Review article

BARRETT'S OESOPHAGUS - DIAGNOSIS AND MANAGEMENT

Anthony Thomas Roger Axon, MD, FRCP

Introduction

In 1950 Norman Barrett, a cardio-thoracic surgeon at St. Thomas's Hospital London described a chronic peptic ulcer of the oesphagus which had arisen in columnar mucosa rather than the squamous mucosa characteristic of normal oesophagus[1]. He postulated that this was the result of a congenitally short oesophagus where the gastric mucosa had been pulled up into the thorax and that in reality it was a gastric ulcer. Since then the columnar lined oesophagus has been referred to as Barrett's oesophagus, though in reality it was Allison in 1953[2] a cardiothoracic surgeon in Leeds who showed clearly that the columnar epithelium was actually part of the anatomical oesophagus and was not part of the stomach. In the seven cases that he described, one of them had a carcinoma of the oesophagus. Today we know that columnar lining characteristic of Barrett's oesophagus is not gastric mucosa but a columnar epithelium characterised by specialised intestinal metaplasia, this mucosa is pre-malignant.

Definition

A concise short definition of Barrett's oesophagus is "intestinal metaplasia within the distal tubular oesophagus". The condition is easily diagnosed at endoscopy if there is a significant length of Barrett's mucosa because there is a sharp delineation between the whitish lining of the squamous mucosa and the salmon pink velvety appearance of the Barrett's mucosa. The diagnosis can then be confirmed by taking biopsies. Certain experts have suggested that spraying with Lugol's iodine (which stains the squamous mucosa but not the columnar) will also help to delineate it, or conversely spraying with methylene blue which is taken up by the columnar epithelium but not the squamous makes the diagnosis easier. In practice however there is little difficulty in identifying the condition without the use of stains. Difficulties do however arise when short lengths of Barrett's mucosa are present because under these circumstances (particularly in cases of hiatus hernia) there may be an area of gastric mucosa which appears to be in the oesophagus but which is in fact in stomach that has prolapsed above the diaphragm. In other words it may be difficult to define precisely where the tubular oesophagus ends and a hiatus hernia begins. Under these circumstances the histology from biopsies taken in that position may be helpful as it may demonstrate merely cardia type gastric mucosa rather than specialized intestinal metaplasia. Nevertheless difficulties even with histological diagnosis may arise if intestinal metaplasia has taken place in the gastric mucosa (as may often occur in patients who are infected with Helicobacter pylori).

A critical question in establishing the diagnosis of Barrett's oesophagus therefore is to define where the oesophagus ends and the stomach begins[3].

The junction of the tubular oesophagus with the stomach may be identified in a number of ways. The identification of the Z-line is not helpful because this merely tells you where the squamous lining changes to columnar, neither is the position of the diaphragm helpful because most patients with Barrett's oesophagus have a hiatus hernia with stomach prolapsing above the diaphragm. The lower oesophageal sphincter which would be a

Professor Axon A.T.R.; Center for Digestive Diseases, The General Infirmary at Leeds, Great George Street Leeds LSI 3EX, UK
Telephone: +44 113 392 2125, Fax:+44 1133926968, Email: anthony, axon@leedsth,nhs,uk

conversely spraying with methylene blue which is taken up by the columnar epithelium but not the squamous makes the diagnosis easier. In practice useful landmark cannot usually be identified endoscopically. The decision therefore as to where the oesophagus ends may be established by three other criteria. The lower end of the oesophagus in many patients is characterized by a network of blood vessels that can be readily seen through the mucosa both in patients with Barrett's mucosa and in normal patients. If this can be identified it is easy to tell whether columnar mucosa is extending into the tubular oesophagus. The second method is to partially deflate the lumen of the lower oesophagus and upper stomach so that the gastric rugae can be seen. The upper limit of the longitudinal gastric rugaie have been taken to represent the upper end of the stomach and thus the gastro-oesophageal junction. The third method is to identify the area where the oesophagus changes from a relatively narrow tubular organ to the wider lumen of the stomach.

It is essential to determine where the junction between the oesophagus and the stomach is because only by doing this is it possible to determine the length of Barrett's mucosa, and this is important because if one is to undertake surveill-ance endoscopy it is necessary to start taking biopsies at the bottom end. It is also important to be able to measure the length of the Barrett's mucosa to see whether treatment is improving it or whether it is extending and finally it is recognized that long segments of Barrett's mucosa are more likely to become malignant than short ones.

Degrees of Barrett's

Barrett's oesophagus has been divided into different grades. Initially Barrett's oesophagus was not considered to be present unless at least 2 cm of abnormal tubular oesophagus was affected, however today most workers would consider that any intestinal metaplasia within the tubular oesophagus indicates some degree of Barrett's. It is important to be able to define the length of Barrett's when undertaking research.

