Peptic ulceration in Crohn’s disease (regional enteritis)

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SUMMARY The incidence of peptic ulceration in a personal series of 300 patients with Crohn’s disease was 8%. Resection of 60 or more centimetres of the small intestine was associated with significantly increased acid output, both basally and following pentagastrin stimulation. Only five (4%) of the 124 patients who received steroid therapy developed peptic ulceration. It is suggested that resection of the distal small bowel may be a factor in the probable increase of peptic ulceration in Crohn’s disease.

Peptic ulceration was observed in 4% of 600 patients with Crohn’s disease by van Patter, Bargen, Dockerty, Feldman, Mayo, and Waugh in 1954. Cooke (1955) stated that 11 of 90 patients with Crohn’s disease had radiological evidence of peptic ulceration whilst Chapin, Scudamore, Bagenstoss, and Bargen (1956) noted duodenal ulceration in five of 39 (12.8%) successive patients with the disease who came to necropsy. In 1958, Jackson found that 13% of his 126 patients had duodenal ulcers whilst Crohn and Yarnis (1958) wrote ‘gastric secretory changes are unusual’ and only 20 of their 542 patients had evidence of peptic ulceration. Atwell, Duthie, and Golligher (1965) reported that 11 or 8.1% of their series had previous evidence of ulceration, and in 1966 Gjone, Myron, and Orning commented that four of 72 newly diagnosed patients with regional enteritis had similar evidence of ulceration.

This paper reports gastric secretory studies in regional enteritis and the incidence of peptic ulceration in a personal series of patients with regional enteritis.

Clinical Materials and Methods

Three hundred patients (143 men and 157 women) with Crohn’s disease have been followed between 1944 and 1969 for a mean period of 11.7 years with a mean duration of the disorder of 13.7 years. Fifty-one of these patients had Crohn’s colitis. Diagnosis in this series was based on macroscopic or histological criteria in 273 patients, on clinical and radiological data in 25 patients, and on clinical data together with minor radiological features in two patients with colonic disease. The presence of peptic ulceration was determined by radiology in association with ulcer dyspepsia and was confirmed in nine patients at surgery. None of the patients had gastroduodenal Crohn’s disease.

Gastric secretory studies were performed on 22 patients (12 men and 10 women) with regional enteritis. None had any history of ulcer type dyspepsia or of treatment with corticosteroids or ACTH within the last 12 months. Of these patients, eight men and three women had had more than 60 cm of small intestine resected; four men had had no resection. Basal gastric secretion was collected for 30 minutes before the intravenous infusion of 6 μg pentagastrin per kilogram for one hour. Four 15-minute collections were made and volumes recorded. The acid content was determined by titration against N/10 sodium hydroxide to end point pH 7.0 using a Radiometer pH instrument. All results were expressed as milli-equivalents of acid per hour. Peak hour output was determined by the sum of the two maximum outputs in 15 minutes multiplied by 2. The results were analysed as a whole and in subgroups.
according to disease activity, sex, age at diagnosis, and length of small intestine resected.

Results

The results of the gastric secretory studies are shown in Table I. There was a significant difference in acid production between the 12 male and 10 female patients with regional enteritis in the hour after stimulation (0.01 > p < 0.001). There was no significant difference between the acid production of eight men who had 60 cm or more resected and that of 20 patients (19 men and one woman) without regional enteritis but with surgically proven duodenal ulcers. Also the gastric secretions of these eight patients were significantly different from those of the four males who had no resection, p being between 0.05-0.02, 0.01-0.001, and 0.02-0.01 respectively for the basal, post-stimulatory, and peak hour outputs. There was no relationship between gastric secretion and disease activity or age at diagnosis.

Amongst the patients with regional enteritis 24 (8%) had evidence of peptic ulceration: 19 men (13-3%) and five women (3-2%): Since none of the patients with Crohn's colitis had peptic ulceration, the incidence of ulceration associated with small intestinal involvement becomes 10%; 19 in 111 men (17-3%) and five in 138 women (3-8%). Of the 19 men, 14 had duodenal ulcers, two gastric ulcers, and three both gastric and duodenal ulcers. These findings are summarized in Table II. The follow-up period for patients with peptic ulcer averaged 11.5 years, ranging from one to 22 years.

