CASE REPORT

Pathological documentation of complete elimination of Barrett's metaplasia following endoscopic multipolar electrocoagulation therapy

M B Fennerty, C L Corless, B Sheppard, D O Faigel, D A Lieberman, R E Sampliner

Abstract

The previous paradigm that Barrett's is an irreversible premalignant lesion has recently been challenged by a proliferation of reports documenting elimination of Barrett's by a variety of endoscopic techniques. Whether Barrett's is entirely eliminated is unknown as endoscopic biopsy samples the surface of the epithelium only. Numerous reports document underlying specialised columnar epithelium in many of these trials. Until now there have been no reports of pathological examination of the entire oesophagus as a specimen. This case documents complete elimination of intestinal metaplasia from the oesophagus and supports the biological plausibility of these research techniques.

(*Gut* 2001;**49**:142–144)

Keywords: Barrett's oesophagus; endoscopy; multipolar electrocoagulation

Department of Medicine, Oregon Health Sciences University, Portland, Oregon, USA
M B Fennerty
D O Faigel
D A Lieberman

Department of Pathology, Oregon Health Sciences University, Portland, Oregon, USA
C L Corless

Department of Surgery, Oregon Health Sciences University, Portland, Oregon, USA
B Sheppard

Arizona Health Sciences Center and Southern Arizona VA Health Care System, Arizona, USA
R E Sampliner

Correspondence to:
Dr M B Fennerty, Oregon Health Sciences University, PV-310, 3181 SW Sam Jackson Park Road, Portland, OR 97201, USA.
fennerty@ohsu.edu

Accepted for publication
14 November 2000

Barrett's oesophagus is an acquired premalignant condition secondary to chronic gastro-oesophageal reflux disease.[1] The intestinalised columnar epithelium in Barrett's oesophagus can develop dysplasia which is the precursor of oesophageal adenocarcinoma. Over the past two decades, oesophageal adenocarcinoma has been the most rapidly rising of any malignancy[2] and now accounts for more than 12 000 deaths per year in the USA.[3]

In the past, Barrett's oesophagus was thought to be an irreversible premalignant lesion, based on numerous studies showing little change in the length of Barrett's oesophagus with either pharmacological therapy (H_2 receptor antagonists, proton pump inhibitors) or surgical antireflux therapy.[4–6] However, since 1994, there have been a number of reports of reversal of Barrett's oesophagus following endoscopic thermal (heater probe, multipolar electrocoagulation (MPEC), laser, argon plasma coagulation) and non-thermal (photodynamic therapy) injury in patients with either surgically or pharmacologically controlled acid reflux.[7–22] Based on follow up endoscopic biopsies, many patients in these trials appear to have complete elimination of Barrett's oesophagus. However, endoscopic biopsies are limited in their depth and area of mucosal sampling. The possibility remains that there is residual Barrett's epithelium underlying the restored squamous epithelium—for example, within the ducts leading to the submucosal oesophageal glands. Indeed, this phenomenon has been documented in a number of series[23–27] and it remains unclear whether Barrett's epithelium is ever fully eliminated.[28–30] Here we report the histological findings in an oesophagectomy specimen from a patient who had received prior MPEC therapy for Barrett's oesophagus. The findings indicate that the premalignant Barrett's epithelium (intestinal metaplasia) can be completely eliminated by endoscopic MPEC therapy.

Case report

RB, a 29 year old male with severe reflux symptoms dating to his early teens, had Barrett's oesophagus confirmed histologically (intestinal metaplasia) at age 18. He underwent a Nissan fundoplication for symptom control but his reflux symptoms returned within six months of operation. He had yearly surveillance endoscopies for Barrett's oesophagus from 1989 until 1998, at which time he was referred by his gastroenterologist for inclusion into the MPEC-Barrett's ablation multicentre study.[31] Following institution of omeprazole 40 mg twice daily for seven days, the patient had an initial protocol endoscopy in May 1998 which revealed 6 cm of Barrett's oesophagus. Barrett's was circumferential in its distal 3 cm with a 3 cm tongue occupying 25% of the mucosa in the proximal 3 cm (fig 1). Intestinal metaplasia without dysplasia was confirmed by biopsy. In addition, he had a large 4 cm hiatal hernia. The entire surface of the metaplastic Barrett's epithelium was treated with MPEC at a setting of 30 until whitening of the metaplastic epithelium was seen. Five follow up treatment sessions (with each session treating the entire residual surface of Barrett's) were performed from July 1998 to November 1998. His December 1998 follow up protocol endoscopy revealed a hiatal hernia but no apparent

Abbreviations used in this paper: MPEC, multipolar electrocoagulation.

