The value of medical imaging in uncomplicated and complicated Barrett's esophagus

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Abstract

Barrett's esophagus is an acquired condition characterized by a progressive columnar metaplasia of the distal esophagus caused by longstanding gastroesophageal reflux and reflux esophagitis. Barrett's esophagus is a premalignant condition associated with a significantly increased risk of developing esophageal adenocarcinoma. The purpose of this article is to provide an overview of the radiologic aspects of Barrett's esophagus and esophageal adenocarcinoma. Review of the literature shows that some findings on esophagography that are relatively specific for Barrett's esophagus are not sensitive, while others that are sensitive have a low specificity. Specific radiologic features allowing a confident diagnosis of Barrett's esophagus are a high esophageal stricture or ulcer associated with a hiatal hernia and/or gastroesophageal reflux. A reticular mucosal pattern is a relatively specific sign particularly if located adjacent to a stricture and is highly suggestive of Barrett's esophagus. Unfortunately, these findings are only present in a minority of cases. More common but nonspecific findings include gastroesophageal reflux, hiatal hernia, reflux esophagitis and/or peptic stricture in distal esophagus. These findings may also be present in patients with uncomplicated reflux disease.

Barrett's esophagus carries a risk of malignant change. Early adenocarcinoma may appear as a plaque-like lesion or with focal irregularity, nodularity, and ulceration of the esophageal wall. Invasive adenocarcinoma may be seen as an infiltrating ulcerated mass. The radiologic diagnosis of Barrett's esophagus is limited by lack of criteria that are both sensitive and specific. The major value of double-contrast esophagography is its ability to classify patients into high risk (high stricture, ulcer or reticular pattern), moderate risk (esophagitis and/or distal peptic strictures), and low-risk (absence of esophagitis or stricture) for Barrett's esophagus determining the relative need for endoscopy and biopsy. Endoscopy and biopsy are generally advocated to make a definitive diagnosis. Endoscopic ultrasound plays a role in the early detection of invasive carcinoma and the staging of proven carcinoma but has no role in the surveillance of Barrett's esophagus. (Acta gastroenterol. belg., **2000**, 63, **22-28**).

Key words : Esophagus, radiology, endoscopic ultrasound — Barrett's esophagus — Esophagitis — Esophagus, neoplasm.

Introduction

The current status of Barrett's esophagus is reviewed with particular emphasis on the role of medical imaging in the diagnosis of uncomplicated and complicated Barrett's esophagus.

Definition, pathogenesis and prevalence

Barrett's esophagus is a metaplastic process in which the squamocolumnar mucosal junction is located above the proximal border of the lower esophageal sphincter (1,2). In the past, a congenital origin for Barrett's esophagus was hypothesized (3). It was postulated that Barrett's esophagus resulted from abnormal embryologic development with incomplete squamous re-epithelialization of the columnar-lined fetal esophagus. However, Barrett's esophagus is currently thought to be an acquired condition (2,4,5). Clinical, morphologic and experimental observations indicate that progressive columnar metaplasia of the distal esophagus develops as a consequence of long-standing gastroesophageal reflux and reflux esophagitis. Recurrent episodes of ulceration may cause the normal squamous epithelium to be denuded and subsequently replaced by a columnar epithelial lining. It remains unclear why some patients with gastroesophageal reflux and reflux esophagitis develop Barrett's esophagus and others do not.

The prevalence of Barrett's esophagus in patients with reflux esophagitis has ranged from 8 to 20%, with an average of about 10% (1). An incidence of only 0.8 to 2.2% is reported in patients without esophagitis symptoms (6). A high prevalence in patients with scleroderma has been described. This is probably related to the severe esophagitis that occurs as a consequence of marked lower esophageal sphincter dysfunction and poor clearance of refluxed peptic acid from the esophagus. Recht *et al.* (7) reported a prevalence of 37% in patients with scleroderma who underwent endoscopy for symptoms of reflux esophagitis.

