# IDIOPATHIC INFLAMMATORY BOWEL DISEASES

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# IIBD CONTD

INTRODUCTION

Inflammatory bowel disease – includes all inflammatory diseases of the intestine including the colorectum.

IIBD is restrictive for:

1. Crohn's disease
2. Ulcerative colitis
3. Indeterminate IIBD – features of the 2 above

# IIBD CONTD

- Differentiation from other colitis can sometimes be difficult
- They are chronic relapsing inflammatory disorders of obscure origin
- Diagnosis depends on clinical and pathological criteria, and exclusion of other causes of inflammatory lesion
- They also exhibit extraintestinal inflammatory manifestations

# AETIOLOGY AND PATHOGENESIS OF IIBD

- Results from loss of dynamic balance between:

1. Factors that activate host immune system (e.g., luminal microbes, dietary antigens, endogenous inflammatory stimuli). AND
2. Host defences that maintain integrity of the mucosa and down-regulate inflammation.

# AETIOLOGY AND PATHOGENESIS OF IIBD

Role of Ethnicity:

- Incidence and prevalence significantly depend geographic location; racial or ethnic backgrounds.
- It occurs worldwide but low incidence in Asian and Middle Eastern countries; while high incidence in Europe, US, Canada, Australia, and New Zealand.
- Incidence in higher in Caucasians than non-Caucasians in US. Jews in US have the greatest risk compared with non-Jewish Caucasians.

# AETIOLOGY AND PATHOGENESIS OF IIBD

Role of Genetics:

- Evidences of familial clustering – 5% to 10% of patients with IBD have affected family member; individuals with a first-degree relative have a 10 to 15-fold increased risk; concordance in monozygotic twin for CD is 42-58% while only 4% in dizygotic twin.
- Susceptibility genes – A no of potential genetic susceptibilty loci for IBD have been identified:

# AETIOLOGY AND PATHOGENESIS OF IIBD

| Locus Designation | Chromosomal Location | IBD Type | Candidate Genes |
|---|---|---|---|
| IBD1 | 16q12 | CD | NOD2 |
| IBD2 | 12q13 | UC | VDR, IFN-γ |
| IBD3 | 6p13 | CD, UC | MHC I, MHC II, TNF-α |
| IBD4 | 14q11 | CD | TCR α/δ complex |
| IBD5 | 5q31-33 | CD | IL-3, IL-4, IL-5, IL-13, CSF-2 |
| IBD6 | 19p13 | CD, UC | ICAM-1, C3, TBXA2R, LTB4H |
| IBD7 | 1p36 | CD, UC | TNF-R family, CASP9 |
| IBD8 | 16p | CD | Unknown |
| IBD9 | 3p26 | CD, UC | CCR5, CCR9, nMLH1 |
| Other | 7q | CD, UC | Multidrug resistance 1 |
| Other | 10q23 | CD | Drosophila discs large homolog 5 |
| Other | 9q32-33 | CD, UC | Toll-like receptor-4 |
| Other | 1q41-42 | CD | Toll-like receptor-5 |
| Other | 7p14 | CD, UC | NOD1/CARD4 |

Crohn disease; IFN, interferon; IL, interleukin; MHC, major histocompatibility complex; UC, ulcerative colit

# AETIOLOGY AND PATHOGENESIS OF IIBD

Other factors:

- Immunological factors – both innate and acquired immunity.
- Autoantibodies – Especially antineutrophil cytoplasmic antibodies (ANCAs)
- Apoptosis – When mucosal T lymphocytes are resistant to apoptosis especially in CD
- Exogenous agents such as diet (food antigen), infectious agents, tobacco use and exposure, use of NSAIDs

# AETIOPATHOGENESIS OF IIBD CONTD

Summary of the interplay of various factors:

1. Genetic predisposition: differential associations with class II HLA (HLA-DR1/DQw5 allelic combination in some patients with CD, HLA-DR2 in patients with UC).
2. Infectious causes: Viruses (measles), chlamydia, mycobacteria, etc, have been implicated.
3. Abnormal host immunoreactivity: Failure to down-regulate after stimulation by luminal antigens.
4. Inflammation as the final common pathway: Products of inflammatory cells cause the tissue injury.

# CROHN'S DISEASE

INTRODUCTION

It is a transmural, granulomatous, inflammatory disease that may affect any part of the GIT but occurs principally in the small intestine and occasionally the colon.

First described in 1932

# CROHN'S DISEASE

EPIDEMIOLOGY

- Occurs throughout the world
- Annual incidence of 0.5 – 5/100,000
- Usually appears in the adolescents or young adults.
- Most common among persons of European origin, higher frequency among Jews
- Slight female predominance, 1.6:1

# CROHN'S DISEASE

MORPHOLOGY

Major features that differentiate CD from other IIBD are:

1. Transmural inflammation – involves all the layers of the bowel
2. The inflammation is discontinuous (skip lesions)

# CROHN'S DISEASE

MORPHOLOGY CONTD

SITES: At presentation 40% of patients show involvement of ileocecal region, 30% have small bowel disease, 25% colonic disease, 15% anorectal region, rarely involves esophagus, stomach, and duodenum.

# CROHN'S DISEASE

GROSS

- Bowel wall appears thickened and edematous and the serosa demonstrates fat wrapping.
- 'Cobblestone' appearance – nodular swelling, fibrosis, and ulceration of the mucosa.
- Ulcers – initially superficial but become deeper and appear as fissures.
- Fistula formation – may penetrate into other organs, including bladder, uterus, vagina, and skin. Perianal fistula is a well-known presenting feature of CD.

