INTRODUCTION
Recently, a number of researches show that COX-2 was expressed at a very high level in gastrointestinal tumors. However, we know less about COX-2 expression in gastric cancer, especially the relationship between COX-2 overexpression and typing, degree, differentiation, lymph node metastasis of gastric cancer. In this paper, we investigated the expression of COX-2 proteins in gastric mucosal lesions and assessed the relationship between COX-2 expression and the type, pathologic stage, differentiation, or lymph node metastasis in gastric cancer and the relationship between expression of COX-2 and H pylori infection in gastric mucosal lesions.

MATERIALS AND METHODS

Abstract

AIM: To investigate the expression of COX-2 proteins in gastric mucosal lesions and to assess the relationship between COX-2 expression and type, pathologic stage, differentiation, or lymph node metastasis in gastric cancer and the relationship between COX-2 expression and H pylori infection in gastric mucosal lesions.

METHODS: Thirty patients with gastric carcinoma underwent surgical resection. Samples were taken from tumor site and paracancerous tissues, and ABC immunohistochemical staining was used to detect the expression of COX-2 proteins. H pylori was determined by rapid urea test combined with pathological staining/14C urea breath test.

RESULTS: The positive rate and staining intensity of mutant COX-2 gene expression in gastric cancer were significantly higher than those in paracancerous tissues (66.7% vs 26.7%) (P < 0.01, P < 0.001). There was a significant correlation between COX-2 and pathologic stage or lymph node metastasis type of gastric carcinoma (76.0% vs 20.0%, 79.2% vs 16.7%) (P < 0.05). No correlation was found between COX-2 expression and type or grade of differentiation (P > 0.05). COX-2 expression of intestinal metaplasia (IM) or dysplasia (DYS) with positive H pylori was significantly higher than that with negative H pylori (50.6% vs 18.1%, 60.0% vs 33.3%) (P < 0.05).

CONCLUSION: COX-2 overexpression was found in a large proportion of gastric cancer tissues compared with matched non-cancerous tissues and was significantly associated with advanced tumor stage and lymph node metastasis. Overexpression of COX-2 plays an important role in tumor progression of gastric cancer. COX-2 may also play a role in the early development/promotion of gastric carcinoma and is associated with H pylori infection.

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Expression of COX-2 proteins in gastric mucosal lesions.

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Expression of COX-2 proteins in gastric mucosal lesions.
New COX isoyme-COX-2, is not expressed in normal tissues, but expressed at a high level in inflammatory tissues. It has been shown in animal studies that COX-2 expression can enhance PGE2 production, which induces cell proliferation and bcl-2 expression. These can destroy the balance between proliferation and apoptosis and induce tumors. More and more studies have shown that COX-2 could express at a high level in human colorectal tumor[1-5] and other gastrointestinal tumors[6-8]. COX-2 overexpression was found in well-differentiated epidermoid carcinoma of the esophagus. Ratnasinghe[9] studied the COX-2 expression in epidermoid carcinoma of the esophagus and found that COX-2 expressed at a high level in well-differentiated tumors, at a low positive level in the normal esophagus, and negative in poorly-differentiated tumors. Hao[10] found COX-2 protein expressed at a high level in adenocarcinoma and adenoma of colon, compared with normal mucosal tissues. COX-2 mRNA expressed in tumor tissues at a significantly higher level than that in normal tissues. There was neither a relationship between COX-2 protein expression and proliferation degree or volume of adenoma, nor a relationship between COX-2 expression and tumor differentiation, Duke’s stage as well as lymph node metastasis (P>0.05). Interestingly, COX-2 expressed in the tissues near adenocarcinoma or adenoma at a higher level than in normal mucosal tissues (P<0.0001), but lower than that in adenocarcinoma or adenoma itself (P<0.001, P<10⁻⁵).

It has been found that the positive rate of COX-2 expression in gastric cancer tissue was 60%-70%[6-8]. Ratnasinghe[9] found that COX-2 expressed positively in 36% cardia adenocarcinoma and 60% gastric body adenocarcinoma in his research on 19 patients with cardia adenocarcinoma and 15 patients with gastric body adenocarcinoma. COX-2 overexpression was found in most of gastric body adenocarcinoma and some cardia adenocarcinoma tissues. It is necessary to further confirm the status of COX-2 expression in gastric cancer tissues, especially the characteristics of COX-2 overexpression related to typing, degree, differentiation and lymph node metastasis[11-15]. We studied the COX-2 expression at gene and protein levels in tissues with gastric mucosal lesion, and explored the relationship between COX-2 expression and gastric carcinoma and H pylori infection at pathological and pathophysiological levels.