Endoscopic and histologic findings

In Barrett's esophagus the squamocolumnar junction is located above the proximal border of the lower esophageal sphincter. This columnar epithelial lining in the distal esophagus may be present as a continuous sheet with finger-like projections extending orally for variable distances, or may be present as islands of columnar epithelium within the distal esophagus surrounded by normal squamous epithelium (2). Barrett's mucosa is often limited to the distal third of the esophagus, but it may extend as far proximally as the aortic arch (1).

Barrett's mucosa causes typical changes in the color and texture of the esophageal epithelium at endoscopy. Usually, Barrett's mucosa has a velvety, pinkish-red

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appearance, less raddish than that of normal gastric mucosa, in contrast to the flat, relatively pale appearance of the normal squamous epithelium (8). These typical findings allow a confident diagnosis of Barrett's esophagus solely on the basis of the endoscopic appearance. However, biopsy and histologic examinations are required to confirm the diagnosis.

Histologically, the columnar-epithelial lining in Barrett's esophagus is not simply gastric mucosa but a mosaic of intimately admixed glandular and cell types from the stomach and small bowel (4,9). Three distinct types of columnar epithelia are seen in Barrett's esophagus : (a) a specialized columnar or intestinal type epithelium with a villiform configuration, mucous glands and intestinal-like goblet cells, (b) a gastric fundic-type epithelium with parietal, chief cells and an atrophic mucosa and (c) a junctional-type epithelium with cardiac mucous glands. Any one of these epithelia, or any combination, constitutes the mucosa seen in Barrett's esophagus. A common histologic finding in all types of mucosa is chronic inflammation characterized by the presence of mononuclear cells (2). One or more foci of low- or high-grade dysplasia, carcinoma-in-situ, or invasive carcinoma may be present in Barrett's mucosa.

Relationship to adenocarcinoma

It is widely accepted that Barrett's esophagus carries a risk of malignant change and that adenocarcinoma evolves through a sequence of progressively severe epithelial dysplasia in preexisting areas of columnar metaplasia (2,10-12). The annual incidence of adenocarcinoma in patients who develop malignancy after a columnar-lined esophagus has been diagnosed varies from one in 52 to one in 441 patient-years of observation, which is about a 30-40 fold increased risk compared to the general population (13-15). Dysplastic changes are classified histologically either as low grade or high grade. This dysplastic epithelium may then progress to carcinoma in situ or invasive carcinoma. Dysplasia has been recognized in all histologic types of Barrett's mucosa, but it is more likely to occur within areas of intestinal metaplasia (2,11,16). A marked association between intestinal metaplasia and esophageal adenocarcinoma has also been reported (11,16). This increased cancer risk and the poor prognosis of advanced adenocarcinomas is the basis for endoscopic screening recommendations and biopsy to detect dysplastic changes and early adenocarcinoma (11,17). Surveillance has been reported to be indicated for those patients in whom esophagectomy is considered as a therapeutic option in case of early malignancy and to be not appropirate for patients whose life expectancy is limited by other diseases (18). However, asymptomatic, early adenocarcinomas could also be detected fortuitously during double-contrast esophagography. Radiologic evaluation could play a role in an optimal surveillance program to detect adenocarcinoma at the earliest possible stage. However, alternating double-contrast esophagography and endoscopy as proposed by Levine is not performed in most centers (4).

