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Diagnosis of Coeliac Disease – an Update

Overall prevalence rate of coeliac disease in both children and adults in the western world is quoted at 1% although some groups have reported a five-fold increase in children when compared to adults.[1] The disease is more prevalent than first thought in Eastern Europe and Asia, with as many as 1% of Latvians and 1.44% of north Indians testing positive with routine screening serology.[2,3] The rise is largely attributed to increased awareness and education resulting on average in 16% annual increases in serological testing for coeliac disease.[1] Large scale studies of healthy school children from Eastern Europe and North Africa have reported prevalence rates similar to those in the western world of between 0.4 and 1.1%.[4,5,6]

In contrast to whites, only one in 300 urban African-Americans investigated for iron deficiency anaemia (IDA) was found to have coeliac disease, although this might be an underestimate of coeliac disease in black communities.[1] European-American differences have also been reported with refractory coeliac disease (RCD), with a lower incidence in North America (1.5%) and a higher type I:II RCD ratio compared to Europe.[6]

Recent prevalence studies in children with type 1 diabetes (T1DM) and adults with irritable bowel syndrome (IBS) have reignited the debate of the timing and frequency of coeliac disease screening in these conditions.

Depending on the use of serology and/or biopsy, the prevalence of coeliac disease in T1DM ranges from 7.2 to 8.6% in Europe[7-9] and even reaches 11% in India.[1] These are almost double the mean prevalence reported in the 1990s,[10] and strongly advocate the need for routine screening of all T1DM patients for coeliac disease, regardless of presence or absence of symptoms. In 2009, the UK's NICE guidelines recommended that children with T1DM should be screened for coeliac disease at the time of diagnosis.[1] But Babiker et al[11] have pointed out that, judging by Cardiff's experience,[12] if the 2009 guidelines were adhered to, only half of the possible childhood coeliac disease cases would be detected, and up to one-third of asymptomatic cases would remain undetected over a 7-year follow-period. Annual screening has, therefore, been suggested, but larger supportive studies are needed.

The need to screen all cases of IBS has recently been challenged by a large American study that found that despite a common finding of coeliac disease antibodies in non-constipated IBS sufferers (7.3%), the presence of histological coeliac disease was almost identical to that of healthy controls (0.41 vs 0.44%, $P>0.99$).[13]

Serological antibody screening and small bowel histology remain the 'gold standard' for coeliac disease diagnosis. Large-population studies have continued to highlight the accuracy of sequential serological antibody testing – high sensitivity of tissue transglutaminase (tTG) and specificity of endomysial antibodies – in detecting symptomatic and asymptomatic coeliac disease.[1] A recent Dutch study of symptomatic children and teenagers suggests that a positive (>100 U/ml) tTG antibody plus symptomatic response to a gluten-free diet (GFD) avoids need for diagnostic biopsy.[1] Infants with chronic diarrhoea and normal serology remain a challenge without a biopsy, but the discovery of a new class of antibodies against deamidated gliadin peptides (α-DGP)[14] have high sensitivity and specificity for coeliac disease in this clinical setting.[1] These α-DGP antibodies can be used to monitor compliance with GFD to a high degree of accuracy in this age group.

Attempts to find non-invasive markers have resulted in novel methods of human leukocyte antigen (HLA) typing techniques. Furthermore, confirming coeliac disease with pre-existing self-prescribed GFD is difficult because both serology and histology can normalise with GFD. In these circumstances, HLA genotyping is of value, but traditional HLA typing methods are costly and labour intensive. Cost-effective HLA typing methods that accurately distinguish risk alleles for coeliac disease have now been reported,[15-17] and they offer promise for screening and diagnosing coeliac disease in developing countries.

To further tackle the problem of detecting a diagnostic immune response to gluten in patients already self-established on GFD, a new subset of peripheral blood gluten-specific T-lymphocytes with better specificity for gut mucosal antigens have been described.[18-19]

Villous atrophy is patchily distributed and the optimal site and number of duodenal biopsies continues to be debated. There is increasing support for duodenal bulb biopsy in addition to D2.[20-22] Furthermore, the diagnostic accuracy of the histological distribution of intraepithelial lymphocytes along the villus for detecting mildly active coeliac cases with otherwise normal villus architecture, has been confirmed.[23-24]

However, the gold-standard status of the histological diagnosis of coeliac disease is under increasing scrutiny and doubt because of the variability of reporting between pathologists, with claims of up to 20% histopathological underdiagnosis of coeliac disease, particularly so with milder forms of the disease. Misinterpretation of poorly oriented biopsies may also lead to overdiagnosis of coeliac disease, mistaken initiation of gluten-free diet, and subsequent unnecessary assessment for misinterpreted failure to respond to the diet.[25]

The author's suggested take-home message is that with the increasing sophistication of serology, where the serological and histological diagnoses do not match up, doubts should be raised about the accuracy of the histological diagnosis. Some authors have recently also put forward the possibility of making the diagnosis and treating patients purely on the basis of serological findings.[26]

References may be accessed at www.thesynapse.net