Many workers now divide Barren's oesophagus into long segment Barrett's (longer than 2 cm), short segment Barrett's (circumferential Barrett's mucosa extending up the oesophagus for less than 2 cm) ultra-short Barrett's where only tongues of the abnormal mucosa extends into the oesophagus and it is not circumferential and finally in patients where intestinal metaplasia is found at or just below the junction of the tubular oesophagus[4] this is referred to as gastro-oesophageal junction specialized intestinal metaplasia (GOJSIM) or intestinal metaplasia at the cardia.

What is the relevance of Barrett's oesophagus?

Most of the epidemiological work that has been done with Barrett's relates to long segment Barrett's. A prospective autopsy series[5] suggests that in a Western population the incidence is roughly 376 per 100,000. However other studies have varied from 7 to 10 per 100,000[6,7]. Short segment Barrett's is much commoner[8,9,10] but the incidence in different series varies from about 2.5 to 36%. These varying results are not surprising because the incidence of Barrett's varies according to the population studied, it is commoner in men, in Caucasians, in individuals with heartburn and hiatus hernia, it tends to occur in older people and there may be a genetic predisposition to the condition. There is some evidence to suggest that bile reflux in addition to acid reflux may be an important aetiological factor[11] but it is still difficult to understand why it should be that some patients develop reflux oesophagitis while others develop the Barrett's change, it is also unclear why the condition is increasing rapidly in Western communities.

Cancer risk[12,13]

It is now recognised that a history of heartburn is strongly associated with development of adenocarcinoma of the oesophagus. It is also known that risk of adenocarcinoma in Barrett's oesophagus is 30-125 fold higher than in the general population. In those patients who are diagnosed as having long segment Barren's the overall risk of developing cancer is between 1 in 50 and 1 in 200 patient years, the risk being considerably higher for men than women. It is believed that cancer of the oesophagus under these circumstances is preceded by dysplastic change within the abnormal epithelium. It is for this reason that patients with Barrett's oesophagus are often recruited to endoscopic surveillance studies in order to identify the dysplasia (or early cancer) so that curative treatment can be provided. There is no doubt from the . literature that if cancer is identified during Barren's surveillance programmes the patients fare very much better than those in whom the cancer is diagnosed as a result of the patient presenting with symptoms of the

order to identify the dysplasia (or early cancer) so that curative treatment can be provided. There is no doubt from the . literature that if cancer is identified during Barren's surveillance programmes the patients fare very much better than those in whom the cancer is diagnosed as a result of the patient presenting with symptoms of the disease.

Management of Barrett's oesophagus

In an ideal world it would be possible to treat the Barrett's oesophagus and return it to normal squamous epithelium, thus obviating the risk of cancer. A number of studies are taking place to determine whether endoscopic therapy can return the epithelium to normal and prevent cancer. Two techniques are commonly used, the first photodynamic therapy (PDT)[14,15,16] The concept underlying this therapy is that the patient is given a photo sensitiser which is taken up by the Barrett's mucosa. The area to be treated is then illuminated, usually using a laser of a specific wavelength. This damages the mucosa causing necrosis. The patient is then treated with acid suppression and re-epithelialisation of the oesophagus occurs with squamous epithelium. This technique is relatively safe but has led to stricturing in some cases. The greater concern however is that islands of specialized intestinal metaplasia may be left not only on the surface of the epithelium but also beneath the newly formed squamous mucosa. There is therefore a theoretical risk that the cancer could arise in one of these islands and it may even be more difficult to detect on surveillance endoscopy than if it had not been so treated. Clearly prospective studies are needed in order to determine whether this therapeutic approach is appropriate.

A second way of dealing with the abnormal mucosa is to use the argon plasma coagulator[17]. The advantage of this method is that it is possible to see exactly which part of the mucosa one is treating and the therapy can be done in several sessions so that circumferential ulceration does not occur and there is a lower risk of stricture formation. A disadvantage of this technique however is that the squamous epithelium may still overgrow areas of intestinal metaplasia leaving the sub-mucosal islands of Barrett's alluded to above.

An alternative approach to managing the Barrett's patient is not to attempt any kind of direct treatment to the mucosa but to undertake regular endoscopic surveillance[18,19]. This is the policy pursued in most gastrointestinal centres. Patients are endoscoped yearly, biannually or every three years and multiple biopsies are taken, using four quadrant biopsies every 2 cm. These are examined for dysplastic change. In the event of there being low grade dysplasia the surveillance is carried out with greater regularity. The presence of high grade dysplasia is associated with roughly a 50% chance of there being invasive cancer. Under these circumstances oesophagectomy, endoscopic mucosal resection of photodynamic therapy has been employed for treatment.