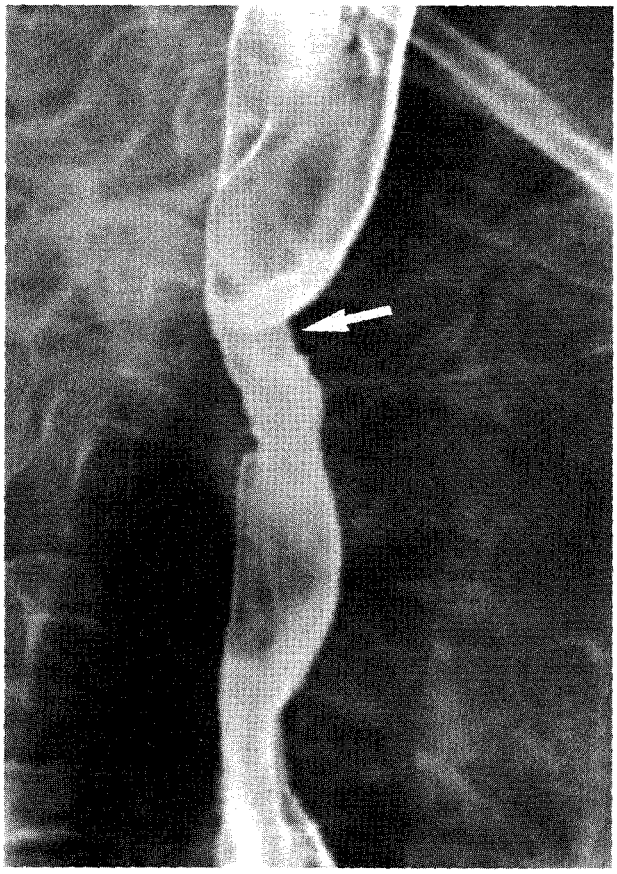
Radiologic diagnosis

Barrett's esophagus

Specific radiologic features allowing a confident diagnosis of Barrett's esophagus consist of a high esophageal stricture or ulcer often associated with a hiatal hernia, gastroesophageal reflux and/or reflux esophagitis (thickened or end-nodular folds, nodular and ulcerative mucosa, and peptic stenosis (Fig. 1) (19-21). The strictures and ulcers seen in Barrett's esophagus often occur in the proximal zone of columnar epithelium at or near the squamocolumnar junction and is responsible for their unusual location (22). The strictures may appear as short constrictions or may be seen as smooth, tapered areas of narrowing in the midesophagus (19). Barrett's ulcers are usually seen as relatively deep ulcer craters within the columnar mucosa at a considerable distance from the gastroesophageal junction. In some patients both a high esophageal stricture and an ulcer may be seen (22). In some patients rather subtle findings consisting of limited distensibility and/or fixed transverse folds may be present. The latter probably represent a mild form of the midesophageal stricture that is associated with Barrett's esophagus (23).

A relatively specific sign of Barrett's esophagus consists of a reticular mucosal pattern which is characterized on double-contrast esophagography by innumerable, tiny barium-filled grooves or crevices on the esophageal mucosa. In most cases, an adjacent, subtle stricture in the mid or distal esophagus is seen, with the reticular pattern extending distally over a short but variable distance from the stricture (Fig. 2) (24). Unfortunately, a high esophageal stricture or ulcer and a reticular mucosal pattern are seen in a minority of patients with Barrett's esophagus (25).

Other, more common findings in Barrett's esophagus consist of gastroesophageal reflux, hiatal hernia, reflux esophagitis and peptic stenosis (Fig. 3, 4). However, these findings may also be present in patients with uncomplicated reflux disease. Inclusion of radiologic evidence of reflux disease in the diagnosis of Barrett's esophagus increases the sensitivity but decreases the specificity. Exclusion of these findings will decrease the sensitivity of double-contrast esophagography and most cases of Barrett's esophagus will be missed (4,25). Thus, esophagography is thought to have limited value as a screening examination for Barrett's esophagus. As a consequence, endoscopy and biopsy are required for accurate diagnosis. However, Gilchrist *et al.* (25) performed a blinded retrospective study in 200 patients who had both double-contrast esophagograms and endoscopy because of severe reflux symptoms. Patients were classified at high risk if specific radiographic signs were present, moderate risk if findings of distal peptic



