Immunoglobulin A Antibodies to Helicobacter pylori

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Received 25 June 1997/Accepted 19 August 1997

Serological testing for immunoglobulin G (IgG) antibodies to Helicobacter pylori has proven useful in supporting the diagnosis of infection with this organism, but the clinical value of IgA antibodies in H. pylori-related gastritis remains controversial. The purpose of our study was to determine the frequency of IgA-positive IgG-negative patients with symptoms of gastrointestinal (GI) disorders, thus assessing the clinical utility of IgA testing for H. pylori-related gastritis. It was found previously that the frequency of infected individuals in this category (IgA positive and IgG negative) is about 2%, but a large number of IgG-negative patients with GI disorders suggestive of H. pylori infection have not been investigated until now.

In the early 1980s, it was found that Helicobacter pylori is associated with gastritis and peptic and duodenal ulcers and more recently, with gastric carcinoma (2, 4, 5, 10, 11, 15). Serological testing is often relied upon to determine the presence or absence of infection with this organism. Moreover, serology may be useful in monitoring the effectiveness of treatment in infected individuals (3, 7, 13). Immunoglobulin A (IgA) antibodies may appear earlier than IgG antibodies in patients who become reinfected after unsuccessful treatment with antibiotics (8, 14). Studies supporting the clinical utility of IgA serology have appeared. In the presence of IgG, IgA has been shown to correlate with active infection in 95 and 74% of cases of duodenal and gastric ulcers, respectively (6). IgA antibodies to H. pylori and low levels of pepsinogen I in patients’ sera increase the risk of gastric carcinoma (1). Yamamoto et al. have shown the IgA antibody to be 100% specific for H. pylori infection compared to Campylobacter-like organism test, culture, and histology (16). Two studies have noted few patients (2%) with confirmed H. pylori infection and with only IgA antibodies (6, 7). We have determined a more realistic frequency of IgA-positive IgG-negative patients with gastrointestinal (GI) disorders suggestive of infection, thus further assessing the clinical utility of IgA testing for H. pylori.

Sera collected from 824 patients and submitted to our reference laboratory for H. pylori IgG testing were included in the study. Patients’ sera were collected over a 3-week period and consisted of 526 negative, 290 positive, and 8 equivocal results for IgG antibody to H. pylori. Patients’ sera were from 453 females ranging from 3 to 95 years of age (mean, 50 years) and 371 males ranging from 1 to 90 years of age (mean, 47 years). All sera were stored at −20°C until all testing was completed. Patients with sera giving IgA-positive IgG-negative results (n = 38) were followed up to obtain additional information from the clinician that would support a diagnosis of infection with H. pylori.

Testing for IgA antibody against H. pylori was accomplished with an enzyme immunoassay (EIA) kit provided by HYCOR Biomedical Inc. (Irvine, Calif.). This EIA detects IgA antibodies against H. pylori-associated antigens (14 to 120 kDa). The performance of this EIA was validated against endoscopy (culture and histology) results from 396 patients with symptoms of GI disorders. One hundred fourteen patients were negative and 282 were positive for H. pylori by endoscopy. Compared with endoscopy, this H. pylori IgA EIA had a sensitivity of 90.2%, a specificity of 99.0%, and an accuracy of 92.8%.

Qualitative IgA values for patients’ sera were determined from the optical densities (ODs) obtained from four calibrator serum samples, and results were reported as negative, equivocal, moderately positive, or highly positive. Sera with ODs greater than that of the moderate control cutoff OD were considered as being positive for IgA antibody to H. pylori. All sera with equivocal results were retested. All assay procedures were followed as stated in the product insert.

All IgG testing was completed with EIA kits purchased from Enteric Products Inc. (Stony Brook, N.Y.). This EIA detects IgG antibodies directed against high-molecular-weight cell-associated proteins of H. pylori. The performance of this EIA kit was validated against the [13C]urea breath test (UBT) with 556 serum samples from patients with symptoms of GI disorders and from nonsymptomatic volunteers. Compared with the UBT, this H. pylori IgG EIA was 97.6% sensitive and 94.1% specific.

Semiquantitative values were calculated for each patient, and the assay results were categorized as follows: ≤1.7, negative; 1.8 to 2.2, indeterminate; and ≥2.3, positive. All sera with indeterminate results were retested. All assay procedures were followed as stated in the product insert.

Other than the IgA EIA kits, no funds were derived from the manufacturers for these experiments. Washing steps for all EIAs were accomplished with a Wellwash 4 automated EIA plate washer from Denley Instruments, Inc. (Durham, N.C.). ODs for EIAs were measured with a Thermomax bichromatic microplate reader from Molecular Devices Corp. (Menlo Park, Calif.).

Of the 526 serum samples that were negative for IgG antibody to H. pylori, 38 were positive for IgA, giving a frequency of 7.2% of IgA-positive IgG-negative sera (Table 1). Follow-up on these 38 patients revealed that all had symptoms of GI disorders which prompted the initial testing for IgG antibody to H. pylori. The possibility of infection with H. pylori was excluded by the clinician for the majority (30 patients [78.9%]) of these 38 patients based on a negative IgG result. No further testing or procedures were utilized (i.e., additional serology, UBT, endoscopy, Campylobacter-like organism test, histological examination, and culture) to further rule out infection with H. pylori.

Of the 38 patients, endoscopy was performed on 6 and ulcers

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Two of the 38 patients were tested for IgA antibody to H. pylori; positive IgA results were obtained for both by another reference laboratory. Symptoms in both patients subsided posttreatment with antibiotics, but one patient relapsed 3 weeks later. Two studies have shown that each of their patients (n = 2; n = 3) who were IgA positive and IgG negative was confirmed as H. pylori positive by culture and histology (6, 7). Moreover, IgA antibody may be specific for GI infection with H. pylori (16). Thus far, we have not found any patients reported in the literature in this category (IgA positive and IgG negative) that were not confirmed as being H. pylori positive. Therefore, a positive finding of IgA antibody to H. pylori in patients who are symptomatic may be of significant clinical value in supporting a diagnosis of infection, especially if IgG serology is negative.

**REFERENCES**


**TABLE 1. H. pylori IgA results compared to IgG results for serum samples from 824 patients**

<table>
<thead>
<tr>
<th>IgA result</th>
<th>No. of serum samples with the following IgG result:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive</td>
<td>121</td>
</tr>
<tr>
<td>Negative</td>
<td>131</td>
</tr>
<tr>
<td>Equivocal</td>
<td>38</td>
</tr>
</tbody>
</table>

| Total      | 290 | 526 |

*Frequency of IgA-positive IgG-negative sera, 7.2%.*