Inflammatory Bowel Disease

by

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IBD

Definition

Inflammatory bowel diseases (IBDs), including ulcerative colitis (UC), Crohn's disease (CD) and microscopic (lymphocytic and collagenous) colitis, are chronic inflammatory diseases of the gastrointestinal tract. They are diagnosed by a set of clinical, endoscopic, and histologic characteristics .

Epidemiology-UC

- The incidence is about 6-15 per 100,000.
- The prevalence is about 80-150 per 100,000.
- The peak age at onset
  - Between 15 and 25 years,
  - Second, lesser peak between 55 and 65 years.
- The incidence in children is low.
- The incidence is equal in men and women.
- Higher incidence in first-degree relatives.
- The epidemiology varies with geographic location.

Epidemiology-CD

- The incidence is about 4-10 per 100,000.
- The prevalence is about 25-100 per 100,000.
- The peak age at onset
  - Between 15 and 25 years,
  - Second, lesser peak between 55 and 65 years.
- The incidence in children is low.
- The incidence is equal in men and women.
- Higher incidence in first-degree relatives.
- The epidemiology varies with geographic location.

Aetiology and pathogenesis

Although the aetiology of IBD is unknown, it is increasingly clear that IBD represents the interaction between several co-factors: genetic susceptibility, the environment (smoking, nutrition, NSAID, appendicectomy, hygiene), the intestinal microbiota and host immune response.

Pathogenesis

- Activated T cells are involved in the pathogenesis.
- Pro-inflammatory cytokines, including interleukin-1 (IL-1) TNF-α, amplify the immune response.
- Failure to suppress the normal, low-grade chronic inflammation of the intestinal lamina propria.
- Colitis could be the result of an abnormal immune response to commensal bacteria.

Pathology-UC

- Inflammation begins in the rectum) Proctitis, E1), extends proximally to involve the sigmoid and descending colon (left-sided colitis, E2), or may involve the whole colon (extensive colitis, E3). In a few of these patients, there is also inflammation of the distal terminal ileum (backwash ileitis).
- Pathological changes vary according to the activity and severity and include one or more of the following;
  - Superficial erosions.
  - Large , superficial ulcers.
  - Mucosal edema and vascular congestion.
  - Inflammatory polyps or pseudopolyps.

Pathology-UC.

- Active UC is marked by
  - Crypt abscesses.
  - Mucosal edema and vascular congestion.
  - Neutrophils in the mucosa and submucosa.
- There are also signs of chronicity, with lymphoid aggregates, plasma cells, mast cells, and eosinophils.
- Pathologic changes in UC
  - Usually limited to the mucosa and submucosa.
  - May not correlate with clinical and endoscopic assessment.

Pathology-CD

- The bowel wall is thickened and stiff.
- The mesentery, which is thickened, edematous, and contracted, fixes the intestine in one position.
- Transmural inflammation may cause loops of intestine to be matted together.
- All intestinal layers are thickened,
- The intestinal lumen is narrowed.
- Colonic inflammation with rectal sparing is more consistent with Crohn's disease than with UC

Pathology-CD.

- Aphthous ulcers are the earliest lesions of CD.
- Aphthous ulcers → stellate or serpiginous → longitudinal and transverse linear ulcers.
- The remaining islands of nonulcerated mucosa give a cobblestone appearance.
- "Skip lesions" suggest Crohn's disease.
- Fissures develop from the base of ulcers and extend down through the muscularis to the serosa .
- Granulomas are common in Crohn's disease.

Anal and perianal complications of CD

- Fissure in ano (multiple and indolent)
- Haemorrhoids
- Skin tags
- Perianal abscess
- Ischiorectal abscess
- Fistula in ano (may be multiple)
- Anorectal fistulae

Clinical Manifestations-UC

- Diarrhea
  - The dominant symptom
  - Usually associated with blood and mucous in the stool
  - Bowel movements are frequent but small in volume.
  - Tensmus, Urgency and fecal incontinence may occur
- Fever and abdominal pain may occur.
- Systemic features “fever, malaise, and weight loss” are more common if most of the colon is involved.

