Letters

Celiac disease: anti-endomysial antibody versus villous atrophy

We report a prospective study done in the Pediatric Gastroenterology clinic (between July 2001 and July 2005) to find the frequency of celiac disease among children with chronic diarrhea (defined as diarrhea lasting for more than 4 weeks) and to determine the sensitivity and specificity of anti-endomysial antibody (EMA) for detection of celiac disease as well as partial villous atrophy (PVA) and subtotal/total villous atrophy (ST/TVa).

All children with chronic diarrhea with associated failure to thrive, short stature, anemia, and abdominal distension were suspected to have celiac disease. All had earlier received broad-spectrum antibiotics for 6-8 weeks. Hematocrit, RBC indices, iron studies, stool for giardia trophozoites, X-ray wrist, EMA and duodenal biopsy were done in all. EMA estimation was not done at a commercial lab (Lal Pathology Laboratories, New Delhi) by indirect immunofloresence using monkey esophagus. Total IgA estimation was not done. Multiple biopsies were taken from the second part of the duodenum and blinded histology reporting was done by the consultant pathologist using Marsh score. The diagnosis of celiac disease was as per the ESPHAGAN criteria, except in the case of symptomatic EMA-positive patients with Marsh scores I and II. All cases and parents were counseled about gluten-free diet (GFD) compliance. Patients were followed up 2 weekly till response to GFD was seen and thereafter 3-6 monthly. Those showing symptomatic improvement within 8 weeks of full compliance with GFD were confirmed as celiac disease.

Sample size was calculated keeping the anticipated prevalence as 48.07%. To estimate the prevalence within 20% of the true value with 95% confidence, we needed a sample size of 110. To see the overall efficacy of EMA, the phi coefficient was also calculated.4

Table: Sensitivity (%) and specificity (%) of EMA in detecting celiac disease and villous atrophy

<table>
<thead>
<tr>
<th>Condition</th>
<th>Positive</th>
<th>Negative</th>
<th>Sensitivity (95% CI)</th>
<th>Specificity (95% CI)</th>
<th>Phi coefficient</th>
</tr>
</thead>
<tbody>
<tr>
<td>Celiac disease</td>
<td>31</td>
<td>8</td>
<td>79.48 (63.23-91.78)</td>
<td>100</td>
<td>0.85</td>
</tr>
<tr>
<td>Non celiac</td>
<td>0</td>
<td>84</td>
<td>100</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Villous atrophy</td>
<td>Present</td>
<td>27</td>
<td>77.14 (66.21-91.78)</td>
<td>95.24 (90.69-99.79)</td>
<td>0.75</td>
</tr>
<tr>
<td></td>
<td>Absent</td>
<td>4</td>
<td>80</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*2 cases where EMA could not be done have been excluded

Of the 346 children with chronic diarrhea, 125 underwent duodenal biopsy and EMA estimation on suspicion of celiac disease. Of the remaining, 104 children had persistent diarrhea, defined as acute-onset diarrhea lasting more than 14 days, usually in children less than 2 years. Small bowel contamination (94), giardiasis (19) or HIV (4) were diagnosed in the rest of the cases. Of the 125 who were suspected to have celiac disease, 54 had normal histology and were EMA negative. The Marsh score of the other 71 was as follows: Marsh score I (19), II (15), IIIA (13), IIIB (17) and IIIC (7). Of these 71, 31 were EMA positive and in 2 cases (with Marsh IIIA and IIIB), EMA could not be done due to financial constraints. Of the remaining 38 EMA-negative cases, 8 were diagnosed as celiac disease on the basis of having partial to total villous atrophy on duodenal biopsy. After excluding the 2 cases where EMA could not be done, we had 39 children with celiac disease among the 123 with suspected celiac disease, giving a frequency of 31.7%.

The sensitivity and specificity of EMA to detect celiac disease were 79.48% and 100%, respectively. The same were lower for the detection of villous atrophy (Table). But the overlap in the 95% CI of the two indicated insignificant difference. The phi coefficient for the overall better prediction was also higher for detection of celiac disease. Eight of the 13 PVA and 19 of the 24 ST/TVa were EMA positive (OR 0.65, 95% CI 0.14-3.01).

All cases reported symptomatic and weight improvement on GFD. Median (range) weight z score improved from -3.08 (-5.7 to -0.37) to -2.76 (-5.3 to 0.16) in the 8 weeks on GFD. We intend to do post-gluten challenge duodenal biopsy for the cases with Marsh scores I and II.

The frequency of 31.7% in the present study is far greater than the 16.5% reported earlier but mirrors recent reports.5,6 This could be due to increase in awareness or a backlog of undiagnosed cases. The recently reported EMA sensitivity and specificity in children is higher.7 Use of monkey esophagus, inclusion of cases without villous atrophy, non-inclusion of serologically screened asymptomatic siblings of the cases, and not excluding IgA-deficient cases could be reasons for the lower EMA sensitivity in the present study. The wide and overlapping 95% confidence intervals imply that EMA as a diagnostic test for detection of villous atrophy has poor precision.
but comparable sensitivity and specificity. High (>0.75) and low (<0.75) phi coefficient for the detection of celiac disease and villous atrophy, respectively, indicate efficacy of EMA as a screening test.

Revision of the diagnostic criteria for celiac disease to include serologically detected cases without typical histological findings has been suggested. Clinical, histological and/or serological improvement on GFD in cases without villous atrophy has been reported. Our study had 5 EMA-positive cases without villous atrophy and all improved on GFD. We cannot explain the higher number of cases who had seronegative celiac disease (some of whom could be IgA deficient) in our series as compared to those reported earlier. As reported earlier too, 20% of our patients could have gone undiagnosed if we depended on EMA alone. There are reports of lower and comparable EMA positivity in PVA versus TVA. This could be due to the variation in gluten content of the diet of untreated celiac disease in different geographical regions.

We conclude that the frequency of celiac disease is 31.7% in suspected cases with chronic diarrhea. EMA sensitivity for detection of celiac disease is 79%; it has comparable sensitivity and specificity to detect PVA and ST/TVA.

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References