# CROHN'S DISEASE

MICROSCOPIC:

- Transmural inflammation that extends through all layers of the bowel wall.
- May be confined to the mucosa and submucosa in early cases.
- Discrete noncaseating granulomas, mostly in the submucosa, are often present.
- NOTE – Absence of granulomas does not exclude the diagnosis.

# CROHN'S DISEASE

CLINICAL FEATURES

- Onset is insidious and manifestations are highly variable, related to anatomical localization of the disease.
- About 75% of patients present with abdominal pain and diarrhea.
- About 50% with recurrent fever.
- Involvement of ileum and caecum may mimick appendicitis
- Ileum – right lower quadrant pain, intermittent diarrhea, and fever.
- Colon – diarrhea and sometimes colonic bleeding
- Diffuse small intestine – malabsorption and malnutrition
- Anorectal region – recurrent anorectal fistulas

# CROHN'S DISEASE

EXTRAINTESTINAL MANIFESTATION

- Uveitis
- Ankylosing spondylitis
- Erythema nodosum
- Pericholangitis and sclerosing cholangitis
- Amyloidosis, etc

# CROHN'S DISEASE

COMPLICATIONS

- Intestinal obstruction and fistulas are commonest
- Occasional free perforation of the bowel
- Strictures
- Risk of small intestinal cancer is increased (3-fold)
- Also predisposes to colorectal cancer (the risk is small compared to ulcerative colitis)

# CROHN'S DISEASE

DIFFERENTIAL DIAGNOSES

- Ulcerative colitis
- Amebic colitis
- Tuberculosis
- Schistosomiasis
- Campylobacter infection
- Acute appendicitis
- Meckel diverculitis, etc

# ULCERATIVE COLITIS

INTRODUCTION

It is an inflammatory disease of the large intestine characterized by chronic diarrhea and rectal bleeding, with a pattern of exacerbation and remission, and with the possibility of serious local and systemic complications.

It is limited to the large intestine and affecting only the musoca and submucosa.

# ULCERATIVE COLITIS

EPIDEMIOLOGY

- Global in distribution
- No sex predominance
- Begins in early adult life, with peak incidence in the 3rd decade
- Childhood onset and old age are not rare
- Whites are affected more than blacks in US

# ULCERATIVE COLITIS

MORPHOLOGY

3 main features differentiate UC from other inflammatory diseases:

1. A diffuse disease – from most distal part of the rectum. When it involves rectum only – ulcerative proctitis, universal colitis – involves the entire large intestine.
2. Inflammation is limited to the colon and rectum. Rarely involves the adjacent ileum – backwash ileitis.
3. It is limited to the submucosa.

# ULCERATIVE COLITIS

Early colitis

Gross:

- Mucosal surface appears raw, red, and granular, and bleeds easily.
- Later ulcer appears.
- Raised areas of mucosa corresponding to inflammatory polyps (pseudopolyps) can be seen.

# Early colitis contd

Histology:

- Mucosal congestion, edema, microscopic hemorrhages, diffuse chronic inflammation infiltrates in the lamina propria
- Damage and distortion of the crypts (crypt distortion), crypts are infiltrated by neutrophils (cryptitis)
- Suppurative necrosis of the crypts results in dilated degenerated crypts filled with neutrophils (crypt abscess).

# ULCERATIVE COLITIS

Progressive colitis –

Gross:

- Mucosal folds are lost as the disease progresses.
- There is tissue destruction with formation of highly vascular granulation tissue in the denuded areas.

Histologic:

- The crypts appear tortous, branched, shortened.
- Mucosa may be diffusely atrophic.

# ULCERATIVE COLITIS

Advanced colitis-

Gross:

- The large intestine is often shortened especially in the left side.
- Mucosal folds are indistinct and are replaced by a granular or smooth mucosal pattern

Histology:

- Chronic inflammatory infiltrates, atrophy.

# ULCERATIVE COLITIS

CLINICAL FEATURES

Highly variable –

- 70% have intermittent attacks with partial or complete remission between attacks.
- 10% have a very long remission after first attack.
- 20% have continuous symptoms without remission.

# ULCERATIVE COLITIS

Clinical features contd

- These include rectal bleeding, tenesmus, recurrent episodes of loose bloody stool, crampy abdominal pain, low grade fever.
- 10% have fulminant ulcerative colitis (about 15% of patient with fulminant UC die of the disease)
- About 30% of patient with UC require colectomy within the first 3 years of onset because of uncontrolable disease.

# ULCERATIVE COLITIS

Extraintestinal manifestations:

- Arthritis – seen in 20% of UC
- Uveitis – seen in about 10%
- Skin lesions e.g., erythema nodosum – 10%
- Liver diseases, e.g., pericholangitis – 3%

# ULCERATIVE COLITIS

Differential diagnosis:

- Crohn's disease
- Shigella colitis
- Salmonella infection
- Amebic colitis
- etc

# ULCERATIVE COLITIS

Complications:

- Fulminant UC
- Toxic megacolon – radiologic diagnosis (diameter of the colon measured at the transverse colon exceeds 6cm). It carries maximum risk of mortality. Occurring in 2-4% of patient with UC. Perforation is common with more than 50% mortality.
- Secondary infection – especially Clostridium difficile
- Backwash ileitis

# ULCERATIVE COLITIS

Complications contd

- Polyps – may be inflammatory or adenomatous
- Colorectal cancer – long standing extensive UC have a higher risk of CRC than the general population. The risk is related to the extent of involvement and the duration of the inflammatory disease.
- Strictures – in about 5% of UC

# INDETERMINATE COLITIS

Overlapping pathologic features of UC and Crohn's disease.