Clinical Manifestations-UC

- In mild to moderate severity
  - There may be tenderness over the affected area.
  - Rectal examination may reveal tenderness
  - Rectal examination may reveal blood on the glove.
- In severe disease, the patient is more likely to have
  - Fever, tachycardia
  - Anemia , Elevated ESR
  - Elevated leukocyte count
  - Electrolyte disorders.

Clinical Manifestations-UC

- The initial attack of UC
  - Usually begins indolently.
  - But it may be fulminant
  - May be seen with any extent of anatomic involvement from proctitis to pancolitis
- UC usually follows a chronic intermittent course .
- A significant % of patients have a chronic continuous course

Clinical Manifestations-CD

- Three major patterns:
  - (1) disease in the ileum and cecum (40 % of patients).
  - (2) disease confined to the small intestine (30 %).
  - (3) disease confined to the colon (25 %).
- Much less commonly, Crohn's disease involves more proximal parts of the gastrointestinal tract.
- Inflammatory→ stricturing and penetrating.
- The predominant symptoms are
  - Diarrhea.
  - Weight loss.
  - Abdominal pain.

Clinical Manifestations-CD

- Patients may complain for months or years of vague abdominal pain and intermittent diarrhea.
- Diarrhea occurs in almost all patients.
- The pattern of diarrhea varies with the anatomic location:
  - Prolonged inflammation and scarring in the rectum may lead to incontinence
  - In disease confined to the small intestine, stools are of larger volume and not associated with urgency or tenesmus.
  - Patients with severe involvement of the terminal ileum and those who have undergone surgical resection of the terminal ileum may have bile salt diarrhea or steatorrhea.

Clinical Manifestations-CD

- The location and pattern of pain correlate with location.
- Abdominal distention, nausea, and vomiting may accompany the pain.
- Weight loss of some degree occurs in most patients with Crohn's disease regardless of the anatomic location.
- Low-grade fever may be the first warning sign of a flare.
- Crohn's disease is a relapsing and remitting disease.

Clinical Manifestations-CD

- **Physical findings**

- Physical findings in Crohn's disease vary with the distribution and severity of the disease.
- Aphthous ulcers of the lips or buccal mucosa are common.
- The abdomen may be tender.
- CD can also present as an emergency with acute right iliac fossa pain mimicking appendicitis.
- Thickened bowel loops, thickened mesentery, or an abscess may cause a mass,
- Perianal disease is suggested by fistulous openings, induration, redness, or tenderness near the anus

Clinical Manifestations

CRITERIA FOR SEVERITY IN IBD	
Mild	Fewer than 4 bowel movements per day with little or no blood, no fever, normal Hb, ESR less than 30 mm/h, Endoscopy Mayo score 1.
Moderate -Severe	>6 bowel movements per day with frequent blood, fever, < 75 % normal Hb, ESR > 30 mm/h, Endoscopy Mayo score 2-3.
Fulminant	>10 bowel movements per day with continuous blood, fever, anemia need transfusion, and sedimentation rate greater than 30 mm/h, Endoscopy Mayo score 3.

Extraintestinal Manifestations of IBD

- **Arthritis**

  Most common extraintestinal manifestation of IBD

- ❑ Type I (Pauciarticular) arthropathy
- ❑ Type II (Polyarticular) arthropathy
- ❑ Arthralgia
- ❑ Ankylosing spondylitis
- ❑ Inflammatory back pain

Extraintestinal Manifestations of IBD

- **Hepatic and biliary complications**

- Sclerosing cholangitis
- Fatty liver
- Chronic hepatitis
- Cirrhosis
- Gallstones

Extraintestinal Manifestations of IBD

- **Dermal manifestations**
  - ❑ Pyoderma gangrenosum
  - ❑ Erythema nodosum,
- **Ocular manifestations**
  - ➢ Uveitis
  - ➢ Episcleritis.
- **Nephrolithiasis**
- **Venous thrombosis**

