Heterotopic gastric mucosa in the duodenum

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SUMMARY Thirteen patients are described who, on routine endoscopy of the upper gastrointestinal (GI) tract, were found to show a characteristic appearance in the proximal duodenum. This consisted of multiple small mucosal nodules, predominantly in the anterior wall. All cases were biopsied, and showed identical histological appearances of heterotopic gastric mucosa of body type.

The incidence of this condition is probably much higher than reported previously, and may be present in up to 2% of the population. In all our patients a diagnosis was reached, other than heterotopic gastric mucosa, to explain the GI tract symptoms. In none was a healed or active duodenal ulcer evident and in none was there a history of a pre-existing ulcer. In our opinion these nodules are probably of little or no clinical significance.

Heterotopic tissue is well known to occur in the alimentary tract. Pancreatic heterotopia is found in both the stomach and duodenum, while in Meckel's diverticulum gastric mucosa or pancreatic tissue can be seen.1 Isolated cases of heterotopic gastric mucosa have been reported at all levels of the alimentary tract from the oesophagus to the rectum.2 These cases are regarded as congenital in origin due to abnormal embryological development.

Epithelium resembling gastric mucosa of the non-specialised antral or pyloric type is seen in a variety of conditions—for example, inflammatory bowel disease. This change occurs secondary to the chronic inflammation and hence is strictly a metaplastic change. Similarly it is well recognised that in duodenitis and peptic ulceration, the surface epithelium may change to a gastric type, this again representing metaplasia, rather than true heterotopia.3 Unfortunately many authors have made the mistake of combining metaplasia and true heterotopia under the term heterotopic gastric mucosa. As a result many of the conclusions drawn seem to be incorrect.

With the increasing use of fibreoptic endoscopy, biopsies from the upper GI tract form a considerable proportion of the work load of pathology departments. It would not be surprising if occasionally a lesion is found incidentally at endoscopy which although unusual may have little or no clinical significance. We wish to report a series of 13 cases which seem to represent a well defined clinico-pathological entity, whose recognition has been obscured by previous reports.

CLINICAL EXAMINATION The 13 cases were seen over an 18-month period in the endoscopy unit of Withington Hospital. Annually 1500 endoscopies are performed. One endoscopist (DFM) identified 12 of the 13 cases and he personally had performed 30% of the total endoscopies. All patients had been referred for investigation of upper GI tract symptoms (Table). There were five men and eight women patients with an age range of 33-82 yr (mean age 56 yr). The characteristic endoscopic appearance was of multiple small mucosal nodules, usually less than 1 cm diameter, situated in the first part of the duodenum. These were more commonly seen in the anterior wall (Fig. 1). In all cases, the endoscopist was absolutely certain that he had passed through the pylorus and was in the duodenum. Five cases had repeat endoscopies at a later date and in all the appearances were essentially unchanged. All cases had complete examination of the upper GI and biliary tracts. In none was an active or healed duodenal ulcer identified. After consideration of the clinical symptoms and radiological, biochemical and endoscopic findings, a final diagnosis was made in all cases (Table).

PATHOLOGY Several biopsies were taken from the abnormal areas. Although many of the biopsy fragments were small and difficult to orientate, sufficient material was obtained in all 13 for histological assessment. All cases

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Investigation of GI tract in 13 patients

<table>
<thead>
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<th>Case</th>
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<th>Diagnosis</th>
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<td>Cholangiocarcinoma</td>
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<td>50</td>
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<td>GI blood loss</td>
<td>Colonic bleeding</td>
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<td>M</td>
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<td>54</td>
<td>F</td>
<td>Retrosternal discomfort</td>
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<td>61</td>
<td>F</td>
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<tr>
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<td>54</td>
<td>F</td>
<td>Heartburn</td>
<td>Gastro-oesophageal reflux</td>
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</table>

Fig. 1  *Endoscopic appearance of heterotopic mucosa in the duodenum, with multiple mucosal nodules projecting into the lumen, as seen through the pylorus.*

Well organised, orderly groups of glands, consisting of a mixture of chief and parietal cells (Figs 2 and 3). These were covered by a surface epithelium of gastric type, which at the edges merged with the adjacent normal duodenal mucosa (Fig. 4). This epithelium was best demonstrated by a periodic acid-Schiff (PAS) stain. In all cases, small fragments of normal duodenal mucosa were present as well as the gastric type mucosa. In no case, was there evidence of significant inflammation either in the duodenal mucosa or in the heterotopic gastric type mucosa. In the five cases where repeat biopsies were performed the histology was identical on both occasions.

**Discussion**

This series of 13 cases represents a well defined clinicopathological entity. The patients, who covered a wide age range, were found to have characteristic endoscopic appearances in the proximal duodenum, and all had identical histological features on biopsy. In none was an active or healed duodenal peptic ulcer identified.

In 1927, Taylor,4 from a series of 150 necropsies, described two cases of heterotopic gastric glands in the duodenum which presented as small slightly raised nodules. Histologically the nodules were composed of fundal glands with chief and parietal cells.

Fig. 2  *Low power appearance of biopsy specimens. The well organised group of body type glands is seen in the largest fragment. × 20.*

The perfect differentiation and orderly arrangement indicated their undoubted congenital origin. In one case, a peptic ulcer was noted one inch (2.5 cm) distal to the heterotopic glands. These two cases appear identical to those reported in our series.

In 1962,5 Gannon described two further cases of heterotopic gastric mucosa in the duodenum at necropsy. One consisted of a single nodule, the other several small polyps. Both these cases and four others from elsewhere in the small intestine showed true fundal type gastric mucosa. A further case was reported eight years later by Lee et al,6 presenting as a polyp 2.5 × 1.5 cm adjacent to the ampulla of Vater.

