

ENDOSCOPIC SEMIOLOGY OF THE OESOPHAGUS

Precancerous lesions and superficial cancers

Emmanuel Coron & Gabriel Rahmi, eds.

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Coordinated by Emmanuel Coron and Gabriel Rahmi

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Foreword

Digital Revolution, technological Revolution, therapeutic Revolution... never before has the term "Revolution" been so present in our daily vocabulary! Regarding endoscopic technologies, and in particular those applied in Hepato-gastroenterology this use of the word Revolution is not unwarranted. To understand that it is indeed a Revolution, it is enough to draw a parallel between the evolution of endoscopic technologies and the evolution of European painting styles at the end of the 19th century and especially at the beginning of the 20th century, with the appearance of Cubist and Surrealist art movements. In a similar manner, the technical progress seen prior to the year 2000 mainly consisted of improving the endoscopes (robustness, field of vision, articulation...) but basically the description and the analysis of the images remained the same, a simple description of what is visible to the naked eve; comparable to simple "macroscopy", as is carried out routinely in Pathology laboratories to describe an operative specimen, with the notable exception that endoscopy deals with living tissues.

To justify the (daring) comparison with the surrealist movement it suffices to mention the famous painting by René Magritte (1898-1967) representing a pipe, entitled "This is not a pipe". Indeed, it is not a pipe but "an image of a pipe"¹. In the same way the treatment of endoscopic images, for example by virtual chromoendoscopy, differs from the simple photograph of a lesion, giving us new information not available by standard macroscopy. In this sense it is SUR (French: above) realistic. It is also cubist or more exactly orphist in the sense of the theory of the simultaneous contrast of colors cherished by Robert Delaunay (1885-1941) and illustrated by the cover of this book. Returning to a more medical discussion, in order to avoid the "betrayal of images", with the development of these new technologies we must learn new semiological vocabulary, essential for rigorous interpretation of digestive endoscopy. This is the rationale for this book.

This book is organised into two parts. The first, more theoretical part consists of a brief update to recapitulate some basics, essential for any gastroenterologist, specialised or not in endoscopy: What is a normal oesophagus? Barrett's oesophagus and its progress to malignancy; superficial carcinomas of the oesophagus and their diagnostic pitfalls. The second part is directly related to medical practice and aims to illustrate the most representative endoscopic aspects using 11 clinical cases as examples. Special attention is paid to the concordance between the endoscopic images and the histological images, since it is true that with the use of modern magnification and high definition techniques in current endoscopy the boundary between macro and microscopy is becoming increasingly vague.

We would like to thank our sponsor Fujifilm Europe not only for their financial support without which the realisation

^{1.} Magritte. Catalogue du Centenaire. Ludion Flammarion Eds 1998.

of this book would have been impossible, but even more so for their real involvement throughout the process that led to its publication. This book is the result of a collaboration between hospital gastroenterologists and the biomedical industry, hopefully showing the appeal of "these common interests" that we assert here. We hope that the readers of this book will consider this topic relevant enough to incite an interest in other organs, such as the colon or the stomach.

> Jean Paul Galmiche, Emmanuel Coron and Gabriel Rahmi

What is a normal oesophagus?

Nicolas Etchepare and Emmanuel Coron, Nantes

The identification and description of the main landmarks of the normal digestive tract are exercises that the gastroenterologist is accustomed to. However, new endoscopic imaging techniques, such as high definition imaging, increasingly high optical zoom levels, Blue Light Imaging (BLI) and Linked Color Imaging (LCI)¹ are changing the analysis of normal mucosa. Indeed, these technologies enable the analysis of the mucosal and vascular architecture with a never before reached precision. In addition, recent therapeutic endoscopic techniques (submucosal dissection and Per Oral Endoscopic Myotomy [POEM] in particular) have brought to the fore the concept of submucosal endoscopy with direct access to the different layers of the oesophageal wall, whose endoscopic appearance needs to be described.

ENDOSCOPIC ANATOMY OF THE NORMAL OESOPHAGUS

The oesophageal wall consists of the classic components of the gastrointestinal tract wall with the following layers (from the inner to the outer layer): mucosa, submucosa, muscularis and outer tunica (adventitia or serosa) (Figure 1).



Figure 1: Histology of the normal oesophageal wall. The values corresponding to the thickness (in mm) of the different layers are given as an indication.

The oesophageal mucosa is composed of a non-keratinised and pluristratified squamous epithelium, with a basal lamina, a lamina propria, which contains muco-secreting glands, blood and lymphatic vessels, and the muscularis mucosae.

^{1.} See page 46 for a description of these techniques.

Under white light endoscopy, the oesophagus has a pink salmon color and the mucosa appears as a thin glossy translucent whitish layer with many luminous reflections. Without zoom, the endoscopic analysis of the microarchitecture shows a perfectly smooth and regular mucosa (Figure 2A). Using the LCI mode, the oesophagus looks pink and the vascular structures of the wall are enhanced, making the parietal vascularisation much more visible (Figure 2B). BLI chromoscopy further increases the contrast of the vascular structures and gives a greenish appearance to the oesophageal mucosa (Figure 2C). Coupled with the zoom, the LCI and BLI modes (and especially the BLI mode) are very effective tools for the analysis of the morphology of intrapapillary capillary loops (IPCL). These structures correspond to fine capillaries emerging at the surface of the epithelium by creating regular loops (Figure 3). Depending on their degree of neoplastic transformation, different aspects can be recognised, as is detailed in the chapter dedicated to squamous lesions of the oesophagus².



Figure 2: Endoscopic appearance of a normal oesophagus using the white light mode (A), Linked Color Imaging (B) and Blue Light Imaging (C).