Diagnosis

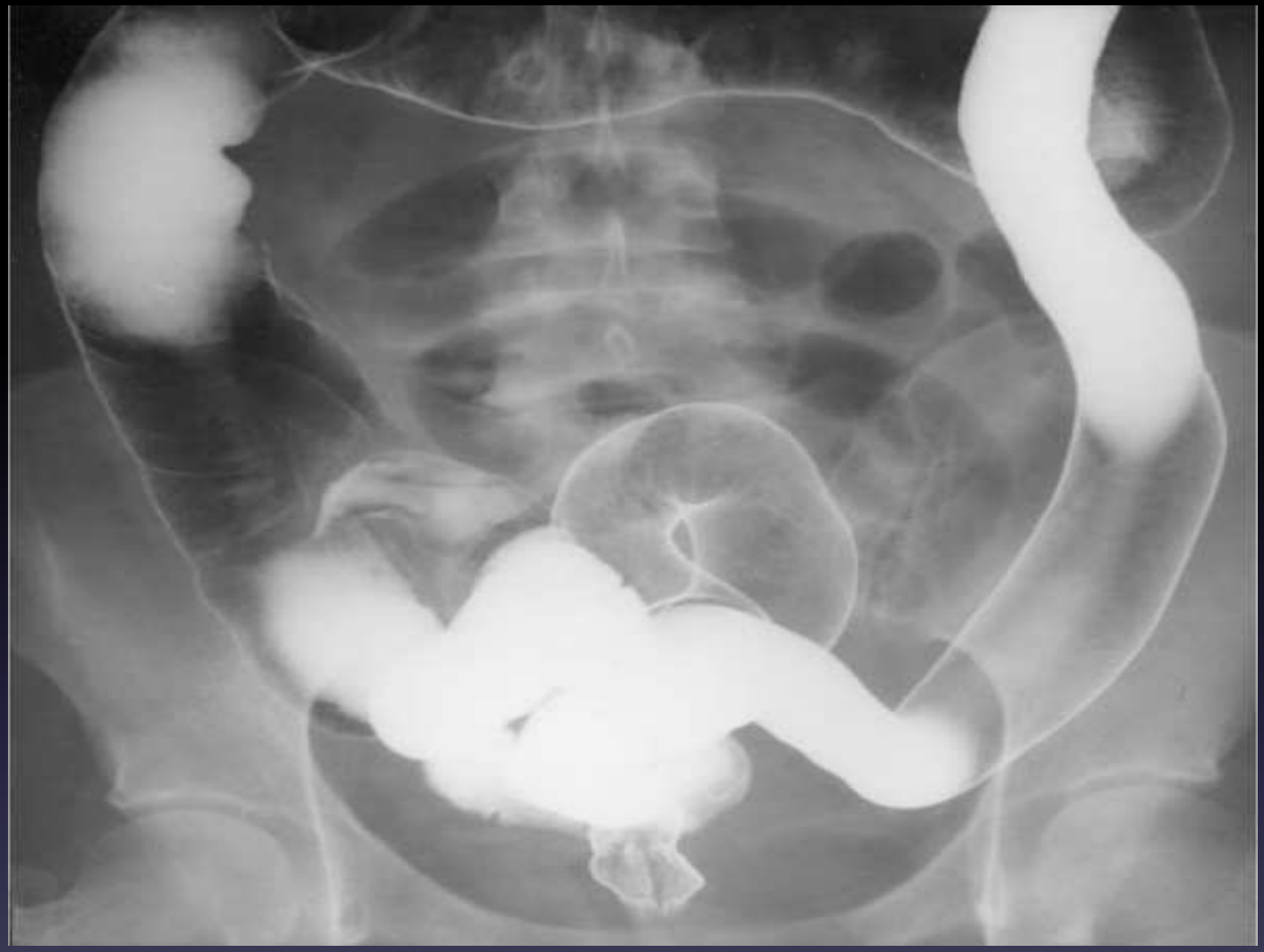
Laboratory tests:

- CBC: White cell and platelet counts are commonly raised in moderate to severe attacks, and iron deficiency anaemia is present.
- ESR and CRP are often raised;
- liver biochemistry may be abnormal, with hypoalbuminaemia occurring in severe disease.
- anti-neutrophil cytoplasmic antibodies (ANCA) positive in UC and anti-Saccharomyces cerevisiae antibodies (ASCA) positive in CD.
- Stool tests and C. difficile toxin: These should always be performed to exclude infective causes of colitis. Stool microscopy to exclude amoebiasis is mandated in patients with a relevant travel history.
- Faecal calprotectin/lactoferrin will be elevated.

