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PAEDIATRIC ESSAY

ACTA PÆDIATRICA NURTURING THE CHILD WILEY

On the diagnosis of childhood coeliac disease: Past and present

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In 1970, the European Society for Paediatric Gastroenterology, Hepatolgy and Nutrition (ESPGHAN) published guidelines for diagnosing coeliac disease based on the morphological changes in the small intestinal mucosa. Very recently, revised criteria were published.[1] Here, we present a short review of the history of coeliac diagnosis and a summary of the current diagnostic guidelines, including the extended use of non-biopsy diagnosis in specific cases.

Seventy years have now passed since the Dutch paediatrician Willem Karel Dicke (1905-1962) made the ground-breaking discovery that gluten is the offensive agent in coeliac disease (CD). During World War II, there was a great shortage of food, particularly bread. He noticed that children with CD improved and saw a connection between low dietary wheat intake and low coeliac rate. He reported his research findings, first in his doctoral thesis in Dutch in 1950, and three years later in two seminal papers in English. At that time, diagnosis of CD was based on standard malabsorption tests such as determination of faecal fat and the xylose absorption test.

A second decisive step forward in the diagnosis of CD was the small intestinal suction biopsy technique developed by the British adult gastroenterologist Margot Shiner (1923-1998). In the 1950s, she was working under the illustrious hepatologist Dame Sheila Sherlock (1918-2001) in London and began to perform gastric biopsies in adult patients with liver disease. As quoted from A Phillips,[2] 'it is thought that Sheila Sherlock prompted Margot Shiner to push on into the duodenum'. So she did, and in 1963 Shiner published a report on the procedure in children.[2] Since then, the introduction of endoscopic biopsy under deep sedation has refined the technique for obtaining small intestinal mucosal material in a fast, safe, and, for the child, more comfortable way.

The histopathologic classification of coeliac enteropathy had no standardised way of reporting until the 1990s when M Marsh published the 'Marsh criteria', further specified by G Oberhuber, the 'Marsh-Oberhuber criteria'. These comprised increased number of intraepithelial lymphocytes, crypt hyperplasia and various degrees of villous atrophy. As time went by, it became evident that the mucosal lesion can be patchy and sometimes confined to the most proximal part of duodenum only, so-called bulbar CD. Thus, multiple biopsies performed endoscopically are now recommended.

Beginning in the 1970s, the use of safe serologic markers indicating CD was successively introduced. First out were anti-reticulin and anti-gliadin antibody tests, soon followed by the more sensitive and specific analyses of antibodies against endomysium (EMA) and against the enzyme tissue transglutaminase (tTGA). Both tests are routinely performed on IgA antibodies, therefore, the patient´s IgA status should be evaluated as part of the serologic workup.

Biopsy of the small intestine made it possible to be more precise when diagnosing CD based on the morphology of the small bowel enteropathy in the biopsy. Thus, in 1970, ESPGHAN published a three-biopsy scheme for diagnosis: Biopsy 1. showing a subtotal/total villous atrophy when the child was on a diet containing gluten; Biopsy 2. showing mucosal recovery while on a gluten-free diet; Biopsy 3. showing mucosal relapse following a period of gluten challenge. This diagnostic procedure gained wide acceptance and was implemented into routine paediatric care.

The added diagnostic value of serological tests was acknowledged by ESPGHAN in their revised criteria formulated in 1990. Accordingly, in a child with suspected CD, a biopsy showing typical coeliac enteropathy at presentation, followed by serologic normalisation and clinical remission on a gluten-free diet, was considered sufficient for the definite diagnosis.

The movement to a non-biopsy based diagnosis was first recommended by ESPGHAN in their revised guidelines published in 2012. Thus, in children with clinical symptoms indicating CD, a tTGA antibody test showing titres more than ten times the upper normal

limit, plus raised EMA titres and positive HLA DQ2/DQ8 genotype test was accepted as a definite CD diagnosis. These criteria reduced the need for biopsy in up to 50% of children investigated for suspected CD. In non-symptomatic children, however, a biopsy was still mandatory. The so-called ProCeDE study showed that children could be accurately diagnosed with CD without biopsy analysis.[3] Of note, the recommendation on omitting biopsy is a 'conditional recommendation' that should be discussed with the family which should be informed about the option of biopsy for diagnosis. Very recently, ESPGHAN published a further revision of the diagnostic guidelines.[1] The recommendation for HLA typing has now been removed and there is no requirement for biopsy in non-symptomatic children with high coeliac serology marker titres. Thus, a diabetic child with high TGA titres but without gastrointestinal symptoms can be diagnosed as CD without biopsy.

In contrast to the situation in Europe, North American paediatric gastroenterologists still rely on 15-year-old guidelines for the diagnosis of CD, which means that small intestinal biopsy is still required in every case with suspected symptoms despite access to modern well established serologic testing, a practice now questioned.[4]

The extended use of non-biopsy diagnosis will reduce the need for endoscopic biopsy and release resources for increasing efforts to find children with hitherto undiagnosed CD. This may pave the way for mass screening projects with the potential of finding many cases of undiagnosed CD in the paediatric population. This is exemplified by a large Swedish screening study including 12-year-old schoolchildren, where a CD incidence of 3% was established.[5] Of the children shown to have CD, only one third had a diagnosis of CD prior to screening. In view of the increased risk for complications in untreated or inadequately treated CD, general screening for CD should be considered if shown to be health economically cost-effective.

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CONFLICT OF INTEREST

The authors have no conflicts of interest to declare.

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