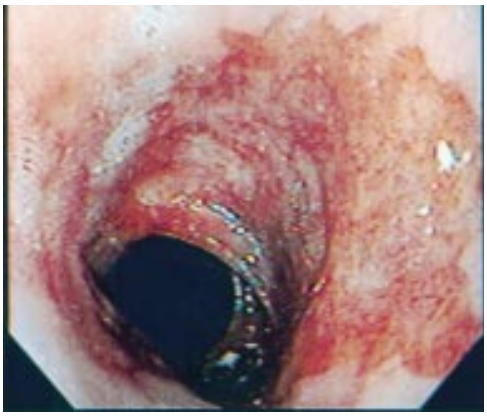

Figure 1 Endoscopic appearance of the proximal margin of Barrett's oesophagus prior to endoscopic therapy.

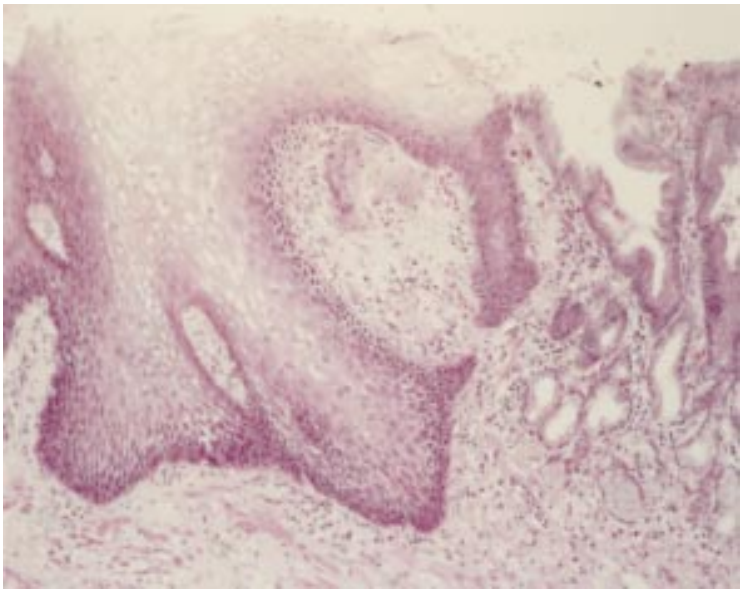

Figure 2 High power photomicrograph of the squamocolumnar junction of the resected specimen.

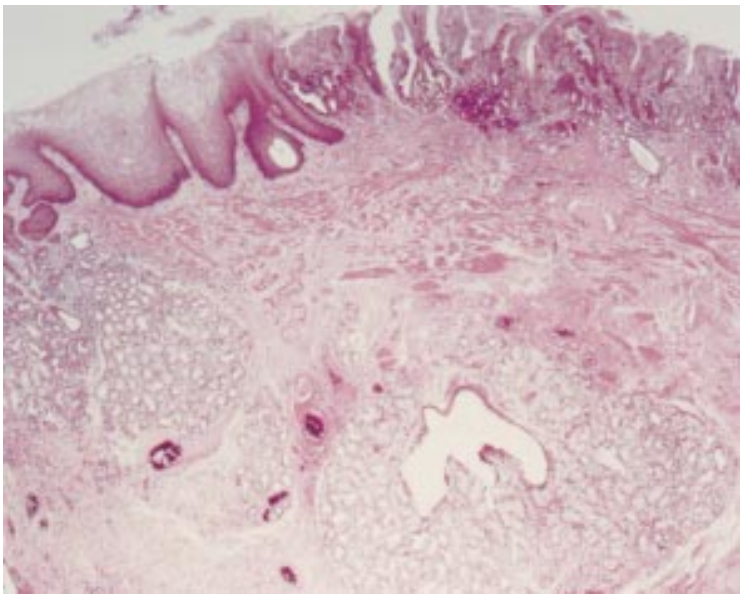

Figure 3 Lower power view of the same region as in fig 2, revealing full thickness squamous epithelium and absence of goblet cells in adjacent columnar mucosa. Note the submucosal scarring.

residual columnar mucosa in the tubular oesophagus (also absent by chromoendoscopy with Lugol's solution). Biopsies from oesophageal sites with prior metaplastic intestinal metaplasia revealed squamous mucosa only. By protocol, he was then placed on maintenance omeprazole 20 mg twice daily and follow up examination was planned for May 1999.

Despite control of his heartburn on this dose of proton pump inhibitor therapy, regurgitation persisted and he sought surgical therapy of his reflux disease. A laparoscopic "toupet-type" fundoplication (because of ineffective oesophageal peristalsis on oesophageal manometry) was performed in March 1999. The wrap became disrupted shortly after operation as a consequence of unremitting vomiting in the recovery room. He subsequently developed a symptomatic paraoesophageal hernia which necessitated open surgical repair in May 1999. At operation the intrathoracic oesophagus was fibrotic and friable with extensive adhesions to the pleura with penetration through into the lingula and left upper lobe requiring an oesophagogastrectomy for repair.

