Expression of HLA-DR antigen in different histological types of gastric polyp

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Abstract

Aims: To study the expression of HLA-DR antigen in the different histological types of gastric polyps.

Methods: Ninety five cases of gastric polyps were histologically classified and examined for the presence of Helicobacter pylori, and for degree and type of inflammation. Further sections were stained immunohistochemically for HLA-DR antigen expression in the epithelium using a monoclonal antibody that was reactive to formalin-fixed paraffin wax embedded tissue.

Results: HLA-DR antigen was expressed in all of the inflammatory polyps studied (20/20), and in most hyperplastic (12/16) and adenomatous (4/6) polyps. Only a few fundic gland polyps (8/51) stained positively for HLA-DR antigen. Gastric polyps seem to have a greater tendency to express HLA-DR antigens than non-papillary gastric mucosa, even after considering the factors that may affect HLA-DR antigen expression, such as inflammation and the presence of H pylori.

Conclusions: Growth disturbances/polyp formation may be associated with increased HLA-DR antigen expression.

Class II HLA antigens comprise the gene products of the HLA-DR, DQ, and DP genes. These genes are located in the HLA-D region of the major histocompatibility complex (MHC) and they are important in the regulation of the immune response to T-cell-dependent antigens. Unlike class I HLA antigens, class II antigens have a more restricted tissue distribution, being present mainly in cells involved in the immune response—B lymphocytes, activated T lymphocytes, monocytes/macrophages and dendritic antigen-presenting cells such as Langerhans' cells. However, recent studies have shown that they can also be present in other tissues. In the stomach, in particular, it has been demonstrated that HLA-DR antigen is expressed in the epithelium in chronic gastritis. This expression was particularly marked when Helicobacter pylori organisms were present but was virtually absent in normal gastric epithelium. HLA-DR expression has also been observed in intestinal-type gastric carcinomas and is only very rarely present in the diffuse type of gastric carcinoma.

Gastric polyps provide a useful model to study HLA-DR expression since the various types of polyps arise through diverse mechanisms and constitute different types of growth disorders. HLA-DR antigen expression of gastric polyps and correspondingly inflamed non-papillary gastric mucosa when H pylori was not present were compared to see whether these growth disorders, of themselves, are able to affect its expression.

Methods

From January 1986 to December 1991, there were 122 gastric biopsies coded under “polyps” in the department files. They were taken from patients who had undergone gastro-duodenoscopy for gastrointestinal symptoms and/or surgical resection of polyps. Patients with gastric carcinoma, submucosal lesions and postgastrectomy polypoid lesions were excluded. A final total of 95 biopsies of gastric mucosal polyps was studied after excluding insufficient material/unsuitable cases (n = 27). The specimens were fixed in 10% buffered formalin. Paraffin wax embedded histological sections 4 μm thick were stained with haematoxylin and eosin and by the periodic acid–Schiff technique.

HISTOLOGICAL ASSESSMENT

Typing of gastric mucosal polyps

Gastric mucosal polyps were classified according to Appleman and Laxen et al with slight modifications.

Fundic gland polyp: short pits, masses of body-type glands close to the surface, and deep cystically dilated glands and/or pits. Inflammatory polyp: inflammation only with or without loss of normal gastric glands. Hyperplastic polyp: disorganised tubular or cystic overgrowth of hyperplastic but otherwise normal foveolar epithelium. Focal foveolar hyperplasia: distinctly elongated, hyperplastic but structurally well organised normal gastric pits; this category was not differentiated from hyperplastic polyps. Adenoma: abnormal tubular or villous structures lined by immature and poorly differentiated intestinal-type epithelium. Peutz–Jeghers polyp: redundant, branching and even cystic pits with few glands; branching of the muscularis mucosae may be minimal. The lamina propria is characteristically sparse and not inflamed.

A patient was counted only once if he had more than one specimen from a single or...
Hyperplastic types
Histological Fundic gland
Type 4
2
10102
No definite
3
Table
System.
of tags
respective
glandular epithelium
pattern
available
(Dako,
presence

Determination of the
expression of HLA-DR
antigen was
performed using
mouse monoclonal
antibody
(Dako, HLA-DR/alpha)
at a concentration of
1 in 50 (streptavidin-biotin
method). The gastric
surface/foveal and
glandular epithelium
were

Assessment of inflammation and H pylori
Histological gastritis was defined by a
modification of the system proposed by
McNulty et al. Mononuclear and
polymorphonuclear cellular infiltration were
each graded from zero to four. Gastritis was
diagnosed when the acute inflammatory score
was one or more, or when the chronic
inflammatory score was three or more. The
inflammation was considered acute if the
polymorphonuclear cellular score was one or more
with a mononuclear cellular score of under
three; and chronic if the mononuclear cellular
infiltrate was three or more with no acute
inflammation. Acute-on-chronic gastritis was
diagnosed when the acute and chronic
inflammatory scores were greater than zero and
two respectively.

