GENERAL, HISTOPATHOLOGICAL AND IMMUNOHISTOCHEMICAL ISSUES OF BARRETT'S ESOPHAGUS

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Keywords: esophageal cancer, Barrett's disease, histopathology **Abstract:** In the Western countries, in the past 30 years, people used to talk only about two major diseases in the oesophageal pathology: esophageal cancer and Barrett's disease. It is interesting that in Oriental countries, the disease is less known. These facts led us to critically analyze the current issues related to Barrett's disease. The purpose of this paper is to present the opinions related to this disease, emphasizing the general aspects, especially the histopathological basis of the diagnosis.

Cuvinte cheie: cancer esofagian, esofag Barrett, histopatologie **Rezumat:** În ultimii 30 de ani, în occident, în patologia esofagiană nu se discuta decât de două maladii: cancerul esofagian și maladia lui Barrett. Este interesant că în țările orientale această boală este foarte puțin cunoscută. Aceste considerente ne-au determinat să analizăm critic aspectele de actualitate legate de maladia lui Barrett. Scopul lucrării este de a prezenta opniile legate de această maladie, subliniind aspectele generale, în special cele histopatologice care stau la baza diagnosticului acestei maladii

Barrett's esophagus is defined as an intestinal metaplasia in association with columnar metaplasia of the gastroesophageal junction, endoscopically recognized.

It occurs in more than 45% of the patients with chronic gastroesophageal reflux disease. The more aggressive the gastroesophageal reflux disease, the higher incidence perspective of Barrett's esophagus.

About 61 years ago, Barrett (1) described for the first time this disease that is the most important complication of the gastroesophageal reflux (GERD). This disease has aroused particular interest as soon as it showed a high percentage of malignancy. Esophageal reflux has been described for a long time and resulted in three classifications: Savary-Miller classification (Ollyo et al.)(2), followed by the Los Angeles classification and more recently, by the Japanese classification that focuses on early diagnosis of this disease.

The diagnosis of certainty is achieved after performing upper gastrointestinal endoscopy and biopsy. According to the Savary-Miller endoscopic classification, Barrett's esophagus meets the level V, meaning the "cure" of the defects of erosive reflux oesophagitis. The cure of these erosions lead to the advancement of fibrosis (in their muscles) in the esophageal walls, which causes a deficiency of the sphincter and subsequently, in the peristalsis of the esophageal body that characterized Barrett's esophagus.

Histologically, two types of metaplasia can be highlighted: the gastric type and the intestinal type.

The first is identically to the lining of the cardia, composed of mucous cells of surface, of foveolar type. Mucous glands of cardial type are found underneath.

The second is the incomplete intestinal metaplasia and refers to a distinct, specialized type (Paull et al.)(3) Complete intestinal metaplasia and Paneth cells accompanied by enterocytes is an unusual combination for Barrett's esophagus. Intestinal metaplasia is characterized in terms of microscopic, the presence of cells, very well shaped, gobletshaped (Goblet cells) (Fig.1) placed in the superficial epithelium or the foveolar region (Chandrasoma and DeMeester).(4) This cell has some large round vacuoles (ready to break) filled with acid mucin.

Figure no.1 Goblet cells (arrows) interspersed among gastric foveolar epithelial cells. Col H & E. (*Sibiu Pathology Archive*



Intestinal metaplasia diagnosis depends on identifying at least one of these cells in a well-defined routine H & E stain. Intestinal metaplasia may be present both in the stomach and the esophagus. The mechanism and etiology of intestinal metaplasia are different for these two organs but, both are defined morphologically by the same criterion: goblet cells present. We can divide these cells into three major categories: (*a*) clear and undisputed goblet cells present, either alone or mixed with pseudogoblet cells; (b) there are doubts about the existence of calceiform cells because of the difficulty to distinguish them from the pseudogoblet cells; (c) certainly no goblet cells. The use of a combination of Alcian blue and PAS (Periodic Acid Schiff) helps in detecting the goblet cells when intestinal metaplasia is present. Pancreatic metaplasia was also reported in 11 of a series of 350 biopsies (Krishnamurthy and Dayal).(5)

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Latest news is based on immunohistochemical and molecular examination. Mucins and cytokeratins immunohistochemistry (IHC), the study of cell cycle abnormalities, as well as the genetic alterations, may represent methods for tracking the progression of dysplasia. Cytokeratins CK 7, 20 can differentiate intestinal metaplasia (MI) of the distal esophagus to cardial metaplasia. DNA flow cytometry and immunohistochemistry for p53 showed a significant increase over the absent sequence dysplasia - defined LGD (low grade dysplasia). Therefore, immunohistochemistry for p53 could be a marker of malignancy risk for Barrett's esophagus. Eendothelial growth factor, overexpression of immunohistochemistry, as well as the overexpression of cyclooxygenase - 2 (COX-2), are commonly found in the patients with adenocarcinoma appeared on a Barrett's esophagus.

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