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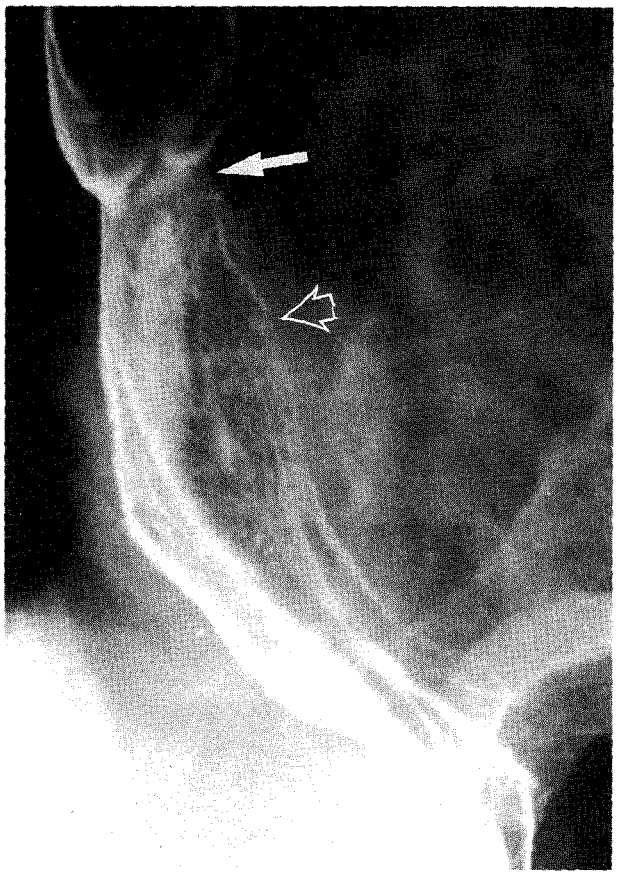

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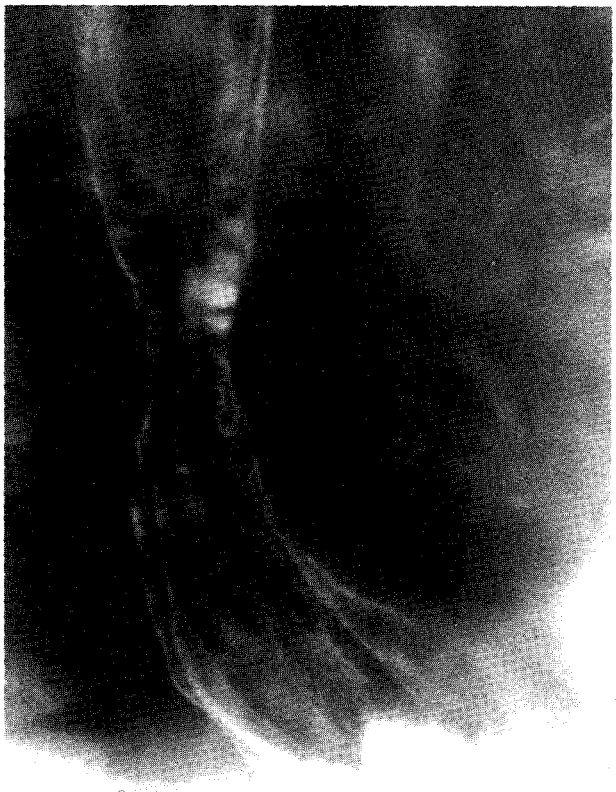

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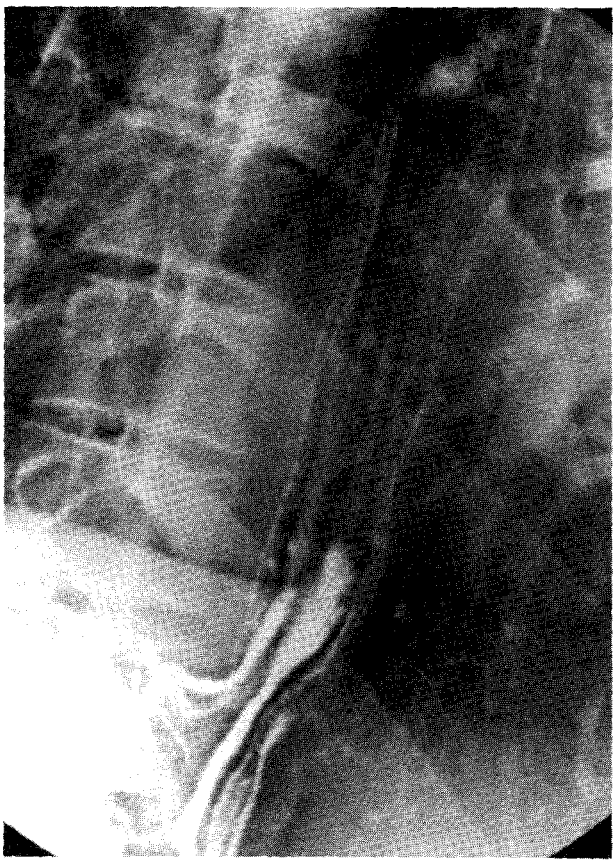