Our study based on 30 tissue samples with gastric cancer as well as paracancerous tissues showed that COX-2 protein expressed at a high level in tumor tissues, which was significantly higher than that in paracarcinoma tissues (P<0.01), and also significantly higher in tumor tissues (P<0.01). COX-2 positive expression in gastric cancer tissues at the developing stage was significantly higher than that at early stage, the positive rate in gastric cancer with lymph node metastasis was significantly higher than that without lymph node metastasis (P<0.05), but the COX-2 positive expression in intestinal type of gastric cancer was the same as that in gastric type of gastric cancer. The positive rate in gastric cancer with low or no differentiation (80%) was not higher than that with high or moderate differentiation (57.1%) (P>0.05), (Table 3).

### Table 1 COX-2 expression in gastric cancer and paracancerous tissues

|          | Number | COX-2 expression intensity | Positive rate n (%) |
|----------|--------|----------------------------|---------------------|
| Gastric cancer | 30     | 10                          | 4                   | 8                   | 8                   | 20 (66.7%) |
| Paracancerous tissue | 30     | 22                          | 6                   | 2                   | 0                   | 8 (26.7%)  |

**a** P <0.001 gastric cancer vs paracancerous tissue; **b** P <0.01 gastric cancer vs paracancerous tissue.

### Table 2 COX-2 expression in gastric mucosa with H pylori infection, n (%)

| Groups                      | Number | COX-2 positive expression intensity | Positive rate n (%) |
|-----------------------------|--------|------------------------------------|---------------------|
| CG (n=30)                   |        |                                    |                     |
| Hp+                         | 25     | 5                                  | 1(0.4%)             |
| Hp -                        |        |                                    |                     |
| IM (n=19)                   |        |                                    |                     |
| Hp+                         | 9      | 11                                 | 5(50.6%)            |
| Hp -                        |        |                                    |                     |
| DYS (n=11)                  |        |                                    |                     |
| Hp+                         | 5      | 6                                  | 3(60.0%)            |
| Hp -                        |        |                                    |                     |
| GC (n=30)                   |        |                                    |                     |
| Hp+                         | 11     | 19                                 | 11(72.7%)           |
| Hp -                        |        |                                    |                     |

**a** P <0.05, IM or DYS (H pylori positive) vs IM or DYS (H pylori negative).

### Table 3 COX-2 expression in gastric cancer tissues

| Groups                      | Number | COX-2 positive expression intensity | Positive rate n (%) |
|-----------------------------|--------|------------------------------------|---------------------|
| Intestinal type             | 24     | 16 (66.7)                          |                     |
| Gastric type                | 6      | 4 (66.7)                           |                     |
| Stage                       |        |                                    |                     |
| Early stage                 | 5      | 1 (20.0)                           |                     |
| Developing                  | 25     | 19 (76.0%)                         |                     |
| Differentiation (Intestinal type) |        |                                    |                     |
| High and moderate           | 14     | 8 (57.1)                           |                     |
| Low and no differentiation  | 10     | 8 (80.0)                           |                     |
| Lymph node metastasis       | 6      | 1 (16.7)                           |                     |
| Without metastasis          | 24     | 19 (79.2%)                         |                     |

**a** P <0.05, developing stage vs early stage; metastasis vs no metastasis.

### DISCUSSION

Yu LZ et al. Expression of COX-2 proteins in gastric mucosal lesions.
We also found that COX-2 expression in tissues with Helicobacter pylori positive intestinal metastasis or dysplasia was significantly higher than that in tissues with H pylori negative infection. H pylori could induce acute and chronic inflammation of gastric mucosa, and the production of cell factors such as IL-8 and IL-1β, and the secondary high COX-2 expression which caused gastric mucosal lesions. H pylori infection could also induce gastric mucosal cell proliferation by COX-2 expression. COX-2 gene expression was one of the related factors mediating the progress from gastritis with H pylori infection to pre-carcinoma lesions even gastric carcinoma. Based on this study, treatment of H pylori infection and special COX-2 inhibitor could be useful for the prevention of gastric carcinoma.

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