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Barretts's oesophagus

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What is Barrett's oesophagus?

Barrett's oesophagus (BO) is defined as the occurrence of metaplastic, specialised columnar epithelium lining the distal part of the oesophagus.¹ Evidence points to this as a metaplastic condition in reaction to ulceration and re-epithelialisation, the columnar epithelium replacing the normal stratified squamous epithelium.² Only specialised columnar epithelium consisting of a villiform growth pattern containing columnar, goblet, Paneth and endocrine cells (i.e. intestinal metaplasia (IM)) located above the lower oesophageal sphincter (LOS) qualifies as BO.^{1,3}

BO has been divided into long-segment (the classic form involving 3 cm or more of the oesophagus) and short-segment (less than 3 cm) forms. Practically, however, these types are managed similarly. Ultra-short-segment BO has also been described where no endoscopic evidence of BO is seen but where IM is found on biopsy. This remains controversial.^{1,4}

BO is furthermore classified as a pre-cancerous condition predisposing to the development of oesophageal adenocarcinoma.⁵

Which patients are affected?

The large majority of patients are adults suffering from gastro-oesophageal reflux disease (GORD).² A genetic predisposition has been reported.⁶ Children suffering from cystic fibrosis and who receive chemotherapy may also develop the condition.⁷ BO is found in 1.6% of the general population and in up to 10% of patients with symptomatic GORD.¹

How is the diagnosis made?

Barium swallow, manometric examinations and intra-oesophageal pH monitoring may provide supporting evidence; however, the definitive diagnosis requires endoscopy and biopsy specifically of the area above the LOS.

On endoscopy the affected mucosa appears red and velvety, extending proximally either circumferentially or advancing in one or several tongues. However, it may be difficult to measure and locate the metaplastic mucosa, and therefore the diagnostic criteria of BO are histological.

On biopsy, IM is the diagnostic feature of BO when located in the oesophagus, not when located in the upper part of the stomach. The mucosa is considered an incomplete form of IM. A villiform growth pattern is observed containing goblet cells with mucous cells, Paneth cells and neuro-endocrine cells.^{1,3} Mature absorptive intestinal cells with a brush border are rare. Foci of cardiac and fundal-type gastric mucosa are also identified in a patchwork fashion.^{1,8}

In addition, *Helicobacter pylori* organisms may be identified in the metaplastic foci, and rarely pancreatic and osseous metaplasia may be identified. Reduplication of the muscularis mucosa is a frequent finding.

What are the complications?

Peptic ulceration and stricture formation may be seen, and in addition dysplasia and adenocarcinoma may develop.^{1,5}

How is Barrett's oesophagus treated?

The surveillance of patients diagnosed with BO entails endoscopy and biopsy. In the absence of dysplasia, medical acid suppression, laser and photodynamic therapy may be used. Various non-surgical treatments of early neoplastic lesions have emerged, including endoscopic mucosal resection (EMR). Surgical options include oesophagogastroplasty, fundoplication or posterior gastropexy. However, the indications for surgical intervention

remain controversial. Factors influencing therapy include possible failure of medical therapy, the length of the BO and dysplasia.^{9,10}

Malignancy

The progression to malignancy in BO follows the familiar metaplasia-dysplasia-carcinoma sequence.

Dysplasia/intra-epithelial neoplasia denotes architectural and cytological abnormalities confined to within the basement membrane of the affected gland. The dysplasia may be low grade (nuclei basally orientated within the cells) or high grade (haphazardly located nuclei).¹¹ Dysplasia may be found in 5 - 10% of cases and is associated with carcinoma in up to 100%. The risk for the development of carcinoma in a patient with dysplasia is therefore much higher than in the general population.¹²

Invasive carcinoma arising from BO is nearly always of the adenocarcinoma type. Five to 10% of all oesophageal tumours are associated with BO. The tumours may be

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multicentric and are often advanced at the time of diagnosis. Most patients are white men with an average age of 57 at the time of diagnosis.

Mutation and over expression of p53, apoptosis-related genes, myc amplification, mutations of the cadherin/catenin membrane complex, microsatellite instability and expression of CD44 are included in the molecular alterations already identified in BO containing dysplastic/carcinomatous changes.¹³

The primary treatment of carcinoma is surgical resection, combined with chemotherapy and radiation.

The prognosis of adenocarcinoma arising from BO is poor, with a 5-year survival rate of 14.5%. The prognosis is, however, similar to that of conventional squamous cell carcinoma of the oesophagus.

Unusual malignancies arising from BO include adenosquamous carcinoma, squamous cell carcinoma, sarcomatoid carcinoma, neuro-endocrine carcinoma, choriocarcinoma and yolk sac tumours.¹⁴

The future

In the future, non-biopsy endoscopic methods including chromo-endoscopy and narrow-band imaging may be used, allowing a reduction in the number of biopsies. Other possibilities include light-induced fluorescence endoscopy, light-scattering spectroscopy and spectroscopy. However, further evaluation is necessary before clinical application will be possible.^{1,9}

References available at www.cmej.org.za

Lymph node biopsy: Some aspects revisited

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Lymph node biopsy, if performed correctly, is likely to yield an optimal diagnostic result.¹⁻³ However, in view of the invasive nature of the procedure, biopsy should only be undertaken in patients with a definitive clinical indication. Less invasive investigations, such as a full blood count and serology, and fine needle aspiration (FNA), may indeed provide a conclusive diagnosis especially if a careful medical history/examination reveals the most likely clinical cause for the lymphadenopathy, which is subsequently confirmed.

FNA as a tool to allow for a reliable diagnosis has gained increasing acceptance.²⁻⁵ Larger/referral laboratories have access to additional specialised investigations, including immunophenotyping, flow cytometry, cytogenetics and other techniques that can be performed as part of FNA sampling aiding in/allowing for a conclusive diagnosis.^{1,2} Unfortunately, of the latter depend on 'on site' sampling. As a very significant percentage of the

population is, at least initially, managed at peripheral healthcare units, lacking readily accessible specialised work-up. More complicated cases in need of ancillary techniques cannot optimally be assessed in this way.

Guidelines for lymph node biopsy are provided in various surgical, medical and pathology textbooks.^{1,2,4,5} In a clinical scenario where other means of arriving at a conclusive diagnosis have failed some of the more important indications for biopsy include:

- Persistent, unexplained lymph node enlargement. Decisions on further management will have to be based on other relevant considerations, i.e. age, general health, findings of clinical examination (site of involvement and whether lymphadenopathy is localised or generalised).
- Confirmation of clinically suspected diagnosis. Medical history and/or findings on examination may indicate that malignant disease is most likely, but conclusive histological diagnosis in most cases remains mandatory to allow for further management. Examination of draining nodes involved by metastatic disease of a primary tumour (i.e. where the latter is far less readily accessible for biopsy) may yield a definitive diagnosis.
- Assist in the investigation of a patient with a lymphadenopathy with associated clinical symptoms/signs that are difficult to explain conclusively (on the assumption that other relevant investigations have failed to provide a diagnosis). In this category conditions inducing non-neoplastic lymphadenopathy, which may have been overlooked, including infections, connective tissue disease and drug-related reactions may be relevant. Lymph node biopsy in these cases may indeed also be indicated to exclude the possibility of malignancy, including lymphomas with unusual presentation or unexpectedly widespread involvement by metastatic disease.
- Localised lymphadenopathy, especially of superficial nodes which are only moderately enlarged and soft, particularly in paediatric patients, may indeed be