Fig. 4.

stricture and/or reflux esophagitis are seen and low risk in absence of these findings. Ten patients were thought to be at high risk, 73 at moderate and 117 at low risk. Endoscopic correlation showed biopsy-proven Barrett's mucosa in 9 (90%) of 10 patients at high risk, in 12 (16%) of 73 at moderate risk, and only one (< 1%) of 117 at low risk for Barrett's esophagus. The major value of esophagography is its ability to classify patients into high-, moderate-, and low-risk groups for Barrett's esophagus and to determine the relative need for endoscopy and biopsy. Patients who are at high risk for Barrett's esophagus almost always have this condition, so that endoscopy and biopsy should be performed for a definitive diagnosis. Clinical judgment (severity of reflux symptoms, age and overall condition of the patient) should be used concerning the need for endoscopy in patients who are at moderate risk for Barrett's esophagus. The risk of Barrett's esophagus is so low in the low-risk group that endoscopy does not seems valuable (25).

Esophageal adenocarcinoma

Most early adenocarcinomas in Barrett's esophagus reported in the radiologic literature have been discovered fortuitously during radiologic evaluation of patients with reflux symptoms. However, barium studies are sometimes performed on patients with known Barrett's esophagus. In these patients, double-contrast esophagograms should carefully be evaluated to detect early malignancy (1). Early adenocarcinomas may appear as plaquelike lesions, flat, sessile polyps with a smooth or slightly lobulated contour, focal irregularity, nodularity and ulceration of the esophageal wall (Fig. 5, 6) (4). In patients with peptic strictures, the earliest manifestation of a developing malignancy may be a localized area of flattening or stiffening in one wall of the stricture. In some patients superficial spreading cancers with diffuse nodularity of the mucosa but no focal lesion may be seen. Rarely, early cancers may be manifested by relatively large polypoid masses that are radiographically indistinguishable from advanced adenocarcinomas (26).

Advanced Barrett's carcinomas have the same radiologic features as squamous cell carcinomas. Usually, they appear as infiltrating, polypoid, ulcerated, or, less frequently, varicoid lesions (Fig. 7) (27,28). However, squamous cell carcinomas tend to be located in the upper or midesophagus, whereas adenocarcinomas tend to be located in the distal esophagus. Thus, the histologic nature of the tumor may often be predicted on the basis of its location in the esophagus (1). Advanced Barrett's carcinoma has a frequent tendency to invade the stomach resembling primary gastric carcinomas secondarily invading the distal esophagus (Fig. 8). In the past, esophageal adenocarcinoma was thought to be a rare entity. However, studies suggest that as many as 20 to 50% of tumors involving the gastroesophageal junction arise in Barrett's mucosa and subsequently spread into the stomach. In these cases examination of resected specimens usually shows one or more areas of esophageal dysplasia and/or carcinoma-in-situ adjacent to or remote from the proximal margin of the tumor (27-30). Although Barrett's esophagus can coexist with primary gastric carcinoma, this finding should normally not expect in case of gastric carcinoma invading the esophagus. Radiologic staging is the same as for other esophageal cancers and comprises barium study, CT scan and echo-endoscopy.

