Coeliac disease in old age: ‘a catch in the rye’

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Keywords: coeliac disease, gluten-sensitive enteropathy, old age

Introduction

Coeliac disease has been viewed as a disease of children and young adults, presenting with weight loss, steatorrhoea, anaemia and evidence of folate, iron or vitamin D deficiency [1]. Early studies reported that only 4% of new diagnoses of coeliac disease were made in patients aged over 60 [2] but the Coeliac Society estimates that 21% of new patient members now fall into this age group [3] and a recent study reports that 34.1% of all new patients diagnosed with coeliac disease are in the seventh decade or above [4]. Swinson et al. [5] demonstrated a bimodal distribution for age at time of diagnosis for adult coeliac disease, with an initial peak in the fourth decade (predominantly women) and a later peak in the sixth and seventh decades (mostly men). The female : male ratio is approximately 2 : 1 in adults overall [6] but may be more even in elderly subjects [7]. However, the recently developed screening tests for the presence of IgA α-gliadin antibody or IgA anti-endomysial antibody have shown that 60% of patients with gluten-sensitive enteropathy may be asymptomatic and have confirmed associations with neurological disorders [8] and insulin-dependent diabetes mellitus [9]. Coeliac disease is therefore likely to be diagnosed more commonly in geriatric practice.

Historical background

Trier [10] defined coeliac disease as “a chronic condition in which there is a characteristic mucosal lesion of the small intestine which impairs nutrient absorption by the involved bowel and which improves on withdrawal of wheat gliadins and barley, rye and oat prolaminues from the diet”. The clinical features of childhood coeliac disease were described by Samuel Gee in 1888 [11]. In 1950 the Dutch paediatrician Dicke [12] noted that wheat and rye cereal grains were harmful to children suffering from coeliac sprue. In 1953 it was demonstrated that the gliadin component of the wheat protein gluten caused fat malabsorption in patients previously diagnosed as suffering from coeliac disease [13] and Paulley described the characteristic histopathological abnormalities of crypt hyperplasia, villous atrophy and lymphocytic infiltrate in the submucosa [14]. These abnormalities arise in genetically susceptible individuals possessing the HLA class 2 DR3 DQW2 haplotype [12] on exposure to the gliadin component of wheat flour or to similar proteins (known as prolamine) in barley (secalin) and rye (hordein) [16]. The severity of malabsorption depends on the length of small intestine exhibiting these histological features. Recent work now suggests that oat prolamine (avenin) may not be toxic to the small bowel in people with coeliac disease [16].

Epidemiology

Older texts report a prevalence for coeliac disease of around 1 : 2000 in Europeans, with an unexpected prominence in the west of Ireland and Sweden [1]. Population-based studies since screening tests have been available suggest that the prevalence of coeliac disease in the community may be as high as 1 : 300 [17]. Gluten-sensitive enteropathy is most common in the northern hemisphere but also occurs in South America, Australia and New Zealand. The condition is rare in the Far East and said never to occur in Afro-Caribbeans.

Classification of adult coeliac disease

Better understanding of the nature of coeliac disease and the availability of screening tests has resulted in most new diagnoses being made in patients with subclinical disease [18]. A new classification of adult coeliac disease into four subsets, covering the full
Anti-gliadin antibodies were positive in 13 of 17 younger patients. However, 20% of patients with a-gliadin antibody titres do not have patients [26]. Over 75% of patients with diarrhoea. Hankey and Holmes [7] reviewed the clinical features of 42 patients aged over 60 and found that 15 had abdominal symptoms or had had abnormal haematological and biochemical indices for a long time (on average 28 years) before diagnosis. Over 75% of these elderly patients were anaemic on presentation and gastrointestinal symptoms were present in 59%. Anti-gliadin antibodies were positive in 13 of 17 patients in whom the titres were measured. A gluten-free diet was well tolerated and associated with substantial clinical improvement in 38 of 40 patients. Iron-deficiency anaemia is common in newly diagnosed elderly coeliac patients [24]. In a study of 30 coeliac patients over 60 [4], anaemia was found in 60% and diarrhoea and weight loss in over 70%. Small bowel lymphoma developed in 17% of patients followed for up to 12 years and there was a 7% incidence of small bowel adenocarcinoma. Although an increased incidence of oesophageal and pharyngeal carcinoma has been reported, none was observed in this study. Yappa [25], in a small study of 10 elderly patients, concluded that clinical features were similar in elderly and younger patients.

Studies in elderly patients

Studies in the late 1970s and early 1980s [21-23] identified malabsorption as an important cause of morbidity and malnutrition in elderly patients. Montgomery et al. [20] identified eight patients with coeliac disease among 70 elderly patients with malabsorption, four of whom presented with bone pain and only two with diarrhoea. Hankey and Holmes [7] reviewed the clinical features of 42 patients aged over 60 and found that 15 had abdominal symptoms or had had abnormal haematological and biochemical indices for a long time (on average 28 years) before diagnosis. Over 75% of these elderly patients were anaemic on presentation and gastrointestinal symptoms were present in 59%. Anti-gliadin antibodies were positive in 13 of 17 patients in whom the titres were measured. A gluten-free diet was well tolerated and associated with substantial clinical improvement in 38 of 40 patients. Iron-deficiency anaemia is common in newly diagnosed elderly coeliac patients [24]. In a study of 30 coeliac patients over 60 [4], anaemia was found in 60% and diarrhoea and weight loss in over 70%. Small bowel lymphoma developed in 17% of patients followed for up to 12 years and there was a 7% incidence of small bowel adenocarcinoma. Although an increased incidence of oesophageal and pharyngeal carcinoma has been reported, none was observed in this study. Yappa [25], in a small study of 10 elderly patients, concluded that clinical features were similar in elderly and younger patients.

