Does the ageing population need to be concerned about coeliac disease?

Coeliac disease is an increasingly recognised autoimmune disease against gluten, a protein found in food such as wheat. This disease is controlled with a gluten-free diet. The consequences of coeliac disease, especially if diagnosed later in life, include anaemia, reduced bone-mineral density, and gastrointestinal tumours.

John S Leeds Honorary Clinical Lecturer in Gastroenterology, Gastroenterology and Liver Unit, Royal Hallamshire Hospital, Glossop Road, Sheffield S10 2JF, UK.

David S Sanders Honorary Reader and Consultant Gastroenterologist, Gastroenterology and Liver Unit, Royal Hallamshire Hospital, Glossop Road, Sheffield, S10 2JF, UK.

*email* john.leeds@sth.nhs.uk

Coeliac disease is a state of heightened immunological response to ingested gluten from wheat, barley, or rye, in genetically susceptible individuals.1,2 Patients with coeliac disease can initially be recognised by using noninvasive serological tests. The reported sensitivity and specificity of these antibodies are variable, depending on the test, or combination of tests, used (table 1).3 When serological tests are positive, a duodenal biopsy (with gastroscopy) is needed to demonstrate villous atrophy. This process remains the gold standard for making the diagnosis of coeliac disease.

Historically, coeliac disease was thought to be uncommon with a population prevalence of around one in 8,000.4 However, reports in 2003 of large studies using the latest serological markers suggested that the population prevalence is 1 in 100–200.5,6 This change is not thought to be due to an increase in disease prevalence, but to a combination of better detection using more sensitive markers, and higher clinical suspicion.

Furthermore, the concept of an iceberg of disease manifestation has been postulated, showing the diversity of presentation of coeliac disease or in some cases the lack of presenting features (figure 1).7 The tip of the iceberg contains those patients with typical clinical features of coeliac disease, particularly malabsorption and gastrointestinal symptoms. The next stratum contains the atypical or silent group presenting with, for example, iron-deficiency anaemia, osteoporosis, or abnormal liver-function tests. Further down the iceberg are those with potential coeliac disease, defined as positive serology but normal duodenal histology on biopsy. The implications of such results are still under investigation.

Since coeliac disease has an autoimmune pathophysiology, its prevalence in combination with several other autoimmune conditions is increased (table 2). Adult presentations are now more frequent than paediatric ones (9:1)8 with more than 25% of patients receiving their diagnosis at the age of 60 years or older.9 Treatment of coeliac disease is exclusion of gluten from the diet, which is effective for most patients. To ensure adequate adherence to a gluten-free diet, discussion with a dietitian is recommended. Non-compliance with the diet is the most common reason for acute or continued symptoms. If symptoms are severe or limit social activities then use of medications such as codeine phosphate or loperamide may be required. In this review, we give specific reference to issues and complications of most relevance to patients older than 50 years.

<table>
<thead>
<tr>
<th></th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Positive predictive value</th>
<th>Negative predictive value</th>
</tr>
</thead>
<tbody>
<tr>
<td>IgG antigliadin antibody</td>
<td>57–78%</td>
<td>71–87%</td>
<td>0.20–0.95</td>
<td>0.41–0.88</td>
</tr>
<tr>
<td>IgA antigliadin antibody</td>
<td>55–100%</td>
<td>71–100%</td>
<td>0.28–1.00</td>
<td>0.65–1.00</td>
</tr>
<tr>
<td>IgA endomyseal antibody</td>
<td>86–100%</td>
<td>98–100%</td>
<td>0.98–1.00</td>
<td>0.80–0.95</td>
</tr>
<tr>
<td>IgA tissue transglutaminase antibody</td>
<td>77–100%</td>
<td>91–100%</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>IgA tissue transglutaminase and endomyseal antibodies</td>
<td>98–100%</td>
<td>98–100%</td>
<td>—</td>
<td>—</td>
</tr>
</tbody>
</table>

**Table 1**: Characteristics of serological markers in detecting coeliac disease
Symptoms

As noted previously, patients with coeliac disease may present with obvious clinical syndromes such as weight loss, abdominal pain, and diarrhoea, but others may have more subtle complaints such as anaemia. Iron deficiency anaemia is a common cause of referral to secondary care, particularly in elderly people. Coeliac disease has been shown to account for 2.7–5.7% of cases of iron-deficiency anaemia.\(^{10,11}\) Additionally, other causes of this anaemia, such as colonic carcinoma\(^ {12} \) and microscopic colitis are also associated with this disorder.\(^ {13} \)

Guidelines from the The British Society of Gastroenterology for the investigation of iron-deficiency anaemia recommend that all patients should be tested for coeliac disease, either by serology or by doing a duodenal biopsy.\(^ {14} \) This guidance is stratified further by suggesting that patients younger than 45 years do not require gastroscopy unless they have upper gastrointestinal symptoms or positive coeliac serological tests. The Society recommends that patients older than 45 years should have gastroscopy and proceed to colonoscopy unless gastric carcinoma or coeliac disease is identified.