^{2.} See page 17.



Figure 3: The appearance of normal intrapapillary capillary loops using high-definition BLI chromoendoscopy. The loops are perfectly regular, elongated and not dilated.

The submucosal layer is a connective tissue containing vessels and the Meissner plexus, the part of the enteric nervous system that controls mucous secretions and motility. The thickness of this layer is about 1,000 microns, but it can be artificially "inflated" by injecting saline with a few drops of indigo carmine to carry out certain therapeutic procedures. It then appears as a translucent, gelatinous layer with long fibers, perpendicular to the wall, or crisscrossed, with many vessels (Figure 4).



Figure 4: The appearance of the oesophageal submucosa using white light imaging. After injection of a saline solution tainted with indigo carmine, the submucosa looks bluish and translucent. A vessel emerging from the muscularis can be seen which then branches out, reaching the oesophageal mucosa.

The muscularis which is about 3 to 5 mm thick is composed of two superimposed layers of smooth muscle: the inner circular layer and the outer longitudinal layer. They are separated by the Auerbach's myenteric plexus, which controls oesophageal peristalsis. Under endoscopic examination, the fibers of the inner circular layer appear white, circular and are clearly distinguishable from each other (Figure 5). In case of a cleavage of this layer, especially during a POEM procedure, the external longitudinal appears in the form of muscle fibers of identical appearance but arranged perpendicularly and divide easily once in contact with the endoscope (Figure 6).

The adventitia is made up of an external fibrous layer of connective tissue, very rich in fat cells, consolidating the oesophagus with the mediastinal organs that surround it. There is no serosa around the oesophagus except in the small portion of intra-abdominal oesophagus (visceral peritoneum). Regarding POEM, myotomy can also involve the external longitudinal muscularis and it allows for the visualisation of peri-oesophageal fat. The adventitia is usually not identifiable.

ENDOSCOPIC ASPECTS WITHOUT ANY PATHOLOGICAL SIGNIFICANCE

Different non-pathological anatomical variations can be observed during endoscopic oesophageal exploration. Furthermore, before examining the oesophagus, a careful



Figure 5: Internal Circular Muscle Layer as seen during an Oesophageal Per Oral Endoscopic Myotomy (POEM) procedure.

exploration of the piriform sinuses should be part of the endoscopic examination by the gastroenterologist when dealing with patients with a history of oesophageal squamous cell carcinoma or a history of ENT issues. Indeed, about 10% of these patients have precancerous lesions in these regions, and their treatment by submucosal dissection is



Figure 6: External longitudinal muscle layer. During the POEM procedure, the complete section of the inner circular shows the fibers of the outer longitudinal.

possible with good outcome (1). At about 15 cm from the dental arches marks the beginning of the oesophagus, entering the oesophageal mouth which corresponds to the upper sphincter of the oesophagus. In difficult conditions, its passage is facilitated by asking the patient to swallow.

The upper third of the oesophagus classically describes the region beginning from the oesophageal mouth to 24 cm from the dental arches. Typically located just below the oesophageal mouth, *gastric heterotopia* is a flat, rounded and well-defined lesion. It is usually subcentimetric in size and pink in color within the whitish squamous mucosa. Its prevalence is at around 5%. Surface analysis, using the BLI, shows regular glandular structures identical to those seen in the stomach. Histological analysis confirms the presence of glands with parietal cells that may correspond to gastric structures. No special management is currently recommended, even though exceptional cases of degeneration of gastric heterotopia have been described.

Glycogenic acanthosis corresponds to flat lesions that are slightly elevated. They are often multiple and less than 10 mm in size, and round in shape. They appear whiter than the adjacent mucosa, almost translucent. When analysed by BLI imaging, they have a squamous appearance. They are "iodine-positive" when stained with Lugol. Histology shows hypertrophy of the squamous epithelium associated with submucosal deposits of glycogen. Glycogenic acanthosis has no pathological significance.

At about 25 cm from the dental arches, the impression of the aortic arch is visible on the left edge of the oesophagus. The left bronchus footprint may also be visible a few centimeters below. Finally, the gastro-oesophageal junction (GOf) is located about 40 cm from the dental arches. It must be carefully examined and described. No consensus exists regarding its definition. In western countries, the top of the longitudinal gastric folds (which pass through the hiatal orifice) is the commonly accepted landmark. The line of demarcation between the oesophageal squamous mucosa and the gastric glandular mucosa is constituted by the Z line, which may be regular or irregular. In Japan, GOJ is defined as the ending of the palissadic vessels, which are thin, longitudinal vessels, located within the submucosa in the body of the esophagus. They become visible by endoscopy, emerging from the lining of the lower oesophagus.

In conclusion, oesophageal examination should be standardised, thorough, and careful so as not to miss any subtle changes in the landscape or color at high definition, as these can be associated with early neoplastic processes. The knowledge of the main endoscopic markers, their detailed description and photographical endoscopy reports make it possible to assure the quality of the examination and facilitate eventual patient follow-up.

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Barrett's oesophagus. From metaplasia to cancer: a direct path

Emmanuel Coron and Nicolas Etchepare, Nantes

Barrett's oesophagus (BE^{1}) is a glandular metaplasia of the lower oesophagus, the diagnosis of which is based on both endoscopic examination and histological confirmation (1). Population screening is not recommended, and testing should be done on targeted at-risk populations. The European Society of Endoscopic Gastrointestinal Endoscopy (ESGE) recommends that oesogatroduodenal screening endoscopy should be provided to patients with previous gastro-oesophageal reflux disease (> 5 years) that have several risk factors from the following: age 50 years or older, Caucasian ethnicity, obesity, first-degree antecedent of BE or oesophageal adenocarcinoma (2). The initial diagnosis is simple and relies on the detection of an oral move of the Z-line of at least 1 cm from the top of the gastric folds. The extension of the BE must be specified by the Prague CM classification (Figures 1 and 2) which is a valuable and reproducible tool with a kappa index > 0.9 (3).