Following fixation in formalin, the entire distal oesophagus, including all areas previously involved by Barrett's, was submitted for histological review. Following intensive sectioning and search there was no residual intestinal metaplasia in the distal oesophagus (fig 2). At the squamocolumnar junction (identified by the submucosal gland) (fig 3), the columnar epithelium was free of goblet cells. The adjacent squamous epithelium was full thickness and showed minimal override of the columnar epithelium. There was some scarring of the submucosa and the squamous epithelium was thickened but there were no signs of intestinal metaplasia.

Discussion

To our knowledge, this is the first documented case of complete elimination of Barrett's oesophagus following combination antireflux therapy and endoscopy thermal injury. This finding confirms the hypothesis that Barrett's oesophagus is a reversible premalignant lesion and complete elimination of Barrett's can occur within six months following therapy.[7 8 30] Whether the majority of patients undergoing endoscopic ablation therapy have complete elimination of Barrett's oesophagus or whether this occurs in patients with dysplasia is not known. However, determination of this will be critical to document whether such therapies can decrease the risk of cancer or eliminate the need for further surveillance endoscopy.

The optimal form of endoscopic and/or antireflux therapy to affect reversal of Barrett's oesophagus is as yet unknown, as is whether elimination of this premalignant epithelium is durable and represents a cure of the lesion.[30 32 33] The fibrotic and scarred oesophagus seen in this case raises concern as to transmural injury to adjacent organs from thermal ablation of Barrett's, the effect of which is unknown. This observation underscores the potential morbidity or hazards of th ese therapies and emphasises

that until improvement in outcome is demonstrated, they remain research techniques. Additionally, Brandt *et al* have documented return of Barrett's oesophagus following cessation of pharmacological antireflux therapy after Barrett's had been apparently eliminated with endoscopic therapy.[34] Thus lifelong pharmacological and/or surgical control of reflux may be necessary to avoid redevelopment of the metaplasia. Further data from resected and/or autopsy specimens following endoscopic ablative therapy are necessary to confirm the findings in this case. However, this report adds to a growing body of literature suggesting Barrett's oesophagus can be totally eliminated, and may be curable, in some patients by endoscopic therapy.