The presence or absence of H pylori was
assessed by staining with haematoxylin and
eosin. In our previous studies and in a blinded
review by the same pathologist (AW) this was
as effective as the Giemsa method.

HLA-DR ANTIGEN
Further 4 µm thick sections were stained for
the presence of HLA-DR antigen with
commercially available mouse monoclonal
antibody (Dako, HLA-DR/alpha) at a
concentration of 1 in 50 (streptavidin-biotin
method). The gastric surface/foveal and

Table 1  HLA-DR antigen expression in gastric polyps

<table>
<thead>
<tr>
<th>Histological type</th>
<th>HLA-DR antigen</th>
<th>No of polyps</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fundic gland</td>
<td>0</td>
<td>51</td>
</tr>
<tr>
<td>Inflammatory</td>
<td>43</td>
<td>1+ 8</td>
</tr>
<tr>
<td>Hyperplastic</td>
<td>6</td>
<td>0</td>
</tr>
<tr>
<td>Adenomatous</td>
<td>16</td>
<td>2</td>
</tr>
<tr>
<td>Peutz-Jeghers</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>50</td>
<td>15</td>
</tr>
</tbody>
</table>

0, No definite staining; 1+, <10% staining; 2+, 10-50%
staining; 3+, >50% staining.

multiple polyp/s of the same histological type,
taken either during one procedure or on
separate occasions. If a patient had histology
of different polyps detected on a single
or separate occasion/s, he was entered as many
times as the different categories of polyps were
encountered.

The presence or absence of H pylori was
assessed by staining with haematoxylin and
eosin. In our previous studies and in a blinded
review by the same pathologist (AW) this was
as effective as the Giemsa method.

Table 2  Prevalence of Helicobacter pylori and inflammation in gastric polyps

<table>
<thead>
<tr>
<th>Histological type</th>
<th>Helicobacter pylori</th>
<th>Inflammation</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Positive</td>
<td>Negative</td>
</tr>
<tr>
<td>Fundic gland</td>
<td>1 (0)</td>
<td>50 (8)</td>
</tr>
<tr>
<td>Inflammatory</td>
<td>14 (1)</td>
<td>6 (6)</td>
</tr>
<tr>
<td>Hyperplastic</td>
<td>3 (2)</td>
<td>13 (10)</td>
</tr>
<tr>
<td>Adenomatous</td>
<td>0 (0)</td>
<td>6 (4)</td>
</tr>
<tr>
<td>Peutz-Jeghers</td>
<td>0 (0)</td>
<td>2 (1)</td>
</tr>
<tr>
<td>Total</td>
<td>16 (16)</td>
<td>77 (29)</td>
</tr>
</tbody>
</table>

Numbers in parentheses indicate the number of polyps showing HLA-DR antigen expression.

Results
Ninety patients were studied, 28 male and 62
female patients with an age range of 1-82 years
(mean 49 years). Thirty seven patients had
more than one gastric polyp—in 32 patients
they were histologically similar and in five each
had two different types of polyp. A total of 95
biopsies were studied and they were classified as
follows: 51 fundic gland (54%), 20 inflammatory
(21%), 16 hyperplastic (17%), six
adenomatous (6%) and two Peutz-Jeghers
(2%) polyps. Overall, 45 polyps stained for
HLA-DR antigen (table 1); 18 polyps were
colonised by H pylori; 45 polyps were
infected with acute-on-chronic inflammation present in
38, just acute inflammation in six and just
chronic inflammation in one polyp (table 2).

FUNDIC GLAND POLYPS
Eight of the 51 polyps (16%) stained for HLA-
DR antigen (table 1). The staining was only 1+
in extent and tended to be localised to the
surface/foveal epithelium rather than
glandular epithelium (fig 1). The polyps were
generally non-inflamed and only one case
tained H pylori. None of the fundic gland
polyps which expressed HLA-DR antigen was
colonised by H pylori; however, two of them were
acutely infected (table 2).

