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Gastric intestinal metaplasia eleven years after randomized selective proximal vagotomy for peptic ulcer

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Summary. The presence of intestinal metaplasia (IM) 11 years after selective proximal vagotomy (SPV), selective proximal vagotomy with pyloroplasty (SPV + PP) and selective vagotomy with pyloroplasty (SV + PP) was investigated in 38 consecutive patients. IM was significantly more frequent in SPV than in SV + PP, SPV + PP or in unoperated controls of matching ages. IM occurred more frequently both at an older age (≥60 years) in SPV and in a larger number of gastric areas than in the other group of patients. Reports in the literature indicate that vagotomy may increase the risk of gastric carcinoma and that IM may antedate malignant transformation. It would thus appear that patients previously operated with SPV (without pyloroplasty) having IM, should be the group of patients to be enrolled in endocospical surveillance programs for detection of possible cancer development.

Key words: Intestinal metaplasia, Selective proximal vagotomy, Selective vagotomy, Pyloroplasty

Introduction

Many reports in the literature have demonstrated that gastric resection for peptic ulcer disease may increase the risk of malignant transformation in the gastric remnants (Nicholls, 1974; Domellöf and Janunger, 1977; Caygill et al., 1986; Carter, 1987; Northfield, 1990). This complication of peptic ulcer surgery has become a matter of much concern in latter years and endoscopic surveillance programmes have been proposed for previously resected patients (Domellöf et al., 1977; Mortensen et al., 1984; Sonnenberg, 1984).

The advent of alternative surgical procedures in the treatment of peptic ulcer disease such as vagotomy and pyloroplasty (Emås and Fernström, 1985), imply the anatomical preservation of that organ. In later years an increased number of cases of gastric carcinoma have been reported for patients previously subjected to vagotomy and drainage (Toten et al., 1983; Watt et al., 1983, 1984). These observations have also been recorded experimentally in rats (Tatsuta et al., 1988a), suggesting that gastric carcinogenesis may be enhanced by a previous vagotomy. More recently it was demonstrated that rats submitted to truncal vagotomy without pyloroplasty and intragastric instillation of 5% NaOH solution (Tatsuta et al., 1988b) or to pyloroplasty with or without vagotomy (Fujii et al., 1985) resulted in a significant increase in intestinal metaplasia of the gastric mucosa. The same phenomenon has been reported in humans (Fujita and Kusama, 1986) after selective proximal vagotomy. The importance of this finding resides in the fact that intestinal metaplasia has been regarded for many years as one of the precursors of gastric carcinoma (Ming et al., 1967; Rubio et al., 1987).

In the present work, we investigated the presence of intestinal metaplasia (IM) of the human gastric mucosa 11 years after selective proximal vagotomy (SPV), selective proximal vagotomy with pyloroplasty (SPV + PP) and selective vagotomy with pyloroplasty (SV + PP) for prepyloric, pyloric or duodenal ulcer.

Materials and methods

The material comprehends 38 consecutive patients undergoing routine endoscopy during the long-term follow-up of a randomized trial of SPV, SPV + PP and SV + P, for treatment of prepyloric, pyloric or duodenal ulcer (Emås and Fernström, 1985). The average interval between surgery and endoscopy was 11.3 ± 1.4 (± SD) years. Nine of the 38 patients had been operated with SPV which preserves the innervation of the antrum, 16 with SPV + PP and 13 with SV + PP. The latter group has accordingly the antrum vagally denervated. In addition, 18 patients of matching ages having no previous gastric surgery and without ulcers or carcinoma were biopsied. The randomized trial was approved by the Ethical Committee at the Karolinska Institute, Stockholm.

In all patients, 7 biopsies were obtained under

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gastroscopic control: 3 from the antrum (1 from the lesser curvature, 1 from the anterior wall and the third from the posterior wall); 1 from the junction zone at the lesser curvature; and the remaining 3 from the fundic mucosa (1 from the lesser curvature, 1 from the anterior wall and the remaining one from the posterior wall). All biopsies were reviewed without knowledge of the type of operation performed, and specimens containing IM were recorded. The histological criteria of IM have been presented elsewhere (Rubio et al., 1987).

The differences between groups were evaluated by Fisher's exact test, and a p-value of 0.05 or less was considered as significant.

Results

Intestinal metaplasia and type of vagotomy performed

Table 1 shows that 88% of the patients with SPV had IM. In patients with SPV or SV both with pyloroplasty, the rates were lower; 43.7% (p=0.037) and 38.5% (p=0.027), respectively. In non-operated control cases, the rate of IM, 44.4%, was similar to that in vagotomized patients with pyloroplasty, but lower (p=0.036) than in patients with SPV alone.

Age and intestinal metaplasia in vagotomy patients

From the results in table 2 it may be deduced that the SPV-patients tended to be younger than the patients with SPV + PP or SV + PP. It is also seen that 55.% of the SPV and of control patients were 60 years of age or more. For SV + PP and for SPV + PP, the percentages were 69.2% and 62.5%. IM occurred at an older age (≥60 years) in 55.6% of 9 SPV-operated patients, in 25.0% of 16 SPV + PP operated and in 23.1% of 13 SV + PP. In control cases the percentage of older patients with IM was 27.8%. Table 2 also shows that all five SPV patients being ≥60 years old had IM (100%) but only 40.0% of SPV + PP patients, 33.3% of SV + PP and 50.0% of control patients.