While the initial diagnosis poses few problems for the endoscopist, surveillance is a more complicated issue. Indeed, BE is to date the only factor known to predispose to oesophageal adenocarcinoma. However, the real risk of cancer is extremely low, estimated at about 0.3% per year. Nevertheless, the perception of this risk is often a source of anxiety for patients and for the endoscopist. Indeed, white light examination makes it difficult to detect flat dysplastic lesions of high grade severity, therefore the interpretation of images obtained with "advanced diagnostic technologies (real or digital stains, zoom, or even





Figure 1: Prague classification.

confocal endomicroscopy) needs adequate training. Unfortunately facilities for such training are still very limited.

In practice, it is essential to perform surveillance endoscopy using high resolution equipment under good examination conditions, ideally on dedicated time-slots. It is therefore necessary to insist on the "basics" of the examination procedure: washing of the mucosa (water and / or mucolytic preparations) to eliminate saliva and mucus, slow and meticulous inspection (about a minute per centimeter of BE) not forgetting a careful examination of the cardia in retrovision. A biopsy should never be performed before having completed the optical exploration phase. Furthermore, quadrantic biopsies should be carried out at the end of the exploration.

Using chromoendoscopy, autofluorescence endoscopy or confocal endomicroscopy is not mandatory in routine.



Figure 2: Initial diagnosis of a Barrett's oesophagus classified as C1M2 according to the Prague classification using white light (A) and LCI (B) mode. Performing biopsies is essential to confirm the presence of intestinal metaplasia and formally retain the diagnosis of Barrett's oesophagus as well as for enabling rigorous surveillance indications.

practice. On the other hand, it seems essential for the endoscopist equipped with previous generation equipment, to become acquainted with the semiology of the macroscopic images enabling the detection, characterisation and prediction of the in depth invasion of the lesions in BE. These methods are frequently used in centers with a large number of patients because they help in the targeting of biopsies and the determination of the margins of lesions before endoscopic treatment.

The number of studies carried out using Blue Light Imaging (BLI) or Linked Color Imaging (LCI) is still limited compared to studies using older methods such as Narrow Band Imaging (NBI). Combined with the use of zoom, these methods make it possible to detect discrete anomalies of the Barrett's mucosa in the form of irregularities or glandular and / or vascular abrasions, and to better characterise them (Figure 3). Any visible abnormality must be photographed in order to facilitate its subsequent identification if endoscopic treatment is required. They must be taken from a separate sample and the endoscopic report must specifically mention the description of the location (in cm in relation to the dental arches and the clockwise orientation), size (in mm) and macroscopic appearance of the lesion using the Paris classification. Finally, even if it is shown that targeted biopsies have a clearly higher benefit compared to random biopsies, it is not currently possible to avoid quadrantic biopsies performed according to the Seattle protocol that still remains the standard recommended by all scientific societies. The extent of BE is a recognised risk factor for malignant progression. The monitoring intervals for nondysplastic BE are therefore coded according to the length of the BE segment:

1. Irregular Z-line: no endoscopic monitoring

2. Glandular appearance < 1 cm (< C1M1): no endoscopic monitoring

3. Maximum extent of BE \geq 1 cm and < 3 cm (M1 to M3): 5-year surveillance

4. Maximum extent of BE \geq 3 cm and < 10 cm (M3 to M10): 3-year monitoring

5. Maximum range of BE \geq 10 cm: monitored at an expert center.

In conclusion, the major interest of early detection of dysplastic or adenocarcinomatous lesions developed in BE is the opportunity to propose a minimally invasive endoscopic treatment with a curative aim, thus avoiding the use of oesophagectomy (4). This strategy is only possible by promoting training in the field of the interpretation of images indicative of superficial lesions, thanks to the newly available technological possibilities that have led to an evolution in endoscopic semiology.



Figure 3: Oesophageal mucosectomy of a flat lesion classified as Paris 0-IIa of a size of 4-5 mm. (A) Locating the lesion at the top of the Barrett's oesophagus. (B) Characterisation using the BLI mode showing the very disorganised appearance of the mucosal microarchitecture, confirming the suspicion of cancer in this region. (C) Aspiration of the lesion using the aspiration-ligation-resection system (Duette). (D) Post mucosectomy ulcer examination showing the completeness of the resection.



Figure 4: Oesophageal submucosal dissection. (A) White light examination showing a suspicious 15 mm nodular band, classified as Paris 0-IIa. (B, C, D) Characterisation of surgical margins before dissection. All images are with BLI + zoom. (E) Examination of the esophageal post-dissection ulcer, to verify the absence of perforation and careful examination of the hemostasis of the visible vessels. (F) Histological examination of the surgical specimen, confirming the curative nature of the dissection (intramucosal adenocarcinoma pT1a, moderately differentiated, L0V0, negative deep and lateral margins).

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Superficial squamous cell carcinoma of the oesophagus. How not to ignore them

Guillaume Perrod, Gabriel Rahmi and Christophe Cellier, Paris

Oesophageal cancer is a pathology with a bad prognosis whose global incidence is increasing. It is the sixth leading cause of cancer deaths in the world. There are two histological types, squamous cell carcinoma (SCC) and adenocarcinoma. Although adenocarcinoma is the most common histological form found in Europe and North America, SCC of the oesophagus remains the most common type in the world. Its prognosis is gloomy due to an often late initial diagnosis and great lymphophilia. In France, the five-year survival at all stages is estimated at 14%. SCC is localised most commonly in the upper or middle third of the oesophagus and is associated with the following risk factors: tobacco, alcohol, ingestion of corrosive substances, chest irradiation and oesophageal motor disorders (achalasia). The two main risk factors are alcohol and tobacco, which, when combined, increase the risk of cancer by a factor of 8.