The value of antibody tests as a screening tool

\(\alpha\)-gliadin antibody titres are raised in 80–90% of coeliac patients [26]. However, 20% of patients with a positive IgA \(\alpha\)-gliadin antibody titre do not have coeliac disease [27]. Chorzelski and colleagues [28] described IgA anti-endomysial antibody as an immunological marker for coeliac disease and this is the best current screening test. Anti-endomysial antibodies are positive in 91–100% of untreated coeliac patients, with a specificity of 99%. With treatment the anti-endomysial antibody titre falls and is positive in 0–68% of patients receiving a gluten-free diet [27]. Thus, a positive test for anti-endomysial antibody has a positive predictive value nearing 100% and a negative predictive value of almost 100%, making it a reliable and accurate screening test for the presence of coeliac disease. However, a false negative result may occur in IgA deficiency, and testing for anti-endomysial antibody is expensive and time-consuming. A small bowel biopsy should therefore be taken in symptomatic patients.

Enteropathy-associated T-cell lymphoma

The association between coeliac sprue and malignant lymphoma was described in 1937 [29]. Evidence of malabsorption frequently predate the diagnosis of lymphoma by 20–25 years [30]. Enteropathy-associated T-cell lymphoma usually presents between the fifth and seventh decades with abdominal pain, weight loss, acute intestinal obstruction or perforation. The reported prevalence of lymphoma in adult coeliac disease is 8%, but these data are from early studies on symptomatic patients [2]. The true prevalence is likely to be much lower given that adult coeliac disease has an estimated population prevalence of 1 in 300. The prevalence of lymphoma in a series of elderly coeliac patients was 23%, suggesting a possible increased susceptibility in aged subjects [31]. Adenocarcinoma of the pharynx, oesophagus or jejunum is associated with celiac disease, but a gluten-free diet will prevent the development of malignant complications even in patients with silent or latent disease.

Bone disease in gluten-sensitive enteropathy

Paterson and Burns [32] reported six patients aged over 60 presenting with bone pain, muscle weakness and biochemical osteomalacia due to vitamin D deficiency associated with coeliac disease. Bone pain may be the only presenting feature of adult coeliac disease [33] and may be difficult to differentiate from other disorders. Fractures are more common and a gluten-free diet may improve but not normalize bone mass in these subjects [34]. Vitamin D deficiency may produce symptomatic proximal myopathy in coeliac patients.

Neurological dysfunction

Neurological complications occur in between 8% [35] and 35% [7] of patients. Peripheral neuropathy [36].
epilepsy [37], cerebellar syndrome [38] myopathy and hyporeflexia [35] have all been reported in association with coeliac disease.

In a study of 53 patients with undiagnosed neurological disorders, 30 (57%) had a positive α-gliadin antibody on screening and, of these, nine (35%) had histological evidence of coeliac disease on jejunal biopsy [8]. It may be that the α-gliadin antibody is neurotoxic or that neurological deficits arise from a vitamin (possibly vitamin E) deficiency [39]. Collin [40] reported five patients with pre-senile dementia, aged 27–58, with villous atrophy or positive anti-reticulin and anti-gliadin antibodies. However, a gluten-free diet was associated with improved cognitive function in only one of them.

Association with insulin-dependent diabetes mellitus
The prevalence of coeliac disease (identified by antibody screening) in patients with insulin-dependent diabetes mellitus is 1.7–8% [9]. Many of these patients are female and asymptomatic, and the commonest laboratory abnormality is iron deficiency. This association may be related to the high frequency of HLA-DR3 genotypes in both patients with coeliac disease and those with insulin-dependent diabetes mellitus. Glucose control is not adversely affected by asymptomatic coeliac disease, although symptomatic patients presenting with weight loss and diarrhoea have increased insulin requirements, better control and fewer hypoglycaemic episodes when treated with a gluten-free diet [9].

Conclusions and future directions
Coeliac disease is being diagnosed for the first time in later life with increasing frequency. These patients may have a long history of gastrointestinal symptoms which may not have been recognized as being caused by gluten-sensitive enteropathy. Alternatively, the diagnosis may have been delayed by a reluctance to investigate mild symptoms or haematological and biochemical abnormalities. As in younger patients, iron-deficiency anaemia is common in elderly subjects with this condition. The availability of antibody-based screening tests suggests that the prevalence of coeliac disease may be far higher than previously suspected and should lead to more cases being diagnosed in old age. Certainly, screening tests should be considered in patients with neurological disorders, memory impairment, insulin-independent diabetes mellitus, mild gastrointestinal symptoms, anaemia, osteopenia, vitamin deficiency and biochemical evidence of malnutrition. This should help identify patients who may benefit from a gluten-free diet.

Future research with the new generation of screening tests may help us to understand the relative proportions of elderly patients with active, latent and silent coeliac disease and to establish whether the sensitivity and specificity values established by the anti-endomysial antibody screening test remain valid into late life.

Key points
- Anti-endomysial antibody is a reliable and accurate screening test for adult coeliac disease.
- Population-based studies using antibody-based screening tests show the prevalence of adult coeliac disease to be 1 in 300.
- The majority of new diagnoses are made in asymptomatic subjects, many of whom are elderly.
- Iron-deficiency anaemia, bone pain and weight loss are common features of adult coeliac disease in elderly patients.
- Adult coeliac disease is associated with neurological complications and insulin-dependent diabetes mellitus.

References
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