COLONIC DIVERTICULAR DISEASE
THE POINT OF VIEW OF THE PATHOLOGIST AND THE GASTROENTEROLOGIST

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THE POINT OF VIEW OF THE GASTROENTEROLOGIST
• Colonic diverticular disease is one of the most frequent pathologic conditions in Western countries, with variable clinical presentation ranging from asymptomatic diverticulosis (incidence 30-63%) to acute diverticulitis (incidence 10-25%) up to perforation (Jacobs DO, NEJM 2007)

Even though DD is more frequent in older individuals, there is a trend toward an increased incidence among younger subjects (Etzioni et al, Ann Surg 2009)

DD: CLASSIFICATIONS AVAILABLE IN LITERATURE

• Hughes et al. Med J Aust, 1963
• Hinchey et al, 1978
• Siewert et al, Chirurg 1995
• Hansen et al, Chirurg 1998
• Sher et al, Surg Endosc 1997
• Wasvary et al, Am Surg 1999 (Hinchey modified)
• Kohler et al, Surg Endosc 1999
• Kohler et al, Surg Endosc 1999 (TC based)
• Ambrosetti et al, Eur Radiol 2002 (TC based)
DD: NEW CLASSIFICATION PROPOSAL

Klarenbeeck et al,
Int J Colorect Dis 2012

*experimental or non evidence-based treatment
DD: PECULIAR ENDOSCOPIC ASPECTS

In DD endoscopy may reveal mucosal aspects that mimic IBD

DIVERTICULAR DISEASE: PATHOPHYSIOLOGY

• genetic predisposition
• aging (wall elastosis)
• fibre-poor diet
• colonic motor abnormalities
• enteric nervous system abnormalities

Bassotti et al, World J Gastroenterol 2003
DD: COLONIC MOTOR ABNORMALITIES

- Overall increased motor activity in the affected segments;
- Increased number of HAPC;
- About 20% of HAPC display abnormal (retrograde) propagation;
- Increased duration of low frequency (2-3 cycles/minute) contractile patterns.

Bassotti et al, Dis Colon Rectum 2001
More than 30% of patients, but none of the controls, reported episodes of abdominal pain (cramping lower abdominal pain with characteristics similar to those experienced at home) during the occurrence of a regular colonic contractile pattern. This was significant by symptom association probability criteria (Bassotti, Villanacci et al, Clin Gastroenterol Hepatol 2005)

Colonic motor abnormalities are frequent in diverticular disease

May these abnormalities be due to abnormalities of the enteric nervous system circuitry?
AND NOW.....

THE PATHOLOGIST

THE POINT OF VIEW OF THE PATHOLOGIST

PATHOGENESIS

TERMINOLOGY

DIFFERENTIAL DIAGNOSIS
DIVERTICULOSIS

PRESENCE OF MULTIPLE DIVERTICULI WITHOUT ACUTE INFLAMMATION

INFLAMMATION
DIVERTICULITIS

MULTIPLE DIVERTICULI WITH ACUTE INFLAMMATION

BRIEF REVIEW

The pathology of diverticular disease

Review Article

Diverticulosis Coli
Update on a “Western” Disease

Hudson YE, MEL, Mariella Lomada, MD, and A. Brian West, MD
Mechanical effects

Lymphatic obstruction

Mucosal ischaemia

Mucosal prolapse

Pre-diverticular disease

Muscle abnormality more important than the presence of diverticula for the genesis of luminal inflammation/diverticular colitis?

Are we missing/ignoring a tranche of significant sigmoid colonic pathology in the diagnosis of diverticular disease by insisting on the demonstration of diverticula to diagnose ‘diverticular disease’?

Mathus-Vliegen & Tytgat, 1986; Ludeman & Shepherd, 2002

MANY DOUBTS!
PROBLEMS ON TWO DIFFERENT POINTS
BIOPSY

GRUPPO ITALIANO MALATTIA DIVERTICOLARE

[Image of bowel lining with apparent abnormalities]
Histopathology of DD

Biopsies should be accompanied by clinical information including the age of the patient, duration of disease and duration and type of treatment.

The Perfect Pathologist for IBD? An Endoscopist’s Vision

Optimally the same handling should allow to perform routine histology, immunohistochemical stains, FISH and DNA extraction...
Normal Mucosa

Morphological elements to be evaluated:

- Crypts
- Lamina Propria
- Cellularity
- Architecture
Histo Statement 1

The vast majority of DD is not associated with any histological change in the mucosa surrounding diverticula (excluding diverticular lesions and their complications).