Superficial squamous cell carcinoma is defined as carcinomatous infiltration limited to the submucosa (T1 stage) (Figure 1). When the invasion does not cross the muscularis mucosa (stages T1m1 or T1m2) and in the absence of any pejorative histological criteria (low differentiation, venolymphatic invasion), the estimated ganglion risk is less than 2% making this lesion type accessible for endoscopic resection.

Figure 1: Superficial oesophageal epidermoid lesion. Histological section with hematoxylin and eosin staining at a 10X magnification, of a moderately differentiated superficial carcinomatous squamous lesion affecting the lamina propria but not crossing the mucosal muscle (T1m2). The resection after submucosal dissection is of the R0 curative type.



The detection and characterisation of these lesions represents a major challenge in endoscopy because it guides the therapeutic decision.

Thus, the French Society of Endoscopy (SFED) recommends carrying out a screening test in case of: a history of squamous cell cancer in the ENT region, a history of ingestion of caustic substances or oesophageal motor disorder that has been evolving for more than 15 years. Since the incidence of squamous cell carcinoma is low in patients with a history of alcohol / smoking, cirrhosis or alcohol-induced pancreatitis, systematic screening is not mandatory (1).

The method of reference for the detection of SCC is 2% lugol chromoendoscopy using a high definition endoscope. After spraying lugol with a spray catheter, the so-called "iodine-negative" tumor zones turn pink after a few minutes ("pink color sign"). The diagnostic accuracy of lugol chromoscopy is high regarding sensitivity (Se) > 90% but low for specificity, therefore resulting in a low negative predictive value of approximately 50 to 60% (Figure 2) (2).

Virtual chromoendoscopy is an alternative approach. It is easy to use and provides better images in real time. Many different systems exist, such as FICE (Flexible Spectral Imaging Color Enhancement), NBI (Narrow Band Imaging, Olympus) and I-Scan (Pentax). Recently the Fujifilm Eluxeo system, with the combination of 4 focused color LEDs, allows the analysis of the mucosa and its vascularisation using BLI (Blue Light imaging) and LCI (Linked Color Imaging) modes. The main advantage of this system



Figure 2: Lugol chromoendoscopy. A demonstration of a negative iodine zone after lugol staining (white arrows), ranked as 0-IIb using the Paris classification. Lugol adheres to the glycogen molecules secreted by the oesophageal mucosa cells. In case of detection of a tumor lesion, there is a loss of glycogen secretion resulting in the creation of a negative iodine zone.

is the acquisition of images that are less dark and of better quality compared to other virtual chromoendoscopy systems. After virtual staining, suspicious lesions that are richly vascularised appear as brownish lesions in contrast with the adjacent mucosa (Figure 3). Regarding detection, virtual chromoendoscopy is superior to the white light approach for lesions < 5 mm, but is equivalent to lugol staining (3). On the other hand, the use of virtual chromoendoscopy is associated with a significant reduction in the analysis time compared to the lugol method.

In order to predict deep invasion, the Paris macroscopic classification should first be used (Table 1). It distinguishes raised lesions (0-I), flat lesions (0-II) and ulcerated lesions (0-III). For the superficial SCC, only flat lesions (0-Iia, 0-IIb or 0-IIc) are associated with a low risk of submucosal invasion (4). In a second step, the analysis of the lesion is completed by virtual chromoendoscopy combined with optical magnification. Numerous classifications exist, but the most appropriate ones are those based on the analysis of the loops formed by the intraepithelial capillaries with or without zoom, which makes it possible to distinguish the intraepithelial lesions from those that cross the muscular mucosa, or IPCL (Intraepithelial Papillary Capillary Loop) (Table 2). Initially based on the use of NBI with zoom, it allows for the distinction between intraepithelial lesions and those that cross the muscularis mucosa with an accuracy of 90% (5).



Endoscopic evaluation of a large suspicious lesion of the upper 1/3 of the oesophagus. Using white light (A), the boundaries seem fuzzy and difficult to characterise. After virtual chromoendoscopy by LCI (B), then BLI (C), the lesion appears brownish with clearly identifiable limits (white arrows), contrasting with the adjacent mucosa. Moreover, by combining the zoom with the BLI mode (C) intraepithelial capillaries can be analysed.

Classification		Definition	Endoscopic resection
Raised 0-I	IP	Pedunculated lesion	NO
	ls	Sessile lesion	
Flat 0-II	lla	Slightly elevated flat lesion	
	IIb	Flat lesion	YES
	lic	Slightly depressed flat lesion	
Ulcerated 0-III		Ulcerated lesion	NO ¹

Table 1: Paris classification and lymph node invasion risk for superficial squamous cell carcinoma of the oesophagus.

The Paris classification is a macroscopic classification that does not require chromoendoscopy or zoom. It classifies lesions into 3 categories: raised, flat and ulcerated. Each class is associated with a risk of deep invasion and thus lymph node involvement. Thus, for squamous cell carcinoma, only flat lesions are associated with a low risk of ganglionic invasion.

^{1.} In Japan the management of small lesions is still debated, but in France endoscopic resection is contraindicated.