Sex and intestinal metaplasia

The material consisted of 24 operated males and 14 operated females. In the control group, 12 were males and 6 females (Table 2). The number of cases was too small for statistical analysis of the frequency of IM in males and females in each of the four groups presented.

Number of biopsies containing intestinal metaplasia

The results in Table 3 show that IM was present in four or more of the seven biopsies in three of the nine SPV-operated patients. In patients with SPV + PP or SV + PP, IM usually occurred at only one localization. Also in control patients, the majority had IM in only one or two localizations.

Discussion

The results of the present investigation have demonstrated that IM of the gastric mucosa is significantly more frequent after SPV than after SV + PP or SPV + PP. Interestingly, the frequency of intestinal metaplasia was similar after the latter two operations as well as in unoperated controls. The difference was more obvious for older patients (i.e. ≥60 years).

Fujita and Kusama (1986), using Congo red staining to detect acid-secreting gastric areas, demonstrated endoscopically that SPV + PP did not result in a rapid development or progress of intestinal metaplasia of the gastric mucosa. Our histological studies (with regard to SPV + PP-operated patients) are thus in accordance with

Table 1. Sex and intestinal metaplasia (IM) in gastric biopsies from 56 patients: in 9 with SPV, 16 with SPV+PP, 13 with SV+PP as well as in 18 unoperated control patients.

	MALES (IM Total)	FEMALES (IM Total)
SPV	5/5	3/4
SPV+PP	6/13	1/3
SV+PP	1/6	4/7
CONTROLS	6/12	2/6
ALL	18/36	10/20

Table 2. Age and intestinal metaplasia (IM) in gastric biopsies from 56 patients: in 9 with SPV, 16 with SPV+PP, in 13 with SV+PP as well as in 18 unoperated controls patients.

	SPV IM/Total	SPV+PP IM/Total	SV+PP IM/Total	CONTROLS IM/Total	ALL
20-29					
30-39		1/1		0/2	1/3
40-49	1/1		2/3	1/2	4/6
50-59	2/3	2/5	0/1	2/4	6/13
60-69	3/3	3/7	1/6	2/5	9/21
70-79	2/2	1/3	2/3	3/5	8/13
80					
ALL	8/9	7/16	5/13	8/18	28/56

Table 3. The number of biopsies containing intestinal metaplasia (IM) in 56 patients: in 9 with SPV, 16 with SPV+PP, 13 with SV+PP as well as 18 unoperated controls. Seven biopsies were taken from predetermined areas of the gastric mucosa in each case.

No. BIOPSIES WITH IM	SPV	SPV+PP	SV+PP	CONTROLS
1	1	5	4	2
2	2	1		6
3	2	1		
4	1			
5	1		1	
6	1			
7				

the findings of Fujita and Kusama (1986).

Previous investigations (Rubio et al., 1987) have demonstrated that IM increases with age. In the present work, age was also an important factor in the occurrence of IM in SPV patients. However, SPV patients had more IM than the other groups in spite of the fact that these were younger than the SPV + PP and SV + PP patients.

The finding that IM was more common after SPV than after SV or SPV, both with pyloroplasty, and the finding that IM was more widespread in the stomach after SPV than following the other two surgical procedures is of particular interest.

It may be argued that IM is focally distributed in the gastric mucosa and therefore pinch biopsies are not able to evidence all areas with IM. However, areas with IM can easily be detected by a trained gastroendoscopist. In fact, all endoscopies in the present work were performed by one of us (H.N). who has many years of experience in gastric endoscopy. Moreover, 3 of the 7 biopsies were taken from the lesser curvature, the preferred site for IM (Rubio et al., 1990).

In a previous work (Rubio et al., 1987) we found a lower percentage of IM (32.3%) in 359 Swedish patients without previous surgery. In that study, only 3 biopsies had been taken from the gastric mucosa; 38.2% of older patients (≥60 years) had IM. When the number of gastric biopsies was increased to 7 (as in the present work), 50.0% of the 34 patients being ≥60 years of age had IM. Thus, by increasing the tissue sampling in the gastric mucosa from 3 to 7, more areas with IM were detected. Thus, the number of biopsies taken at endoscopy is important when comparing results of IM between different hospitals.

By studying the same number of biopsies, we found here that SPV patients had twice as much IM than the other groups investigated.

This is the first study in which 7 gastric biopsies have been taken from predetermined areas in vagotomized patients with long follow-up as well as in unoperated controls. If the results of the present work are confirmed in a large number of patients, it would appear that patients previously operated with SPV without pyloroplasty should be the group of patients to be included in proposed (Domellöf et al., 1977; Mortensen et al., 1984; Sonnenberg, 1984) endoscopical surveillance programmes for detection of possible cancer development.

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