Definition of Barrett's oesophagus

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Abstract

Barrett's oesophagus is the eponym applied to the columnar epithelium-lined lower oesophagus. In 1976, Paull *et al.* described three types of columnar epithelia lining the distal oesophagus : a junctional or cardiac-type epithelium, a gastric fundic-type epithelium and a distinctive type of intestinal metaplasia referred to as specialized columnar epithelium. Even the normal oesophagus can be lined by 2 cm of columnar epithelium. To avoid the problem of false-positive diagnoses, arbitrary criteria for the extent of oesophageal columnar lining necessary to include patients in studies of Barrett's oesophagus were established in the early 1980s. The latter criteria require a circumferential segment of columnar lined epithelium of 2 or 3 cm in length. There are, however, a number of technical and conceptual problems related to this approach. The traditional definition excludes shorter segments and tongues of columnar lined epithelium. Only the specialized columnar epithelium defined by intestinal type goblet cells carries an inherent risk of malignancy. Therefore, a number of investigators currently define Barrett's oesophagus as any amount of columnar mucosa in the lower esophagus that has histologic evidence of goblet cells (highlighted in biopsies using the alcian blue pH 2.5 stain). Recently, short segments of specialized intestinal metaplasia in the distal oesophagus ("short segment Barrett's oesophagus") have attracted considerable attention. It has also become clear that intestinal metaplasia can occur at a normally located gastro-oesophageal junction. The etiology and clinical significance (in terms of possible relationship to the adenocarcinoma of the cardia) of this "intestinal metaplasia of the gastric cardia" and its potential relationship to Barrett's oesophagus are not yet completely understood (Acta gastroenterol. belg., **2000**, 63, **10-12**).

Key words : Barrett's oesophagus, intestinal metaplasia.

Historical notes

In 1906, Tileston (1) reported several patients with "peptic ulcer of the oesophagus". He noted "the close resemblance of the mucous membrane about the ulcer to that normally found in the stomach". Over the subsequent four decades, a number of investigators described similar patients who had peptic ulcerations in an oesophagus lined by a gastric type of columnar epithelium (for review see (2)). Most investigators, however, considered the columnar-lined organ not oesophagus but rather a tubular segment of stomach. In his landmark paper entitled "The lower oesophagus lined by columnar epithelium" (3) the influential British surgeon Norman Barrett argued that the columnar-lined organ was in fact oesophagus and not stomach. Following his paper, the columnar-lined oesophagus became known eponymically as "Barrett's oesophagus".

Histopathologic features of Barrett's mucosa

A wide spectrum of histopathologic features can be seen. The macroscopic architecture can include glands with deep and shallow pits, as in gastric mucosa, and villous structures resembling small-intestinal mucosa. *Cardiac-type mucosa* resembles gastric cardiac mucosa. In contrast to normal gastric cardiac mucosa, however, there is often glandular distortion, oedema and chronic inflammation (4). *Fundic-type Barrett's mucosa*, as the name implies, resembles gastric fundic mucosa in having shallow pits lined by mucus-containing columnar cells with underlying glands composed of parietal and chief cells (4). The glands may be distorted or short and the surface may be villiform. Intestinal metaplasia is also referred to as *distinctive-type Barrett's mucosa* and is characterized by the presence of goblet cells (4). This type of mucosa has a villiform configuration and cryptlike glands. It is present in the majority of patients with Barrett's oesophagus but is found less frequently in children (4). In a study by Paull *et al.* (5) a zonal distribution of the various types of Barrett's mucosa was seen. The distinctive-type mucosa occurred most proximally, the fundic-type most distally and the cardiac-type mucosa interspersed between the other two (5). Studies of resection specimens, however, often reveal a mosaic distribution of the various types of mucosa (4). The lamina propria of all types of Barrett's mucosa can show varying severity of congestion, oedema, acute and chronic inflammation and fibrosis (4). A discussion of dysplasia in Barrett's oesophagus is beyond the scope of this review.

Two or three centimeter rules

By the 1970s, it was clear that the columnar-lined oesophagus was associated with severe gastro-oesophageal reflux disease ((2)). If an endoscopist inadvertently biopsied the columnar epithelium of the proximal stomach, this would result in a false-positive diagnosis of Barrett's oesophagus. Furthermore, Hayward, a surgeon, had contended that the lower 1 to 2 cm of the normal oesophagus is lined by columnar epithelium (6). To avoid false-positive diagnoses of Barrett's oesophagus, arbitrary criteria for the extent of oesophageal columnar lining necessary to include patients in studies of Barrett's oesophagus were established

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requiring anywhere from 2 cm to as many as 5 cm of columnar-lined oesophagus (for review see (2)). This "classical" definition requires a circumferential segment of columnar-lined oesophagus, and thus excludes short segments or tongues. As pointed out by Spechler and Goyal (2) there are both technical and conceptual problems in defining Barrett's oesophagus by the extent of oesophageal columnar lining. The primary technical problem lies in the precise identification of the gastro-oesophageal junction. Anatomic landmarks such as the peritoneal reflection or the character of the muscle bundles in the oesophageal wall are not clinically applicable. Manometric and endoscopic localization of the lower oesophageal sphincter often differs by several centimeters (7). According to McClave *et al.* (8) the proximal margin of the gastric folds is a fixed reproducible anatomic landmark at endoscopy designating the junction of the muscular wall of the oesophagus and stomach. Even though this criterium has gained widespread acceptance (9), there is no "gold standard" for localizing the precise junction (2). Another technical problem is one of endoscopic measurement. It has been demonstrated that endoscopic measurements are subject to considerable imprecision (7). The major conceptual problem in defining Barrett's oesophagus is that any length chosen as a diagnostic criterion is necessarily arbitrary (2).