INFLAMMATORY POLYPS
All of the 20 inflammatory polyps (100%)
stained positively for HLA-DR antigen and
staining was often extensive (table 1) (fig 2). Most
of them contained H pylori (70%).

Acute-on-chronic inflammation was present in
17 (85%) of the polyps and acute inflammation
alone in the remaining three (15%) (table 2).

HYPERPLASTIC POLYPS
Most polyps, 12 out of 16 (75%), stained
positively for HLA-DR antigen and the extent
of staining was evenly distributed between 1+
and 2+ (table 1, fig 3). Only three contained
organisms (19%). Most of the polyps were
infected: 13 showed acute-on-chronic (81%) and
one chronic inflammation only.

ADENOMATOUS POLYPS
Four out of six polyps (67%) were positive for...
HLA-DR antigen expression in gastric polyps

Figure 1 Immunoperoxidase staining of a fundic gland polyp showing only focal HLA-DR antigen expression in a gland.

Figure 2 Immunoperoxidase staining of an inflammatory gastric polyp showing extensive HLA-DR antigen expression in the epithelium.

Figure 3 Immunoperoxidase staining of a hyperplastic gastric polyp showing focal HLA-DR antigen expression in the hyperplastic mucus-secreting epithelium.

Figure 4 Immunoperoxidase staining of an adenoma showing HLA-DR antigen expression in neoplastic epithelium.

HLA-DR antigen (table 1, fig 4). None of the polyps contained any organisms. Five (83%) showed acute-on-chronic inflammation and the other polyp had acute inflammation only.

PEUTZ-JEGHERS POLYPS

There were only two cases of which one showed HLA-DR antigen staining. Only one polyp was inflamed with acute-on-chronic inflammation. None of the polyps contained any organisms.

Discussion

We previously studied HLA-DR antigen expression in non-inflamed and inflamed gastric mucosa. In our experience, HLA-DR antigen was not expressed in histologically normal mucosa. In inflamed mucosa—acute-on-chronic and chronic gastritis—the expression of this antigen was low in the antrum, being present in only seven of 18 cases (39%) and lower still in the body mucosa when *H pylori*...
was not present. When *H. pylori* was present, the expression of the antigen was markedly increased, rising to 92% or 11 out of 12 cases in the antrum. For this study on gastric polyps we employed the same methodology for the study of HLA-DR antigen expression in the gastric epithelium. When we considered only those polyps which were negative for *H. pylori*, the percentage of cases showing HLA-DR antigen expression was unexpectedly high—100% of the inflammatory (6/6), 77% of the hyperplastic (10/13), 67% of the adenomatous (4/6) and 50% of the Peutz-Jeghers (1/2) polyps stained positively for the antigen (table 2). Overall, the percentage of gastric polyps, excluding fundic gland polyps, expressing HLA-DR antigen in the absence of *H. pylori* was 78% (21/27) (table 2). In this comparison, we have excluded fundic gland polyps because the overwhelming majority were non-inflamed. Since normal gastric mucosa does not express HLA-DR antigen, we expected fundic gland polyps to be similarly negative for HLA-DR antigen expression. Despite this, eight fundic gland polyps expressed HLA-DR antigen although six of these were not inflamed and none contained *H. pylori* (table 2).

Our results would seem to indicate that aside from inflammation and the presence of *H. pylori*, gastric polyp formation may be associated with aberrant HLA-DR antigen expression. It was not unexpected for adenomas to have a high rate of HLA-DR expression (67%) since previous studies showed the antigen to be expressed in 74% of intestinal-type gastric carcinomas. It was surprising that the prevalence of antigen expression was higher than expected, considering the inflammatory status and the presence of organisms, even for inflammatory, hyperplastic, and fundic gland polyps. One possible explanation is that all gastric mucosal polyps, neoplastic and non-neoplastic in nature, are in some way associated with the release of growth factors that may in turn be able to affect the expression of class II HLA antigens. It is interesting to note that both platelet-derived growth factor (PDGF) and epidermal growth factor (EGF) may have the ability to regulate the production of gamma interferon, a potent inducer of class II HLA antigens, by T cells and increase the expression of class II MHC antigens on antigen-presenting cells. The increase in HLA-DR antigen expression in the epithelium of gastric polyps could be affected by these or similar growth factors.

The functional significance of HLA-DR antigen in gastric polyps is not known. Since T helper cells are able to recognise antigens in association with class II antigens, the expression of class II antigens on the surface of gastric epithelial cells may lead to the development of gastric antibodies. Further studies are necessary to test this hypothesis.

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