Stage	De	efinition	Invasion	Endoscopic resection	BLI with ZOOM
A	Normal or abnormal vessels without irregularity		No dysplasia or low grade dysplasia	Yes	
B1	Marked irregularity and/or significant dilatation of micro-vessels	Loop persistence	High grade dysplasia	Yes	3 2 7
B2		Disappearance of loops	T1a Muscular mucosa or T1b Sm1	To be discussed	AL.
B3		Large dilatation> 3x	T1b Sm2	No	

Table 2: Japanese classification of intraepithelial capillaries or IPCL.

Table based on Oyama T, et al. (5).

The IPCL classification is based on the analysis of micro-vessel loops by virtual chromoendoscopy (here using BLI) with zooming. Using this approach, the degree of tumor invasion can be predicted to guide the therapeutic strategy. Only stages A and B1 represent low risk of crossing the muscularis mucosa.

Diagnostic endoscopic ultrasound is not recommended for the initial assessment of superficial SCC (6). Indeed, identification of the muscular mucosa is difficult by endoscopic ultrasound, not allowing the operator to differentiate with certainty between T1a and T1b lesions. Endoscopic ultrasound should be reserved for the evaluation of doubtful lesions (macroscopic appearance suggestive of submucosal invasion) and for advanced lesions when looking for mediastinal adenopathy and for the evaluation of parietal extension.

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List of clinical cases¹

CC1: Non-dysplastic Barrett's oesophagus
CC2: Non-dysplastic Barrett's oesophagus
CC3: Low grade dysplasia in Barrett's oesophagus
CC4: High grade dysplasia in Barrett's oesophagus
CC5: Intramucosal adenocarcinoma
CC6: Adenocarcinoma with superficial submucosal invasion
CC7: Adenocarcinoma with deep submucosal invasion
CC8: Squamous lesion with high grade dysplasia
CC9: Intra-mucosal squamous cell carcinoma
CC10: Squamous cell carcinoma with deep submucosal invasion
CC11: An example of a rare tumor: oesophageal melanoma

List of abbreviations used in the text DA: dental arches BE: Barrett's oesophagus ESD: Endoscopic submucosal dissection HGD: high grade dysplasia LGD: low grade dysplasia LCI: Linked Color Imaging BLI: Blue Light Imaging

^{1.} The collection of clinical cases and the constitution of the data base were carried out by Nicolas Etchepare.

CC1 Non-dysplastic Barrett's oesophagus



- 1 -



-2-







1/200 3:REC 4:0M_DH 5:0M_UP G-760Z

- 5 -



24

CASE REPORT

A 59-year-old man was referred for surveillance of Barrett's oesophagus (BE). He had no other notable antecedents except for gastro-oesophageal reflux during the past twenty years, which was well controlled with standard proton pump inhibitors. Oesophagogastroduodenal endoscopy classified the BE as C3M4 according to the Prague classification, with multiple areas of squamous mucosa in the BE (Image 1). There were no suspicious macroscopic lesions within the BE, nor was there any evidence of overlying oesophagitis.

ENDOSCOPIC DESCRIPTION USING BLUE LIGHT IMAGING (BLI) WITH ZOOM

► Images 2 to 4: Better characterisation of the mucosal microarchitecture was made possible by carefully exploring the BE with a moderate level of magnification using white light imaging (Image 2), LCI (Linked Color Imaging - Image 3) and especially the BLI mode (Blue Light Imaging - Image 4). The latter technique enabled the clearest identification of the network of regular capillary vessels within the BE.

▶ Images 5 and 6: Using high magnification coupled with BLI, in the lower part of the BE there were clear areas of gastric metaplasia (Figure 5) with round or oval holes in the glands (red arrows) and areas of complete intestinal metaplasia (Figure 6) with very elongated glands (yellow arrows) and many capillaries of different caliber but regular shape (green arrows).

HISTOLOGICAL DESCRIPTION

Four quadrant biopsies performed at every 2 cm according to the Seattle protocol confirmed the diagnosis of BE with gastric or intestinal metaplasia, without dysplastic lesions. A 3-year surveillance endoscopy was therefore proposed according to the actual European recommendations (1).

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CC2 Non-dysplastic Barrett's oesophagus







-2-



- 3 -





- 5 -





CASE REPORT

A 32-year-old patient referred by his doctor for the exploration of gastro-oesophageal reflux disease complicated by dysphagia during the last month. Endoscopy using white light imaging and virtual chromoendoscopy showed a typical C1M2 short Barrett's oesophagus (BE) extending circumferentially over 1 cm from the Z line (39 to 38 cm from the dental arches) showing a 1 cm band (from 38 to 37 cm from the dental arches) (1). BE mapping by planimetry confirmed the presence of non-dysplastic mucosa. Also noted was the presence of grade A Los Angeles oesophagitis.

ENDOSCOPIC DESCRIPTION

▶ Images 1 and 2: Using white light imaging, the Z line is identified located just above the gastric folds, opposite the palissadic vessels (white arrows). Typical appearance of circumferential BE of 1 cm in length was observed from 39 to 38 cm from the DA. It also had an aspect of a bifurcated tongue extending from 38 to 37 cm from the DA at 12 o'clock. Note the presence of a 5 mm longitudinal erosion consistent with a grade A Los Angeles oeso-phagitis lesion (black arrow).

▶ Images 3-5: Mucosal analysis with intermediate zoom using 3 modes: white light, BLI (Blue Light Imaging) and LCI (Linked Color Imaging). A mucous membrane with elongated regular glands with a villous appearance without any vascularisation anomalies can be seen. This observation is compatible with nondysplastic intestinal metaplasia.