Diagnosis- UC

Radiography

- Findings are not correlate well with disease activity.
- Barium enema may be normal in early UC.
- The involved segment may reveal
  - limited distensibility.
  - Narrow, short, and tubular lumen.
  - The haustral markings disappear.
  - Straightening of the colon.
  - Fine granular appearance of the mucosa.



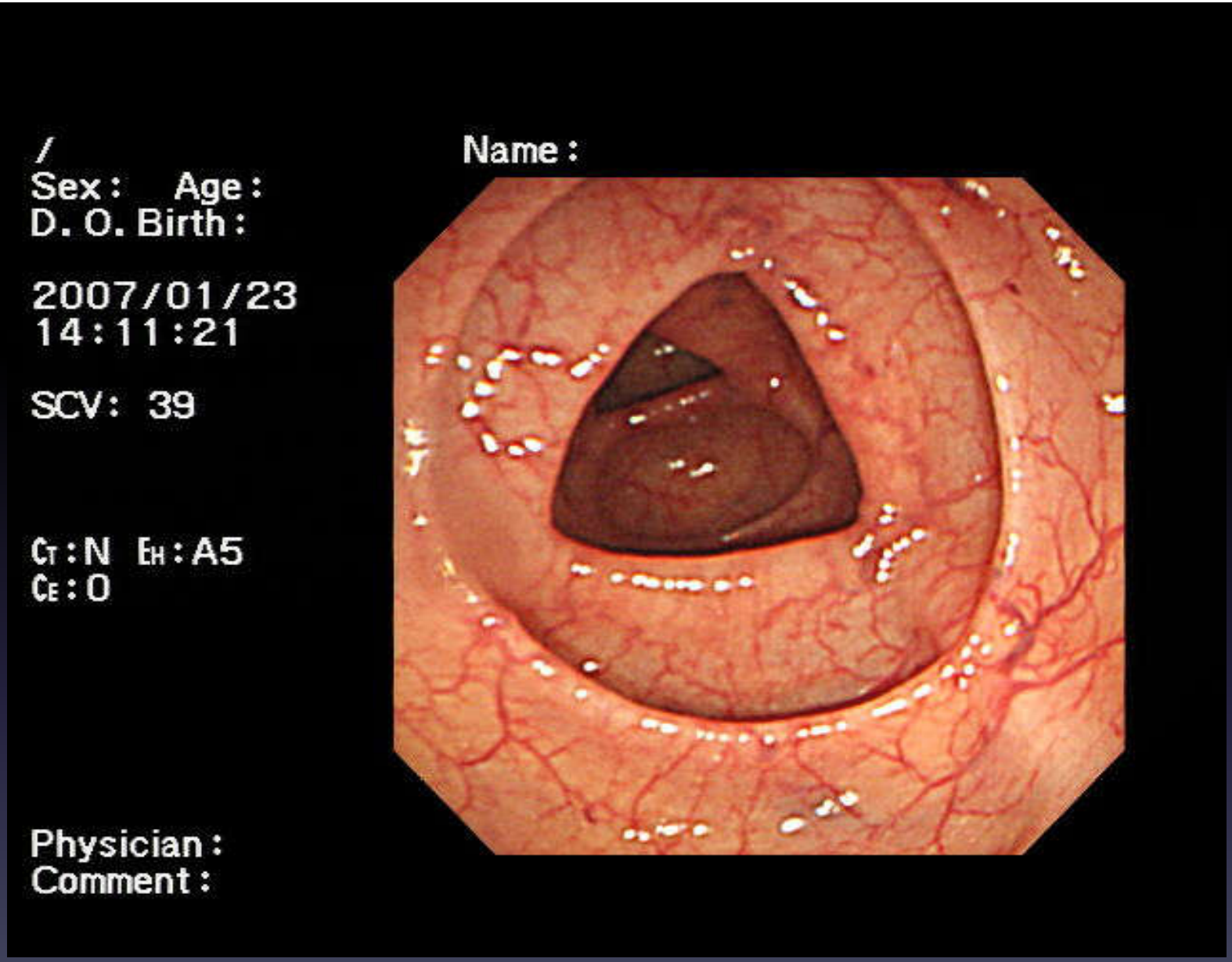
Ulcerative colitis. An air contrast barium enema demonstrates luminal narrowing and loss of haustral markings in the sigmoid and descending colon in a patient with ulcerative colitis.