The problem with surveillance program-mes is that to date there have been no properly designed prospective studies that have demonstrated this policy to be effective and it is therefore even more difficult to know how frequently patients should be endoscoped and how many biopsies should be taken. It would be very much better if it was possible to identify areas of potential dysplasia during the surveillance study because that would enable one to target the biopsies to areas of suspicion. A great deal of research in this area is ongoing, in particular the use of the magnifying endoscope, chromo-endoscopy, fluorescence endoscopy, optical coherence tomography, light scattering spectroscopy and there are other newer methodologies in the pipeline. Time will tell whether these techniques are truly beneficial or whether an attack on the Barrett's epithelium itself with newer technologies will in the end produce better results[20].

References

1. Barrett NR. Chronic peptic ulcer of the oesophagus and "oesophagitis". BrJ Surg 1950; 38: 175-182.
2. Allison PR, Johnstone AS. The oesophagus lined with gastric mucous membrane. Thorax 1953; 8: 87-101.
3. Spechler SJ. The columnar-lined esophagus. Histology, terminology and clinical issues. Gastroenterol Clin North Am 1997; 26: 455-466.
4. Spechler SJ, Zeroogian JM, Antonioli DA, Wang HH, Goyal RK. Prevalence of metaplasia at the gastro-oesophageal junction. Lancet 1994; 344: 1553-1556.
5. Cameron AJ, Zinsmeister AR, Ballard DJ, Carney JA. Prevalence of columnar-lined Barrett's esophagus. Comparison of population based

4. Spechler SJ, Zeroogian JM, Antonioli DA, Wang HH, Goyal RK. Prevalence of metaplasia at the gastro-oesophageal junction. Lancet 1994; 344: 1553-1556.
5. Cameron AJ, Zinsmeister AR, Ballard DJ, Carney JA. Prevalence of columnar-lined Barrett's esophagus. Comparison of population based clinical and autopsy findings. Gastroenterology 1990; 99: 918-922.
6. Cameron AJ, Lomboy CT. Barrett's esophagus: age, prevalence, and extent of columnar epithelium. Gastroenterology 1992; 103: 1241-1245.
7. Gospe: Cruppo Operative Per Lustudio Delle Precanorsi Del'esofago. Barrett's esophagus: epidemiological and clinical results of a multicentric survey. Int J Can 1991; 48: 364-368.
8. Johnston MH, Hammond AS, Laskin W, Jones DM. The prevalence and clinical characteristics of short segments of specialised intestinal metaplasia in the distal oesophagus on routine endoscopy. Am J Gastroenterol 1996; 91:1507-1511.
9. Nandurkar S, Talley NJ, Martin CJ, Ng TH, Adams S. Short segment Barrett's oesophagus: prevalence, diagnosis and association. Gut 1997; 40: 710715.
10. Sharma P, Morales TG, Sampliner RE. Short segment Barrett's esophagus: the need for standardisation of the definition and of endoscopic criteria. Am J Gastroenterol 1998; 93: 1033-1036.
11. Dixon MF, Neville PM, Mapstone NP, Moayyedi P, Axon ATR. Bile reflux gastritis and Barrett's oesophagus: further evidence of a role for duodenogastro-oesophageal reflux? Gut 2001; 49: 359-363.
12. Williamson WA, Ellis FH Jr, Gibb SP, Shahian DM, Aretz HT, Heatley GJ, Watkins E Jr. Barret's oesophagus. Prevalence and incidence of adenocarcinoma. Arch Intern Med 1991; 151; 2212-2216.
13. Hameeteman W, Tytgat GNJ, Houthoff HJ, van den Tweel JG. Barrett's oesophagus: development ofdysplasia and adenocarcinoma. Gastroenterology 1989; 96: 1249-1256.
14. Brown SG. A light at the end of the tunnel. Gut 1998; 43: 737-741.
15. Barr H, Shepherd NA, Dix A, Roberts DJH, Tan WC, Krasner N. Eradication of high-grade dysplasia in columnar-lined (Barrett's) oesophagus by photodynamic therapy with endogenously generated protoporphyrin IX. Lancet 1996; 348: 584-585.
16. Overholt BF, Panjehpour M, Haydek JM. Photodynamic therapy for Barrett's esophagus: follow-up in 100 patients. Gastrointest Endosc 1999; 49: 1: 1-7.
17. Van Laethem J-L, Cremer M, Peny MO, Delhaye M Deviere J. Eradication of Barrett's mucosa with argon plasma coagulation and acid suppression: immediate and mid term results. Gut 1998; 43: 747-751.
18. McGarrityTJ. Barrett's oesophagus: the continuing conundrum. Br Med J 2000;321: 1238-1239.
19. Bani-Hani K, Sue-Ling H, Johnston D, Axon ATR, Manin IG. Barren's oesophagus: results from a 13 year surveillance programme. Eur J Gastroenterol Hepatol 2000; 12: 649-654.
20. Rollins AM, Sivak Jr. MV. Potential new endoscopic techniques for the earlier diagnosis ofpre-maiignancy. In:Best practice & Research Clinical Gastroenterology. Ed. Tytgat GNJ. Balliere Tindall, London Uk2001; 15:2:227-247.