HISTOLOGICAL DESCRIPTION

▶ Image 6: Histological presentation of BE with normal squamous oesophageal mucosa and metaplastic mucosa defined by regular mucoid secreting cells without nuclear abnormalities or significant mitotic activity. No reason to suspect dysplasia.

REFERENCE

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CC3 Low grade dysplasia in Barrett's oesophagus



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CASE REPORT

An oesogastroduodenal endoscopy was performed in this 71-year-old patient due to the occurrence of heartburn. The presence of grade C oesophagitis according to the Los Angeles classification was demonstrated and a short Endoscopic Barrett's oesophagus (BE) ranked C1M3 using the Prague classification was diagnosed. The biopsies confirmed the presence of intestinal metaplasia associated with a typical appearance of low grade dysplasia with an inflammatory infiltrate. After treatment with a double dose of proton pump inhibitors for 6 months, control endoscopy showed that the oesophagitis and the BE were healed, with no visible lesions. A new series of biopsies confirmed the presence of low grade multifocal dysplasia.

ENDOSCOPIC DESCRIPTION

▶ Image 1: Oesophageal examination using white light shows a 1 cm hiatal hernia, topped with a C1M3 Barrett's oesophagus

according to the Prague classification, without any obvious nodular lesions but with suspected ulceration at 8 o'clock from the BE.

▶ Image 2: Using LCI mode with zoom shows a typical BE appearance with elongated, regular glands, and very regular vascularisation along the glands.

▶ Image 3: The suspected ulceration at 8 o'clock corresponds to a patch of regular whitish epidermoid mucosa, with intrapapillary capillary loops typical of non-dysplastic squamous mucosa.

▶ Images 4 and 5: BLI mode with zoom enables the identification of some areas with a rarefaction of the glandular structures but with a normal appearance of the adjacent vessels.

HISTOLOGICAL DESCRIPTION

• Image 6: Histological appearance of intestinal metaplasia and low grade dysplasia. At a magnification of x 5 and after HES staining, the presence of packed, basophilic glands with pseudo-stratified hyperchromatic oval nuclei with mitosis is visible. The chorion is fibro-inflammatory. This histological appearance corresponds to low grade dysplasia.

CC4 High grade dysplasia in Barrett's oesophagus



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CASE REPORT

An oesogastroduodenal endoscopy was performed on a 69-year-old patient because of gastroesophageal reflux disease. The presence of a long BE classified as C9M9 was demonstrated with a centimetric flat, sessile lesion. The patient was referred for re-evaluation of his BE with four quadrant biopsies.

ENDOSCOPIC DESCRIPTION

Follow up endoscopy identified 2 distinct lesions with endoscopic and histological features.

▶ Images 1-3: The flat, sessile lesion (0-IIa) previously described at 38 cm from the dental arches (DA) (6 o'clock) was classified as Paris 0-IIa and measured approximately 8-10 mm. It was characterised by white light imaging, Linked Color Imaging (LCI) and Blue Light Imaging (BLI). It appeared to have a modified architecture of the glands which looked smaller and denser. The vascular network was difficult to analyse. The lesion was biopsied. ▶ Images 4, 5: Immediately below the Z line at 35 cm from the dental arches (DA), i.e. at the superior pole of the BE, there was a pseudopapillary lesion classified as Paris 0-Is measuring 5-6 mm in diameter. This lesion was examined using white light imaging and BLI. It was then resected by mucosectomy.

HISTOLOGICAL DESCRIPTION

▶ Image 6: Biopsies of the flat, sessile lesion located 38 cm from the DA. Classed as a BE mucosa made up of crypts lined with metaplastic intestinal epithelium, presenting with high grade dysplastic lesions. There was no overexpression of the P53 protein. The proliferation index using MIB1 was high. The pseudo-papillary lesion resected by mucosectomy at 35 cm from the DA also corresponded to a BE mucosa with high grade dysplastic lesions but consisted of crypts or villous papillary structures, lined with a dedifferentiated epithelium. There was intense overexpression of the P53 protein throughout the dysplastic epithelium. The proliferation index evaluated by MIB1 was high. The rest of the BE was non-dysplastic as determined by four quadrant biopsies performed according to the Seattle protocol.

CC5 Intramucosal adenocarcinoma







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CASE REPORT

This 68-year-old patient presented with a lesion of \sim 1 centimeter located immediately above the cardia within a BE band classified as C0M2. The biopsies were supportive of the diagnosis of adenocarcinoma.

ENDOSCOPIC DESCRIPTION

▶ Images 1 to 3: Examination using white light imaging, LCI and BLI, showed a flat, sessile lesion at 4 o'clock (Paris 0-Is) with a 15 mm diameter in the largest axis.

▶ Images 4 and 5: Using the BLI mode with zoom allowed for a precise characterisation of the lesion. The glands were very small or absent in an irregular microarchitecture (yellow arrow). The micro-vasculature was irregular but thin (red arrow). This presentation supports the verdict of a superficial adenocarcinomatous lesion (1).

▶ Image 6: Submucosal dissection allowed for the performance of a monoblock resection (2). Large submucosal vessels were

present under the lesion (yellow arrows). Also visible were submucosal fibers of the dissection plane which were tugged by gravity (blue arrow) as well as the muscular fibers of the inner circular layer (red arrow).

HISTOLOGICAL DESCRIPTION

The analysis confirmed the presence of a 9 mm (largest axis) moderately differentiated adenocarcinoma and lesions with variable levels of dysplasia. It infiltrated the mucosal chorion and the muscular mucosa as far as the interface between the two layers of the muscular mucosa, which was split. No vascular embolus was present and the resection limits were healthy (pT1a lesion).

