Serologic Testing for Celiac Disease

To the Editor:

We read with interest the report by Martini et al. (1). The authors compared the accuracy of five commercially available IgA anti-tissue transglutaminase (anti-tTG) ELISAs with data from anti-endomysial antibodies (EmAs) in the diagnosis and follow-up of adult patients with celiac disease (CD) and supported the superiority of the EmA test over ELISAs. They reported high sensitivities and specificities for some ELISAs that overlapped those of the EmA test.

We studied 285 children (107 males, 178 females; mean age, 8 years; range, 2–18 years), of whom 134 had CD and had been on a gluten-free diet for 3 (n = 17), 6 (n = 9), 12 (n = 16), 24 (n = 19), or >24 (n = 73) months. Histology in 108 children after 1 year on the diet showed a consistent improvement or complete recovery in all cases. One hundred fifty-one of the patients were children who consecutively underwent upper gastrointestinal endoscopy: CD was histologically diagnosed in 81 and excluded in 70 control cases. Diagnoses included absence of any lesion (n = 20), mild antral gastritis (n = 27), Helicobacter pylori infection (n = 15), reflux gastritis (n = 2), antral erosions (n = 2), Crohn disease (n = 2), graft-vs-host disease (n = 1), and portal hypertension (n = 1).

IgA or IgG anti-tTG autoantibodies in the sera were measured with seven different quantitative ELISAs that use human (h) or murine (m) antigen: h-tTG 1 IgA (EU-tTG IgA; Eurospital S.p.A.); h-tTG 2 IgA (Inova Diagnostics Inc.); h-tTG 3 IgA (CelikeyTM; Pharmacia & Upjohn); h-tTG 4 IgG (Inova); h-tTG 5 IgG (Celikey); m-tTG 6 IgA (EU-tTG IgA); and m-tTG 7 IgA (Inova). The areas under the ROC curves (95% confidence intervals) and the sensitivities (at cutoffs corresponding to a 95% specificity for control cases) were as follows: 0.88 (0.77–0.97) and 86% (7 arbitrary units) for h-tTG 1 IgA; 0.97 (0.92–1.00) and 96% (20 units) for h-tTG 2 IgA; 0.98 (0.96–1.00) and 95% (1.0 unit/mL) for h-tTG 3 IgA; 0.82 (0.73–0.91) and 54% (6.0 units) for h-tTG 4 IgG; 0.93 (0.87–0.99) and 89% (1.75 units/mL) for h-tTG 5 IgG; 0.92 (0.85–1.00) and 86% (5.0 arbitrary units) for m-tTG 6 IgA; and 0.92 (0.87–0.97) and 86% (10.0 units) for m-tTG 7 IgA. The three CD patients with false-negative results in one of the two more sensitive ELISAs (h-tTG 2 IgA) had negative results with all the other ELISAs. These three patients were EmA-negative, and although they did not have complete deficiency, total IgA values were low enough (0.41–0.82 g/L) to cause false negativity with any assay based on IgA antibody. Fig. 1 shows the h-tTG 2 IgA, m-tTG 7 IgA, h-tTG 3 IgA, and h-tTG 5 IgG results for the CD patients subdivided on the basis of the period of gluten withdrawal. Similar results were obtained with other ELISAs.

The study by Martini et al. (1) was prospective and concerned adults, whereas ours was retrospective and concerned children. Both studies show that ELISAs that use the human antigen have a very high sensitivity and specificity in diagnosing CD in both children and adults (e.g., Celikey had 95% sensitivity and specificity in our hands and 91% sensitivity and 94% specificity in the adults).

Fig. 1. Mean values and SE (error bars) obtained with four different ELISAs in CD children after gluten withdrawal. (A), comparison of anti-tTG antibodies of the IgA and IgG classes; (B), comparison of anti-tTG antibodies of the IgA class that recognize human or murine antigens.
hands of Martini et al.). Similar results were reported by Clemente et al. (2) and overlap those obtainable with EmA testing (3,4), which is subject to interobserver variation and is more time-consuming than ELISAs. Use of anti-tTG antibodies of the IgG class does not enhance the results obtained with anti-tTG antibodies of the IgA class. Gluten withdrawal in CD patients is accompanied by a decrease in anti-tTG antibodies that correlate with the duration of diet. We suggest that ELISAs that include human recombinant antigens can be used as a first-level investigatory tool in the diagnostic panel for CD. Actually, EmA testing appears to have limited clinical value in dubious cases. In fact, any result does not allow the clinician to avoid biopsy to confirm or exclude a diagnosis of CD (5). The quantitative ELISAs also seem to be useful indices for monitoring compliance with a gluten-free diet, especially in children.

References

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