Wolff7 then reported a large series of 87 cases of gastric heterotopia in the alimentary canal, 15 involving the duodenum. She subdivided heterotopia into congenital and acquired groups, the latter representing an abnormal regenerative process as exemplified by pyloric type epithelium in Crohn's disease. This, as we have suggested earlier is probably best termed metaplasia to avoid confusion. Pathologically, this so-called heterotopia "consisted of small numbers of parietal cells and sometimes chief showed identical appearances. Centrally there were
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The presence of both parietal cells and oxyntic cells is evident. × 525.

cells, or small groups of fundic glands, rather than fully developed fundic mucosa.” In Wolff’s view this description of scattered isolated parietal cells amongst otherwise indigenous cells was probably an acquired phenomenon, only the fully formed fundic mucosa representing true congenital heterotopia. We would support this interpretation of the pathology.

However other workers, predominantly German and Scandinavian, have taken a different view. Hoedemaker examined the duodenal cuff in 158 gastrectomy specimens and found 52 cases where parietal and occasional chief cells were found. These were commoner in cases of duodenal ulcer and a relation was postulated with hyperacidity. In no case was a macroscopic abnormality seen. Although in a few cases the duodenal mucosa was entirely replaced by gastric type mucosa, usually only a few glandular structures lined by some parietal cells were found. A similarly designed study by Scandinavian workers examined 250 gastrectomy specimens and 2 duodenal resections. These workers showed parietal cell heterotopia in 61 of the 272 cases (22.5%). This was diagnosed even if only a few parietal cells were demonstrable in only one of the three sections. Again a relation was found with acid output.

Although a few of their cases may have represented true congenital heterotopia, the vast majority appear to resemble those described by Wolff, where, again, there was a strong association with peptic ulceration.

In 1970, the first case diagnosed endoscopically was reported. Three years later Scandinavian workers described six cases of heterotopic gastric mucosa in the duodenum, three diagnosed at endoscopy and three at operation. Four of the cases consisted of multiple polyps; the others only a single
polyp. However their statement that “histological examination revealed fully developed gastric mucosa with parietal and pepsinogen cells in nearly all the polyps. Only a few were composed solely of gastric surface epithelium surrounding an oedematous lamina propria” is imprecise. Certainly some of the six cases are genuine heterotopic gastric mucosa as shown by their Fig. 5, which shows an identical appearance to our cases but we feel that these six cases may not all represent the same entity, although it is difficult from the text to be sure. Certainly we do not agree with their conclusion that this epithelium is a response to an “extraordinarily strong stimulus forcing the heterotopic tissue to grow beyond the level of the normal mucosa. The growth is hyperplasia not neoplasia.”

In 1977,11 Kratzsch described 14 polypoid lesions in the duodenum, seen during 3140 endoscopic examinations. Eight of these were reported as showing gastric mucosa, but in only four was it of body type. One of these had erosive bulbitis, the other three having no evidence of duodenal ulceration. Unfortunately the pathological description is not sufficiently clear to enable us to assess whether all four represent true heterotopia.

Lastly in 1980,12 22 cases were described—17 diagnosed on double contrast barium meal and five seen at endoscopy, from a series of 7400 barium meals and 2700 endoscopies. However the pathology is only briefly discussed, “parietal cells with or without chief cells were demonstrated in all cases.”

Having reviewed the literature critically, it seems that there are five definite cases diagnosed at necropsy and at most 30, but probably fewer, cases diagnosed at endoscopy.

The term heterotopic gastric mucosa has been applied, in the past, to three different entities:

Firstly, gastric type surface epithelium lining the duodenum is recognised as a prominent feature of duodenitis and is regarded as metaphastic. Interestingly, Dutch workers13 have shown this epithelium to be present in 64% of apparently normal individuals.

Secondly, nodules of pyloric type glands may be seen in the mucosa and termed heterotopic, although we suspect that most of these represent Brunner’s glands, which are difficult to differentiate from pyloric-type glands. In addition, it appears that occasional parietal cells and less commonly chief cells may be present, although usually in very small numbers. These cases we regard not as congenital and heterotopic but as metaphastic. There seems convincing evidence that this entity is related, as is the surface change, to hyperacidity, being most common in association with duodenal ulcer. In our opinion, most of the cases described by Wolff,2 Johansen8 and Hoedemaker7 fall into this category.

Thirdly, true heterotopic body type mucosa in the duodenum as in our patients. This is identified by a well organised mass of perfectly differentiated body type glands covered by gastric surface epithelium replacing the entire thickness of the duodenal mucosa. This is congenital in origin, and is present in up to 2% of the population. One case was described in a study of 50 normal people by a group from the Netherlands.12 The interesting point related to its frequency in this series is that 12 of the 13 cases were identified by one endoscopist who performed only 30% of the examinations in the unit. It appears that endoscopists are failing to recognise this entity. If the pathologist is also unaware of the entity, a duodenal biopsy will be reported as “consisting only of gastric mucosa.” As yet this condition appears of no clinical significance and there is no evidence of an association with peptic ulceration. This is understandable in that any acid and pepsin produced will be quickly neutralised in the duodenum and as the nodules themselves are very small, the quantity produced is presumably insignificant.

This report may help to clarify this area of confusion in the literature, but further studies are needed. However it can only be studied when endoscopists and pathologists are aware of the entity and pathologists are aware of the strict criteria which should be applied.

References

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