Level 1b Grade A

Terminology

- Segmental Colitis
- Sigmoid Colitis
- Sigmoiditis
- Crescentic Colitis
- Segmental Colitis Associated with Diverticula (SCAD)
- Diverticular Associated Colitis (DAC)
- Diverticular Disease-Associated Segmental Colitis
- Diverticular Colitis
Diverticular Associated Colitis (DAC)

**DEFINITION:**
chronic colitis localized in the colonic segment presenting diverticulosis.

By definition, both the rectum and the right colon are spared from inflammation both endoscopically and histologically.

DAC involves the interdiverticular mucosa

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The spectrum of histological lesions associated with Diverticular Disease Associated Segmental Sigmoid Chronic Colitis (DAC) is wide.

**It includes**

- 1) mild non-specific inflammation,
- 2) IBD-like changes
Pathological spectrum of luminal disease in diverticulosis

- Minor Inflammation
- Cistically Dilated Crypts
- Mucosal Prolapse Change (segmental colitis)
- Mild Active Inflammation
- CIBD mimicry: Ulcerative Colitis, Crohn’s disease

Sladen et al 1984; Gore et al, 1992;
Makapugay & Dean, 1996; Ludeman & Shepherd, 2002;
Peppercorn, 2004; Lamps & Knapple, 2007;
Freeman, 2008; Mulhall et al, 2009

Minor Inflammation
Cystically Dilated Crypts
REVIEW

Histopathological mimicry in mucosal prolapse

B Singh, N J McC Mortensen and B F Warren
Nuffield Department of Surgery, 1Department of Colorectal Surgery and 2Department of Cellular Pathology, John Radcliffe Hospital, Oxford, UK

Singh B, Mortensen N JMcC & Warren B F
(2007) Histopathology 50, 97–102

Histopathological mimicry in mucosal prolapse

Mucosal prolapse solitary rectal ulcer syndrome is a condition which has frequently confused both pathologists and surgeons alike. Despite its recognition in the nineteenth century, it continues to be a diagnostic challenge. The significance of correctly diagnosing this condition is that it avoids the morbidity and mortality associated with major surgery or the side-effects of long-term medical treatment. This review considers the histological features of mucosal prolapse and how it may mimic other pathological conditions.

Keywords: histology, mimicry, solitary rectal ulcer syndrome

Abbreviation: MPSRUS, mucosal prolapse solitary rectal ulcer syndrome
Term used to describe isolated finding of neutrophilic crypt injury

Histological features:
- single/multiple foci of cryptitis
- single discrete crypt abscess
- multiple crypt abscesses
- no significant chronic inflammation

Follow-up (1-74 mths, mean = 25 mths)

- acute self-limited infectious colitis (45%)
- incidental finding (25%)
- irritable bowel syndrome (14%)
- ischaemia (10%)
- antibiotic associated colitis (5%)

No patient developed CIBD

Greenson et al, 1997
Secondary Colitis

26 cases in a 10 year period: single centre study
initial biopsy pathology suggestive of CIBD
• subsequent information indicated an underlying mass lesion
• no evidence of CIBD on follow-up / resection
• nearly all in the sigmoid colon / rectum

Significant mimicry of CIBD (both UC & CD) by:
• primary adenocarcinoma 6
• secondary carcinoma 7
• complicated diverticular disease 7
• pneumatosis cystoides intestinalis 4
• Endometriosis 7

Unifying factor: underlying mass lesion causing biopsy mimicry of CIBD

Histopathology of DAC may closely mimic IBD: this point represents a potential diagnostic pitfall

Level 2A

Grade B
**Infections**
- Viral
- Bacterial – TB, yersinia, chronic enterocolitides
- Mycotic
- Protozoal
- Helminthic

**Drugs, enemas & suppositories**

**Endoscopic preparation**

**Immunopathology**
- Immunodeficiency syndromes
- GVHD
- Granulomatous disease of childhood

**Ischaemic enterocolitis**

**Radiation enterocolitis**

**Behcet’s syndrome**

**Diversion proctocolitis**

**Diverticular/segmental colitis**

**Secondary colitis**

**Focal active colitis**

**Pouchitis and pre-pouch ileitis**

**Microscopic colitis (MC)**
- Lymphocytic colitis
- Collagenous colitis
- Granulomatous MC
- Giant cell MC

**Obstructive colitis**

**Pneumatosis cystoides intestinalis**

**Endometriosis**

**Malignant lymphoma and other tumours**
**EPITHELIOID CELL GRANULOMATA IN COLORECTAL BIOPSIES**

- Crohn’s disease
- sarcoidosis
- tuberculosis, yersiniosis
- infective enterocolitis, especially microgranulomas
- diversion proctocolitis
- diverticular colitis
- ulcerative colitis, especially cryptolytic granulomata
- pouch mucosa and pouchitis
- granulomatous disease of childhood
- drugs, especially with ‘microscopic colitis’
- pneumatosis cystoides intestinalis
- For a diagnosis of Crohn’s disease, even granulomas are beholden to context
  - location – basal, submucosal
  - commoner the more distal in the gut
  - size is important
  - effete in diverted CD
  - microgranulomas
  - cryptolytic granulomas