1 Fennerty MB. Barrett's esophagus: What do we really know about this disease? *Am J Gastroenterol* 1997;**92**:1–3.
2 Devesa SS, Blot WJ, Fraumeni JF. Changing patterns in the incidence of esophageal and gastric carcinoma in the United States. *Cancer* 1998;**83**:2049–53.
3 Landis SH, Murray T, Bolden S, *et al.* Cancer statistics, 1999. *CA Cancer J Clin* 1999;**49**:8–31.
4 Sampliner RE, Garewal HS, Fennerty MB, *et al.* Lack of impact of therapy on extent of Barrett's esophagus in 67 patients. *Dig Dis Sci* 1990;**35**:93–6.
5 Sampliner RE. Effect of up to 3 years of high-dose lansoprazole on Barrett's esophagus. *Am J Gastroenterol* 1994;**89**: 1844–8.
6 Kim SL, Waring UP, Spechler SJ, *et al.* Effects of antireflux therapy on the extent of Barrett's epithelium. *Gastroenterology* 1993;**104**:A118.
7 Berenson MM, Johnson TD, Markowitz NR, *et al.* Restoration of squamous mucosa after ablation of Barrett's esophageal epithelium. *Gastroenterology* 1993;**104**:1686–91.
8 Sampliner RE, Hixson LJ, Fennerty MB, *et al.* Regression of Barrett's esophagus by laser ablation in an antacid environment. *Dig Dis Sci* 1993;**38**:365–8.
9 Grade AJ, Shah IA, Medline SM, *et al.* The efficacy and safety of argon plasma coagulation therapy in Barrett's esophagus. *Gastrointest Endosc* 1999;**50**:18–22.
10 Byrne JP, Armstrong GR, Attwood SEA. Restoration of the normal squamous lining in Barrett's esophagus by argon beam plasma coagulation. *Am J Gastroenterol* 1998;**93**: 1810–15.
11 Dumoulin FL, Terjung B, Neubrand M, *et al.* Treatment of Barrett's esophagus by endoscopic argon plasma coagulation. *Endoscopy* 1997;**29**:751–3.
12 Gossner L, May A, Stolte M, *et al.* KTP laser destruction of dysplasia and early cancer in columnar-lined Barrett's esophagus. *Gastrointest Endosc* 1999;**49**:8–12.
13 Lightdale CJ. Ablation therapy for Barrett's esophagus: Is it time to choose our weapons? *Gastrointest Endosc* 1999;**49**: 122–5.
14 Sampliner RE, Fennerty MB, Garewal HS, *et al.* Reversal of Barrett's esophagus with acid suppression and multipolar electrocoagulation: preliminary results. *Gastrointest Endosc* 1996;**44**:523–5.
15 Kovacs BJ, Chen YK, Lewis TD, *et al.* Successful reversal of Barrett's esophagus with multipolar electrocoagulation despite inadequate acid suppression. *Gastrointest Endosc* 1999;**49**:547–53.
16 Montes CG, Brandalise NA, Deliza R, *et al.* Antireflux surgery followed by bipolar electrocoagulation in the treatment of Barrett's esophagus. *Gastrointest Endosc* 1999;**50**: 173–7.
17 Michopoulos S, Tsibouris P, Bouzakis H, *et al.* Complete regression of Barrett's esophagus with heat probe thermocoagulation: mid-term results. *Gastrointest Endosc* 1999;**50**:165–72.
18 Overholt BF, Panjehpour M, Haydek JM. Photodynamic therapy for Barrett's esophagus: follow-up in 100 patients. *Gastrointest Endosc* 1999;**49**:1–7.
19 Gossner L, Stolte M, Sroka R, *et al.* Photodynamic ablation of high-grade dysplasia and early cancer in Barrett's esophagus by means of 5-aminolevulinic acid. *Gastroenterology* 1998;**114**:448–55.
20 Overholt BF, Panjehpour M. Photodynamic therapy for Barrett's esophagus: Clinical update. *Am J Gastroenterol* 1996;**92**:1719–23.
21 Overholt BF, Panjehpour M. Barrett's esophagus: photodynamic therapy for ablation of dysplasia, reduction of specialized mucosa, and treatment of superficial esophageal cancer. *Gastrointest Endosc* 1995;**42**:64–9.
22 Laukka MA, Wang KK. Initial results using low-dose photodynamic therapy in the treatment of Barrett's esophagus. *Gastrointest Endosc* 1995;**42**:59–63.
23 Sampliner RE, Steinbronn K, Garewal HS. Squamous mucosa overlying columnar epithelium in Barrett's esophagus in the absence of anti-reflux surgery. *Am J Gastroenterol* 1988;**83**:510–12.
24 Sharma P, Jaffe PE, Bhattacharyya A, *et al.* Laser and multipolar electrocoagulation ablation of early Barrett's adenocarcinoma: long-term follow-up. *Gastrointest Endosc* 1999;**49**:442–6
25 Biddlestone LR, Barham CP, Wilkinson SP, *et al.* The histopathology of treated Barrett's esophagus: squamous re-epithelialization after acid suppression and laser and photodynamic therapy. *Am J Surg Pathol* 1998; **22**:239–45.
26 Sharma P, Morales TG, Bhattacharyya A, *et al.* Squamous islands in Barrett's esophagus: what lies underneath? *Am J Gastroenterol* 1998;**93**:332–5.
27 Sharma P, Bhattacharyya A, Garewal H, *et al.* Durability of new squamous epithelium after endoscopic reversal of Barrett's esophagus. *Gastrointest Endosc* 1999;**50**:159–64.
28 Fennerty MB. Endoscopic ablation of Barrett's esophagus. *Curr Gastroenterol Rep* 1999;**1**:210–13.
29 Haag S, Nandurkar S, Talley NJ. Regression of Barrett's esophagus: the role of acid suppression, surgery, and ablative methods. *Gastrointest Endosc* 1999;**50**:229–40.
30 Fennerty MB. Perspectives on endoscopic eradication of Barrett's esophagus: who are appropriate candidates and what is the best method? *Gastrointest Endosc* 1999;**49**:S24–8.
31 Sampliner RE, Camargo E, Faigel D, *et al.* Efficacy and safety of reversal of Barrett's esophagus with high dose omeprazole and electrocoagulation. *Gastroenterology* 1999; **116**:A298.
32 Bremner RM, Mason RJ, Bremner CG, *et al.* Ultrasonic epithelial ablation of the lower esophagus without stricture formation. A new technique for Barrett's ablation. *Surg Endosc* 1998;**12**:342–6.
33 Johnston MH, Schoenfeld P, Mysore JV, *et al.* Endoscopic spray cryotherapy: a new technique for mucosal ablation in the esophagus. *Gastrointest Endosc* 1999;**50**:86–92.
34 Brandt LJ, Blansky RL, Dauvar DR. Repeat laser therapy of recurrent Barrett's epithelium: success with anacidity. *Gastrointest Endosc* 1995;**41**:267.