Five patients, all men, had the duodenal ulcers before and not obviously related to the onset of Crohn's disease. Another eight patients (four men and four women) had peptic ulceration diagnosed at the same time as the intestinal disorder. Four men developed ulceration after

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Table I  The mean and standard error of the gastric acid secretion in men and women with regional enteritis and in patients with surgically proven duodenal ulceration

<table>
<thead>
<tr>
<th>Group</th>
<th>No. of Patients</th>
<th>Acid Secretion (m-equiv/hr)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Basal</td>
<td>One Hour after Stimulation</td>
</tr>
<tr>
<td>Regional enteritis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Males</td>
<td>12</td>
<td>3.11 ± 0.87</td>
<td>28.75 ± 2.35</td>
</tr>
<tr>
<td>Resection (&gt; 60 cm)</td>
<td>8</td>
<td>4.12 ± 1.17</td>
<td>33.56 ± 2.29</td>
</tr>
<tr>
<td>Females</td>
<td>10</td>
<td>2.05 ± 0.60</td>
<td>18.85 ± 2.08</td>
</tr>
<tr>
<td>Duodenal ulcer</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No resection</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Males (19) Females (1)</td>
<td>20</td>
<td>6.73 ± 1.28</td>
<td>32.18 ± 2.93</td>
</tr>
</tbody>
</table>

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Table II  Sex and age at onset of Crohn's disease and of peptic ulcer, the relationship to resection and amount resected, the incidence of gastric and duodenal ulcers, and the type of operation carried out
the diagnosis of Crohn’s disease and before resection of the small intestine. One of these (case 225) had duodenal ulceration at the time of diagnosis and is included amongst the four cited above. Twenty years later, this patient who had involvement of more than 150 cm of small intestine with fibrosing regional enteritis, developed a gastric ulcer which responded to medical treatment only to relapse following resection of small intestine thus necessitating partial gastrectomy. Case 122, who had diffuse jejuno-ileal involvement, developed a duodenal ulcer necessitating operation for its relief. Cases 26 and 326 had less severe involvement of the small intestine. One woman, case 285, a sister of case 122, developed duodenal ulceration following bypassing 150 cm of small intestine. Of the remaining seven patients, all men, who developed ulceration following resection of varying lengths of intestine, one developed gastric ulceration and severe haemorrhage following the administration of butazolidin. Three had received steroid therapy, two developing duodenal ulcers and one an ulcer on the greater curvature of the stomach. This latter case had previously developed duodenal ulceration following his first intestinal resection.

Discussion

Resection of 60 cm of small intestine resulted in the three female patients secreting the same amount of gastric acid as men without resection and the eight men secreting comparable quantities to those encountered in patients with surgically proven duodenal ulcers and significantly more than the men with no resection. Such results are perhaps to be expected, for the small intestine has been thought to exert an influence on gastric acid secretion for many years. Kosaka and Lim (1930) showed that mucosal extracts of small intestine exposed to oil had an inhibitory effect upon the acid production of a denervated gastric pouch and suggested the term ‘enterogastrone’ to describe this mucosal agent. The innervated stomach may also be affected by bowel resection, for Frederick, Sizer, and Osborne (1965) showed that gastric secretion in dogs could be increased progressively by increasing lengths of intestinal resection, 75% resection producing 176% increase in gastric secretion. Menguy (1960) demonstrated that bile salts were involved in gastric inhibition by fat and speculated that this inhibition was mediated by re-absorbed bile salts. Whether the failure of adequate bile salts re-absorption is a factor in the increased gastric secretion in some patients with regional enteritis will need further investigation, but it is clearly an attractive hypothesis.

It is debatable whether the incidence of peptic ulceration in this series represents an increase as compared with the general population, for adequate representative figures are difficult to obtain. Doll and Jones (1951) found the incidence of peptic ulceration between the ages of 15 and 65 in a London population in men to be 5.8% and in women 1.9%. The incidence of peptic ulceration in men before the onset of Crohn’s disease was 4.9%, so that in men of this series there may well have been an increased incidence later. Certainly the occurrence of peptic ulceration in a brother and sister both with diffuse jejuno-ileal involvement which necessitated, in both, operation before the age of 22 argues in favour of some influence being exercised by Crohn’s disease. In these two patients, in two other patients (cases 26 and 326) there was extreme fibrosis of the intestine following diffuse jejuno-ileitis and this may well have had a similar effect to that of resection. Of the 22 male patients who had more than 60 cm resected, five (23%) subsequently developed duodenal ulcers.

Only five (4%) of the 124 patients who received steroid therapy developed peptic ulcers. The influence of this therapy was clear in two patients who developed ulcers on the greater curvature of the stomach. The remaining three patients developed duodenal ulcers after resection of more than 60 cm in two of them and 40 cm in the third so that the influence of steroid therapy must remain doubtful in these patients.

The frequency of peptic ulceration in this series is such that it has been of some clinical importance. Though the increase in women was slight, approximately one male patient in six with small-intestinal involvement was troubled symptomatically with peptic ulceration.

References

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