**DIVERTICULAR DISEASE AND CROHN’S DISEASE**

A Crohn’s-like reaction can be a localised reaction to diverticulitis alone.
Gledhill and Dixon, 1998

Crohn’s-like changes are an idiosyncratic inflammatory response to diverticulosis rather than coexistent Crohn’s disease in the vast majority of patients.
Goldstein et al, 2000

Pathologists should be wary of making a diagnosis of sigmoid colonic Crohn’s disease in the context of diverticulosis.
Goldstein et al, 2000

Whilst we do not deny that Crohn’s disease and diverticulosis can co-exist and that their coincidence may worsen the prognosis of either disease, we believe that extreme caution is required before making the diagnosis of coexistent disease, in the absence of collateral evidence to support a diagnosis of Crohn’s disease.
Ludeman, Warren & Shepherd, 2002
Formerly believed that the two conditions coexisted much more often than would be expected.

More recently it is clear that many, if not all, of the classical pathological hallmarks of CD can be mimicked by complicated DD.

Meyers et al, 1978; Berman et al, 1979; McCue et al, 1989

- Granulomas
- Focal active inflammation
- Transmural inflammation in the form of lymphoid aggregates
- Fissuring ulceration and fistulae

Makapugay & Dean, 1996; Burroughs et al, 1998; Gledhill & Dixon, 1998; Goldstein et al, 2000; Ludeman & Shepherd; 2002
<table>
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<th>Total number and pathology</th>
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<td>Goldstein et al, 2000</td>
<td>27: CD-like changes</td>
<td>4 (2 before; 2 after sigmoid resection)</td>
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</table>

Look elsewhere for evidence of Crohn’s disease!

Diverticular Colitis and Ulcerative Colitis

Mimicry of UC by diverticular colitis  
The rectum should always be biopsied!

Some cases progress from diverticular colitis to classical UC  
Similar pathogenesis in some cases?
Chronic inflammation and crypt changes in luminal mucosa in diverticulosis: mimicry of ulcerative colitis

<table>
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<tr>
<th>Author</th>
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Histo Statement 5

Limitation of mucosal lesion to the diverticular segment is the most important diagnostic criterion for DAC (distal and rectal sparing)

Rectal biopsies are crucial for DAC

DAC vs UC distinction
59 years old female, rectal bleeding. Endoscopy, mucosal congestion edema, patchy iperemia with exudative inflammation. Presence of diverticuli in sigma

SIGMOID COLON
Colitis related to diverticular disease (DAC)!

87 years old female; hypertrophic rectal mucosa with hyperemia.

RECTUM
Colitis related to diverticular disease (DAC)!
Diverticulosis provides some intriguing relationships with CIBD

Cryptolytic granulomas/pericryptal granulomas and focal active colitis are certainly not specific to, and are variably predictive of Crohn’s disease

Intramural mass lesions cause significant mimicry of CIBD in mucosal biopsies

Pathologists often confuse focal active colitis and microscopic colitis with CIBD but.....

Nowhere is context more important in gastroenterology than in colorectal biopsies taken for potential CIBD
**DD: RECENT ADVANCES**

- Patients with DD undergoing both elective and emergency surgery have an increased number of colonic mast cells compared to controls.
- All patients with DD undergoing emergency surgery (n=12) had myenteric plexitis (eosinophilic, 4, and lymphocytic, 8).

*Bassotti, Villanacci et al, Int J Colorect Dis 2012*
DD: RECENT ADVANCES

- Patients with DD needing surgery display a higher number of colonic MC
- This finding might explain some symptoms (pain, dysmotility) found in these patients
- The presence of myenteric plexitis in patients undergoing emergency surgery might represent a histological marker of more aggressive complicating disease

Bassotti, Villanacci et al, Int J Colorect Dis 2012
CONCLUDING REMARKS

A COMMON POINT OF VIEW

Vincenzo

Gabrio

- DD is a complex entity, both from a gastroenterological and pathological point of view
- In addition to mucosal aspects, the neuroenteric circuitries of the large bowel are also involved
- And…
…a strict collaboration is of paramount importance to better elucidate the pathophysiological mechanisms of DD