Endoscopic ultrasound

The role of endoscopic ultrasound in the evaluation of Barrett's esophagus is the early detection of invasive carcinoma and the staging of proven carcinoma. The latter can be done with classic endoscopic ultrasound using either 7.5 or 12 MHz and showing a 5 layer wall and the presence of lymph nodes. Increased wall thickness has been reported in Barrett's esophagus but it is impossible to differentiate between benign and malignant thickening of the wall. Endoscopic ultrasound is not able to differentiate among the different grades of dysplasia. For detecting cancer in 17 patients with Barrett's esophagus and adenocarcinoma, endoscopic ultrasound has been reported to have a sensitivity of 82% and a specificity of 87% (31). Recently miniature ultrasound probes using 20 MHZ were introduced and are able to detect 9 layers (32). Even with these probes miniature ultrasound is unable to identify patients with dysplasia. On the other hand miniature ultrasound probes are able to detect early esophageal carcinoma and to select the patients for endoscopic mucosal resection (Fig. 9). However miniature ultrasound probes are not widely available and the experience is rather

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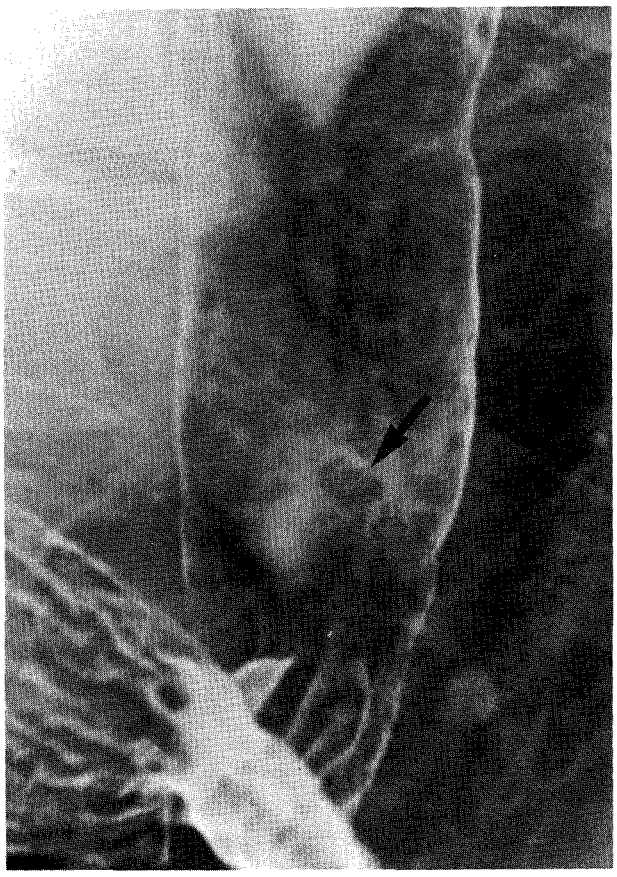
Fig. 1. — Barrett's esophagus with a high stricture. A stricture (arrow) is seen in the midesophagus. This patient also had a hiatal hernia and gastroesophageal reflux. In the presence of a hiatal hernia and gastroesophageal reflux, a high stricture should strongly suggest Barrett's esophagus. Fig. 2. — Barrett's esophagus with a reticular mucosal pattern and a high stricture. A reticular pattern (open arrow) adjacent to the distal aspect of the stricture is seen (arrow). This combination of findings is strongly suggestive for Barrett's esophagus but is seen in only a minority of patients. Fig. 3. — Barrett's esophagus with a distal stricture. Peptic scarring with sacculations and transverse folds are present. These findings are at moderate risk for Barrett's esophagus (Gilchrist's classification). Fig. 4. — Reflux esophagitis with thickened folds and irregular mucosa in a patient at moderate risk for Barrett's esophagus (Gilchrist's classification). Note how the folds are diffusely thickened in the distal esophagus due to submucosal edema and inflammation. Endoscopic biopsies showed Barrett's mucosa.