Using HES staining, a disorganisation of the glands was seen, which appeared more rectilinear with a decreased size of the interglandular chorion. The cells were cylindrical with a nucleolar nucleus and numerous images displayed mitosis. The tumor did not cross the muscular mucosa.

REFERENCES

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2. Pimentel-Nunes P, Dinis-Ribeiro M, Ponchon T, Repici A, Vieth M, De Ceglie A, *et al.* Endoscopic submucosal dissection: European Society of Gastrointestinal Endoscopy (ESGE) Guideline. *Endoscopy* 2015; 4: 829-54. doi:10.1055/s-0034-1392882.

CC6 Adenocarcinoma with superficial submucosal invasion





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CASE REPORT

This 72-year-old man was referred for surveillance of a BE which was not previously treated endoscopically.

ENDOSCOPIC DESCRIPTION

▶ Images 1, 2 and 3: Examination using white light imaging and virtual chromoendoscopy. The mucosal and vascular patterns appear very irregular, with a submucosal invasion visible due to a small peripheral extension of the lesion. The margins were delineated using coagulation points, respecting a safety margin of 10 mm.

HISTOLOGICAL DESCRIPTION

▶ Images 4, 5 and 6: An ESD resection specimen (35 × 25 mm after fixation). Well differentiated adenocarcinoma invading the

submucosa by 150 microns (sm1). The distance between the deepest tumor gland and the margin was greater than 500 μ m. The 5 mm lateral oral part of the adenocarcinoma was mostly buried and covered with normal squamous epithelium. The lateral resection margin consisted of normal squamous epithelium on the oral side and dysplastic mucosa on the aboral side.

COMMENTS

ESD is an effective technique for resecting superficial neoplasia of the BE, including those larger than 15 mm. The presence of mucosa buried beneath the normal squamous epithelium with in some cases dysplasia or adenocarcinoma has already been reported (0-28%) (1, 2). The buried components seem difficult to detect by endoscopy leading to an underestimation of the size of the lesion (3). This justifies enlarging the safety margins to more than 10 mm (4).

REFERENCES

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CC7 Adenocarcinoma with deep submucosal invasion













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An endoscopy was performed in a 78-year-old patient with a clinical history of reflux disease and many antecedents of vascular disorders. It showed a supracentimetric lesion developed within a long Endoscopic Barrett's oesophagus (BE) which was classified as C9M10. The biopsies indicated the presence of an adenocarcinoma, classified as usT1N0M0 after endoscopic ultrasound.

ENDOSCOPIC DESCRIPTION

Images 1 to 3: Within the BE, there was an elevated sessile and micro-ulcerated zone of about 15 mm (classified as Paris 0-Is + 0-IIc). This area was friable and spontaneously haemorrhagic.
Images 4, 5: High magnification zoom combined with white light imaging and with using the LCI mode, and even more strikingly with the BLI mode, demonstrated the presence of tumor nodules with major architectural disorganisation and complete disappearance of the vascular framework. This appearance supports the diagnosis of a deep adenocarcinoma. Nevertheless, considering the age of the patient and the contraindication to a possible surgical treatment, a submucosal dissection was performed.

► Image 6: Appearance of the submucosal dissection piece which was extended before it was sent for anatomopathological

examination. A second suspected zone of 8-10 mm, corresponding to a zone of high grade dysplasia was resected by mucosectomy at the same time.

HISTOLOGICAL DESCRIPTION

• Image 7: Adenocarcinoma coming into contact with the deep margin (blue arrows) with lymphatic and vascular emboli (yellow arrow: lymphoid islet). The tumor infiltrated the muscular mucosa and extensively infiltrated the submucosa by over 500 μ m. Perineural invasion was also observed.



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CC8 Squamous lesion with high grade dysplasia



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A 67-year-old patient, monitored for chronic calcifying pancreatitis due to alcohol use, was referred for epigastralgia and heartburn. Upper digestive endoscopy revealed a flat, rounded lesion, about 15 mm in diameter, located 29 cm from the dental arches. Using virtual chromoendoscopy, this lesion seemed suspicious and well limited. Lugol 2% staining confirmed the presence of an iodine-negative area with a "pink color sign", i.e. an erythematous appearance associated with dense vascularisation. Note the absence of oesophageal metachronous lesions and the absence of any signs of portal hypertension.

ENDOSCOPIC DESCRIPTION

▶ Images 1 (white light) and 2 (BLI chromoendoscopy): there was a well-defined vascularised oval area (black arrows),

contrasting with the adjacent mucosa. It represents a non-ulcerated flat lesion classified as 0-IIb according to the Paris classification.

▶ Images 3 and 4: Intraepithelial capillary analysis was performed using BLI and LCI with zoom. The structure was regular, marked by persistent loops, sometimes irregular but without major dilation. This analysis enabled the classification of the lesion as stage B1 according to the IPCL classification (1).

► Image 5: Lugol 2% staining confirmed the suspicion of neoplastic lesions in this iodine-negative and well-defined zone. It also importantly confirmed the absence of other associated lesions.

HISTOLOGICAL DESCRIPTION

► Image 6: High-grade squamous intraepithelial lesion characterised by cytological abnormalities and major architectural abnormalities present throughout the layers of the epithelium, reaching the muscularis mucosa without invading it.

REFERENCE

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Intra-mucosal squamous cell carcinoma CC9







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A 74-year-old patient with a smoking habit of 30 pack-years and history of alcohol consumption was treated for squamous cell carcinoma of the left tonsil, classified as T4N2. In accordance with the recommendations of the ESGE (1), upper GI endoscopy for screening synchronous oesophageal lesions was performed.

