biopsy should be performed.¹³ Elderly patients following a gluten-free diet will see improvements in their symptoms and be committed to the diet despite their age.¹⁶

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Endpiece

A practical man

If there be one species of cant more detestable than another, it is that which eulogises what is called the practical man, as contradistinguished from the scientific. If by practical man is meant one who, having a mind well stored with scientific and general information, has his knowledge chastened, and his theoretic temerity subdued, by varied experience, nothing can be better; but if, as is commonly meant by the phrase, a practical man means one whose knowledge is only derived from habit or traditional system, such a man has no resource to meet unusual circumstances; such a man has no plasticity; he kills a man according to rule, and consoles himself, like Molière's doctor, by the reflection that a dead man is only a dead man, but a deviation from received practice is an injury to the whole profession.

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