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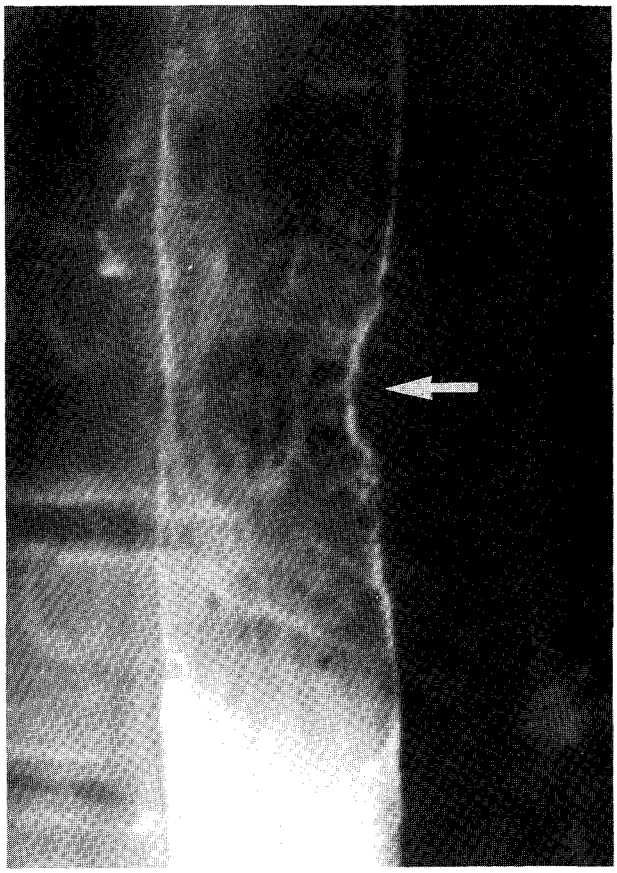

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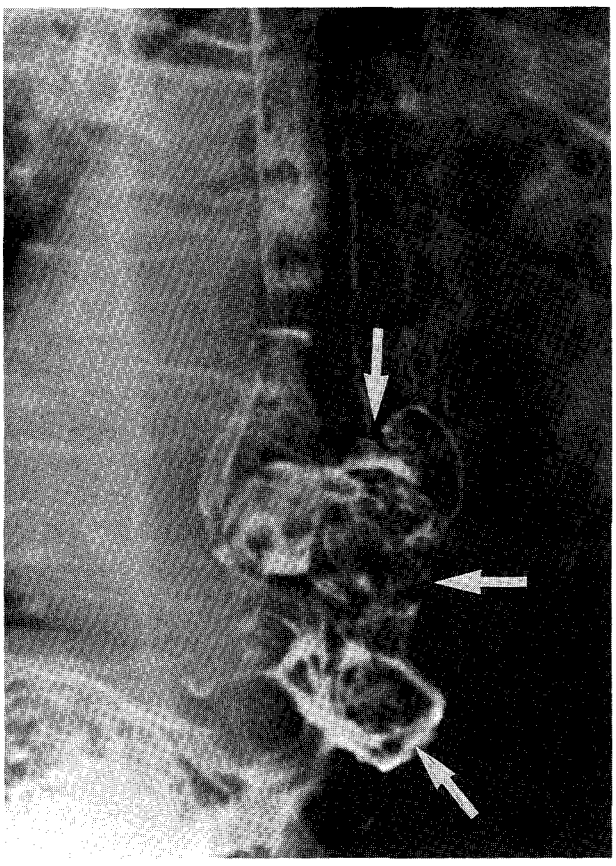

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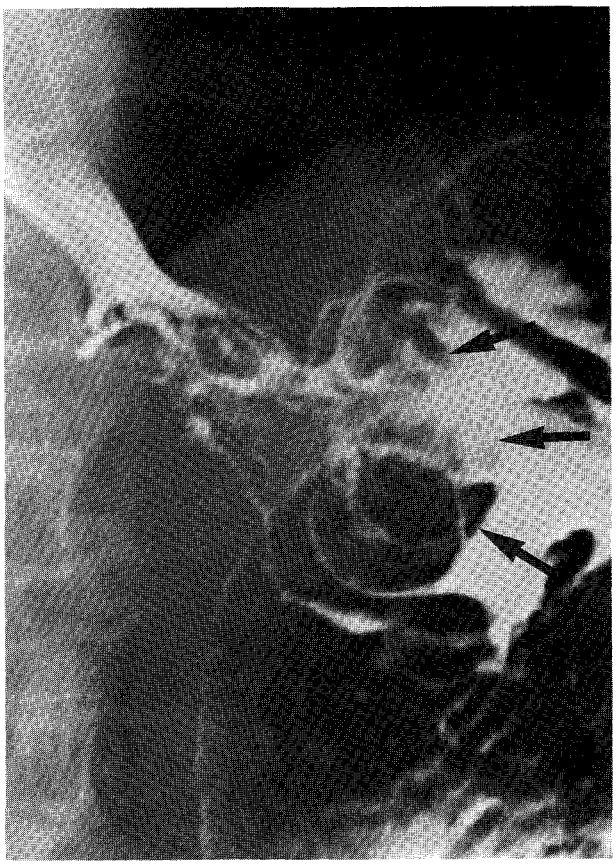