ENDOSCOPIC DESCRIPTION

- ▶ Images 1, 2: Oesophageal examination using white light imaging followed by Linked Color Imaging (LCI) showed a flat lesion ranging from 28 to 31 cm from the DA, occupying about 50% of oesophageal circumference. This lesion was irregular, granular, with several micro-ulcerations. It was ranked as 0-IIa + IIc using the Paris classification.
- ▶ Image 3: The oesophageal instillation of lugol 2% confirmed the suspicious iodine-negative nature of the lesion and enabled the estimation of its exact size before resection.

▶ Images 4, 5: Using the Blue Light Imaging (BLI) mode with zoom allowed for the visualisation of the epithelial vascular loops which appeared sinuous, dilated and of irregular caliber. No new vessels were seen. As previously suggested (2), the BLI mode also enables a more precise detection of the lesion and an estimation of its margins. A mucosectomy was then performed.

HISTOLOGICAL DESCRIPTION

This lesion corresponded to moderately differentiated squamous cell carcinoma, infiltrating the mucosal chorion in the form of lobules, without keratotic maturation. No infiltration of the muscularis mucosa or lymphatic or vascular emboli were observed. This lesion developed on top of squamous dysplastic lesions of variable grade, going up to the grade of squamous cell carcinoma. Endoscopic resection passed through a deep, healthy margin.

▶ Image 6: At magnification x 5, after HES staining, the diagnosis of squamous cell carcinoma was confirmed, infiltrating the mucosal chorion in the form of lobules.

REFERENCES

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CC10 Squamous cell carcinoma with deep submucosal invasion







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An 80-year-old woman with a history of smoking and alcohol use underwent upper GI endoscopy in the context of an anemia work-up.

ENDOSCOPIC DESCRIPTION

▶ Images 1-3: There was a suspicious raised lesion of 6-7 mm, classified as Paris 0-IIa + c examined using white light imaging followed by Linked Color Imaging (LCI) plus Blue Light Imaging (BLI). The center of the lesion was very disorganised with an amorphous appearance and large vessels (B3 in the IPCL classification).

▶ Image 4: The oesophageal instillation of lugol 2% confirmed the suspicious iodine-negative nature of the lesion and showed a fairly large lateral flat extension of about 20-25 mm.

▶ Images 5, 6: Because of its size > 10 mm, submucosal dissection was performed rather than a mucosectomy. The 30 × 15 mm specimen was extended and stretched, then sent for pathological examination.

HISTOLOGICAL DESCRIPTION

The lesion was a moderately differentiated squamous cell carcinoma. The lateral and deep boundaries were in the healthy zone but the lesion was classified as pT1bsm2 using the Japanese classification. Indeed, the lesion infiltrated the muscular mucosa and the submucosa by $300 \,\mu$, thus justifying the indication of a complementary treatment. Because of her age, the patient opted for simple clinical surveillance.

CC11 An example of a rare tumor: oesophageal melanoma



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A 71-year-old patient, with no notable antecedents, complained of early satiety with heartburn that had been evolving for several weeks. Upper GI endoscopy was performed, showing the presence of a polypoid lesion of the lower oesophagus, 5 cm in height, occupying 3/4 of the oesophageal circumference, with a stenosis but still allowing the passage of an endoscope.

ENDOSCOPIC DESCRIPTION

▶ Images 1 and 2: Oesophageal exploration using white light showed the presence of a prominent and sessile lesion of bluish and blackish pigmentation occupying almost the entire circumference of the oesophagus. At the periphery of the raised lesion, a sub-mucosal planar development of this pigmented lesion was observed.

▶ Images 3 and 4: The lesion protruded in the sub-cardiac region as shown by endoscopic retrovision. On this side the lesion was much more fragile and budding, with spontaneous bleeding, probably related to mechanical phenomena. There was also a whitish fibrin coating on the lesion.

HISTOLOGICAL DESCRIPTION

• Images 5 and 6: Histological analysis showed the presence of a tumor with pigmented cells at high cellular density underneath the squamous epithelium (magnification \times 2.5). At high magnification (x10), the cells exhibited moderate to marked cytonuclear atypia, with the presence of intra-cytoplasmic melanin pigment.

COMMENTS

Primary oesophageal melanoma is a rare disease with a poor prognosis. The main differential diagnoses are vascular lesions, Kaposi sarcomas and leiomyosarcomas. The diagnosis is made through histology and is simple in the presence of intracytoplasmic melanin pigment. On the other hand, diagnosis of the other forms of this disease, those without melanin is more difficult and in such cases it is important to describe the endoscopic black pigmented aspect of this lesion which is very evocative. The treatment does not differ from that used for cutaneous forms, namely surgical treatment when the disease is localised, and immunotherapy and chemotherapy treatments in case of disseminated disease (1).

Reference

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The **BLI** is targeted illumination that provides excellent visibility of the mucosal surface and better contrast of its vascular network.

Associated with zoom endoscopes from the 700 series, with a magnification capacity of up to 135x, the images obtained are more detailed **facilitating the characterisation of neoplastic lesions**.



Los Angeles grade B esophagitis

ELUXEO



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Los Angeles grade B esophagitis

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Pr Emmanuel Coron, MD, PhD - CHU de Nantes - France







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Mr. Takemasa KOJIMA - Senior Manager Marketing & Sales for Endoscopy European department.

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Switching between the BLI (Blue Light Imaging) and LCI (Linked Color Imaging) endoscopic modes allows for a more precise characterisation of the lesions and a more cautious estimation of any unusual topography. From here on, the whole of the digestive system can be analysed, facilitating diagnosis with a sharpness and quality of contrast never before reached.

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The study of oesophageal lesions and angiogenesis is greatly modernised by this innovative device. This technology allows the practitioner to finely categorise precancerous lesions.