However, two recent studies have challenged this stance. Both studies found that the prevalence of neoplastic lesions in the colon of patients with coeliac disease and anaemia was around 12%.\(^ {15,16} \) Bidirectional endoscopy may be troublesome for patients at the extremes of age. The factors involved include difficulty taking bowel preparation, increased risk secondary to higher comorbidities, therapeutic futility, and perceived unwillingness on the patients’ behalf. Yet, colonoscopy has a low complication rate (0.2%) even in elderly patients and has a higher diagnostic yield in those older than 65 years.\(^ {17} \) However, in both studies most patients with clinically significant colonic lesions were more than 65 years old.

Similarly, change in bowel habit is a frequent reason for elderly patients to be referred for gastrointestinal investigations. Carcinoma of the colon is usually the most pressing concern, however, coeliac disease is a common cause of chronic diarrhoea and national guidelines recommend exclusion of coeliac disease in patients with this symptom.\(^ {18} \) Furthermore, functional symptoms are prevalent in all age groups accounting for 2.4–15.5% of consultations in general practice.\(^ {19} \) Coeliac disease has a higher prevalence in patients with irritable bowel syndrome, compared with controls matched by age and sex.\(^ {20} \)
Bone-mineral density

The association between coeliac disease and reduced bone mineral density, both osteopenia and osteoporosis, is well known. The most common skeletal complication of coeliac disease in adults is reduced bone-mineral density with studies reporting around 30–50% of patients with coeliac disease having either osteoporosis or osteopenia.21 Few studies have specifically examined whether patients who present with coeliac disease at age 75 years or older are at additional risk. Of the available studies, data show no significantly increased rate of hip fractures in patients older than 75 with coeliac disease when compared to population-based controls.22,23 The absolute number of excess hip fractures is about 24 per 10,000 person years. This estimate correlates to an extra 2–3 hip fractures over a 10-year period compared with that expected in the general population.

In one study, patients with coeliac disease were more likely to be non-smokers and more likely to have used hormone replacement therapy—thus these confounding factors may have protected them from reduced bone mineral density.21 Furthermore, the elderly group with coeliac disease had a lower body-mass index which could have led to a higher rate of osteoporosis or an increased risk of fracture, or both, but no increased risk was observed.

On the basis of these data, the risk of fracture in elderly patients with coeliac disease seems to be increased only modestly. When investigating elderly patients with reduced bone-mineral density for possible secondary causes, trying to identify coeliac disease in these patients should be restricted to those with either gastrointestinal symptoms or anaemia.24

Cancer

Patients with coeliac disease do seem to be at increased risk of several neoplastic conditions in the gastrointestinal tract and elsewhere. Two long-term follow-up studies show a 30–40% increase in mortality in patients with coeliac disease, most commonly attributed to malignancy and, in particular, lymphoma.25,26 Interestingly, people with coeliac disease appear to have lower rates of breast and lung cancer, although the mechanism of this finding is not entirely clear.25 Other studies have shown increased incidence of cancer at all sites, with the highest risk being 10-fold in people not on a gluten-free diet and a 5-fold increase in those in a partly gluten-free diet.

Those maintaining a strict diet had a similar incidence of cancer to the general population.27 Furthermore, a recent Italian study suggested that the risk of developing a neoplasm in coeliac disease is higher when it is diagnosed later in life with many patients being diagnosed simultaneously with coeliac disease and cancer.28 Imaging the small intestine for lymphoma, has historically been difficult. Cross-sectional imaging modalities miss lesions, and small-bowel meal has a low sensitivity for subtle mucosal

<table>
<thead>
<tr>
<th>Prevalence of coeliac disease in other autoimmune disorders</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prevalence</td>
</tr>
<tr>
<td>Dermatitis herpetiformis</td>
</tr>
<tr>
<td>Addison’s disease</td>
</tr>
<tr>
<td>Autoimmune thyroid disease</td>
</tr>
<tr>
<td>Sjogren’s syndrome</td>
</tr>
<tr>
<td>Autoimmune hepatitis</td>
</tr>
<tr>
<td>Type-1 diabetes mellitus</td>
</tr>
<tr>
<td>Primary biliary cirrhosis</td>
</tr>
</tbody>
</table>
changes. With the advent of wireless capsule endoscopy and double balloon enteroscopy, pan-intestinal endoscopy is achievable and safe.

Neurological disease

Coeliac disease can present with neurological manifestations,
and it affected up to 23% of patients in one study. Furthermore, not all patients with gluten sensitivity and neuropathy had evidence of villous atrophy on duodenal biopsy or significant gastrointestinal symptoms. Further work has shown changes in the humoral response, irrespective of macroscopic duodenal changes. Treatment of such patients with a gluten-free diet can arrest or reverse the neurological changes. These manifestations are not specific to coeliac disease, and, therefore, patients could be misdiagnosed and treated incorrectly. The most common neurological manifestation of coeliac disease is ataxia followed by peripheral neuropathy, cognitive impairment, and Parkinsonism. Conceivably, patients referred to elderly-care physicians with these features may have neurological coeliac disease, which is unlikely to respond to conventional therapies.

Conclusion

Coeliac disease is a common condition that can occur at any time in life, often having a delayed time to diagnosis because of atypical features. The ageing population is at risk of complications related to coeliac disease, particularly osteoporosis and malignancy. Early diagnosis and treatment of this disorder leads to reductions in risk of complications and, therefore, morbidity and mortality. Increased awareness of the atypical presentations of coeliac disease with an active case-finding approach will aid detection of patients, thereby reducing delay in diagnosis and treatment.

We have no conflict of interest.

References