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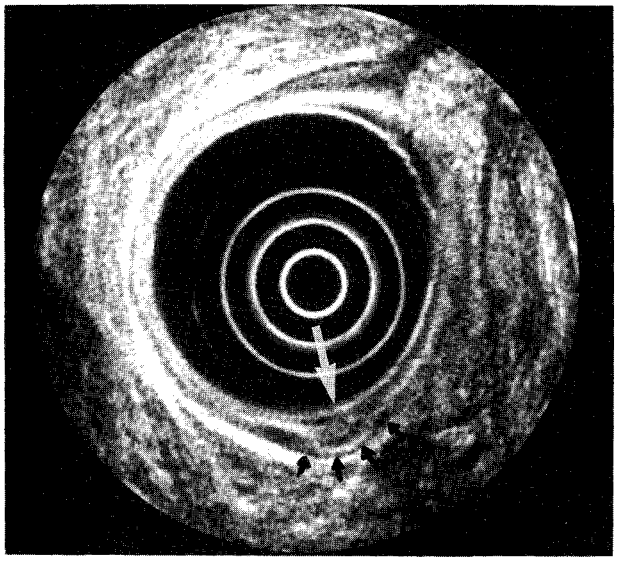

Fig. 9. — Endoscopic ultrasound image of a hypoechoic tumor (large arrow) limited to the mucosa and submucosa, leaving the muscularis propria (small arrows) intact. There are no lymph nodes. These data are consistent with a T1sm cancer in a patient with Barrett's esophagus.

limited. From all these data it can be concluded that endosonography is not an alternative for endoscopic surveillance in patients with Barrett's esophagus.

Conclusion

Barrett's esophagus is an acquired condition in which there is progressive columnar metaplasia of the distal esophagus caused by longstanding gastroesophageal reflux and reflux esophagitis. Prevalence in patients with esophagitis ranges from 8 to 20%. Endoscopy and biopsy are the most accurate diagnostic methods. Although the classic radiologic findings of Barrett's esophagus are present in only a minority of patients, this condition should be suspected whenever reflux esophagitis or peptic strictures are demonstrated on double-contrast esophagography. Barrett' esophagus carries an increased risk of developing esophageal malignancy. This risk is at least 30 fold increased compared to the general population. Advanced adenocarcinoma evolves through a sequence of progressively severe dysplasia and carcinoma in situ. The increased cancer risk tends to occur essentially in those patients exhibiting specialized columnar metaplasia. The increased cancer risk is the basis for endoscopic screening recommendations and biopsy to detect dysplastic or carcinomatous changes at the earliest possible stage. Once malignancy has been detected, endoscopic ultrasound is indicated for further staging. When barium studies are performed on patients with known Barrett's esophagus, the radiographs should be carefully evaluated for signs of early adenocarcinoma, so these patients may be referred for appropriate management prior to the development of advanced, unresectable tumors.

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Fig. 5. — Early adenocarcinoma in Barrett's esophagus. A plaquelike lesion is seen in the distal esophagus above a hiatal hernia (arrow). Fig. 6. — Early adenocarcinoma in Barrett's esophagus. A small mucosal mass (arrow) is seen in the midesophagus. Fig. 7. — Barrett's esophagus and advanced, infiltrating carcinoma. A polypoid and ulcerative tumor in distal esophagus invading the stomach is present (arrows). Fig. 8. — Barrett's carcinoma invading the stomach. A double-contrast view of the fundus shows obliteration of the normal anatomic landmarks at the cardia (arrows) and involvement of the distal esophagus with stenosis.

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