Goblets, goblets, goblets

By the 1970's another important feature of Barrett's oesophagus was well established : the association between Barrett's oesophagus and adenocarcinoma. By the late 1980s, it was clear that the specialized intestinal metaplasia was the epithelial type that especially predisposed patients to cancer development (for review see (2,9)). In the light of this observation and to bypass the insurmountable technical and conceptual problems described above, some investigators have chosen to define Barrett's oesophagus by the presence of specialized intestinal metaplasia. In a recent editorial, Weinstein and Ippoliti (9) clearly state that "our prerequisite for the diagnosis of Barrett's oesophagus is the presence of intestinal-type goblet cells in at least one biopsy from the lower oesophagus". In their opinion, when an endoscopist sees short ($\leq$ 2 cm) pink tongues in the lower oesophagus and biopsies reveal only oxyntic gland or cardiac-type mucosa, that corresponds to an eccentric Z-line and not to Barrett's oesophagus. Straightforward as it may seem, the "goblet cell approach" does not obviate diagnostic difficulties. First, the goblet cells may be overlooked on standard hematoxylin and eosin stained tissue sections (resulting in underdiagnosis of Barrett's oesophagus). In a recent study, goblet cells would have been overlooked in 50% of cases if hematoxylin and eosin had been the sole staining method used (10). The identification of goblet cells can be greatly enhanced by a combined hematoxylin and eosin-alcian blue pH 2.5 stain since the mucins within the goblet cells turn blue (9,10). Cells that look like gastric columnar cells but unlike them stain positively with the combined hematoxylin and eosin-alcian blue pH 2.5 stain ("columnar blues" or "transitional cells") are not diagnostic of Barrett's oesophagus (9). Secondly, there are several reports describing patients with endoscopically evident long segments of columnar lining in whom biopsies (sometimes obtained 7-9 cm above the lower oesophageal sphincter!) only show junctional or fundic-type mucosa (for review see (2)). These patients would not be considered to have Barrett's oesophagus by the modern diagnostic criteria. Thirdly, there is also a conceptual problem with defining Barrett's oesophagus by the presence of intestinal metaplasia : Barrett himself did not mention an intestinal type of epithelium in any of his reports. By this modern definition, therefore, none of the patients that Barrett described had Barrett's oesophagus (2). Finally, intestinal metaplasia in the stomach can be histologically indistinguishable from the specialized intestinal metaplasia of Barrett's oesophagus, and an inadvertent biopsy of such a stomach could result in a false-positive diagnosis of Barrett's oesophagus (11).

Short segment Barrett's oesophagus and intestinal metaplasia of the gastric cardia

Short segments of intestinal metaplasia in the distal oesophagus are being reported with increasing frequency (12-16). Adenocarcinomas can arise in tongues or short segments of Barrett's oesophagus (17). Unfortunately, the definition of "short segments" of Barrett's oesophagus varies among investigators and endoscopic criteria have not been uniformly defined. Consequently, the reported prevalence of this condition varies widely (for review see Sharma *et al.* (14)). Recently, Sharma *et al.* (14) proposed the following working definition for short segment Barrett's oesophagus : " an abnormal appearing oesophageal lining at endoscopy that is $<$ 3 cm in length with intestinal metaplasia documented on biopsy". Short segment Barrett's oesophagus, in particular its pathogenesis and clinical implications in terms of cancer risk and need for follow-up, is currently the focus of intense scientific research. The observation that the frequency of cancer of the gastro-oesophageal junction is increasing, has also triggered interest in another condition, intestinal metaplasia of the cardia. As opposed to short segment Barrett's oesophagus, intestinal metaplasia of the cardia lacks distinguishing endoscopic characteristics from normal cardia mucosa and is defined as histologic evidence of intestinal metaplasia by biopsy of the proximal stomach within 2 cm of the oesophagogastric junction (14). The clinical implications of this condition are still under investigation but some studies suggest that its pathogenesis is distinct from that of short segment Barrett's oesophagus (12,18).

Conclusions

In an outstanding review, Spechler and Goyal state that "the question "what is Barrett's oesophagus" inappropriately has assumed metaphysical proportions. There is no fundamental truth to be discerned by slavish attention to this question. The term Barrett's oesophagus is artificial and the condition has been defined by investigators who have imposed arbitrary criteria that fit their personal perspectives" (2). Weinstein and Ippoliti hold a different view and believe "that it is justified to change the definition of a disorder based on new knowledge and yet keep the original name" (9). Rather than fueling this debate, most pathologists favor a pragmatic approach. A recent authoritative textbook of gastrointestinal pathology (4) suggests the following. If goblet cells are present, a biopy from the distal oesophagus can confidently be reported as "Barrett's mucosa of the distinctive type". Specimens with only cardiac or fundic-type mucosa can be interpreted and reported in the light of clinical data e.g. "cardiac-type mucosa consistent with Barrett's mucosa if the specimen was obtained from the oesophagus" (4). It is thus clear that the diagnosis of Barrett's oesophagus is as much a matter of specimen site as histopathologic findings in the specimen. It follows that the pathologist should be aware of the endoscopist's observations. The importance of this dialogue between the gastroenterologist and the pathologist cannot be overemphasized. As to short segment Barrett's oesophagus and intestinal metaplasia of the cardia, further studies are needed to unravel their pathogenesis and to define their clinical importance.

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