Diagnosis-UC

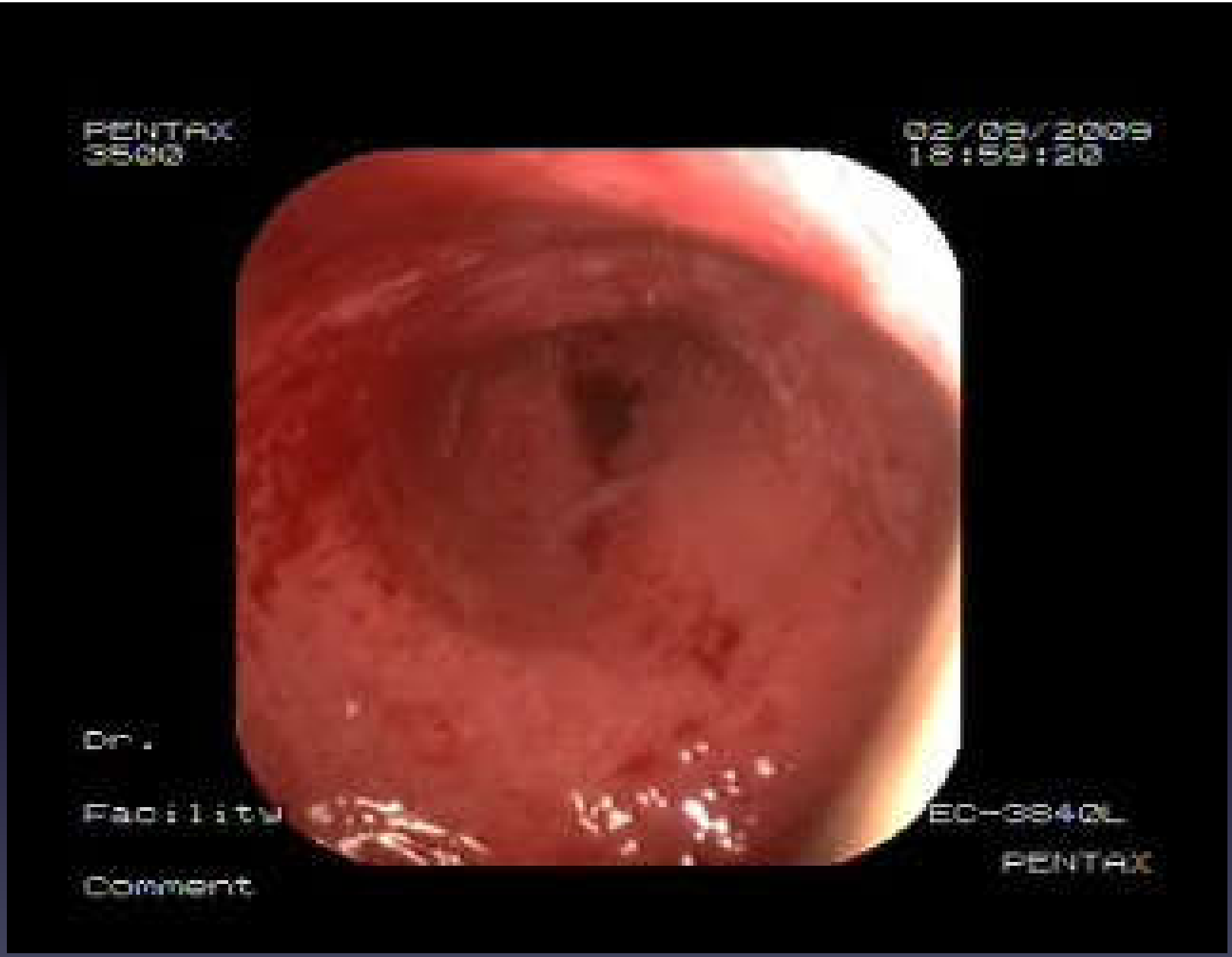
Colonoscopy and mucosal biopsy

Endoscopic features include

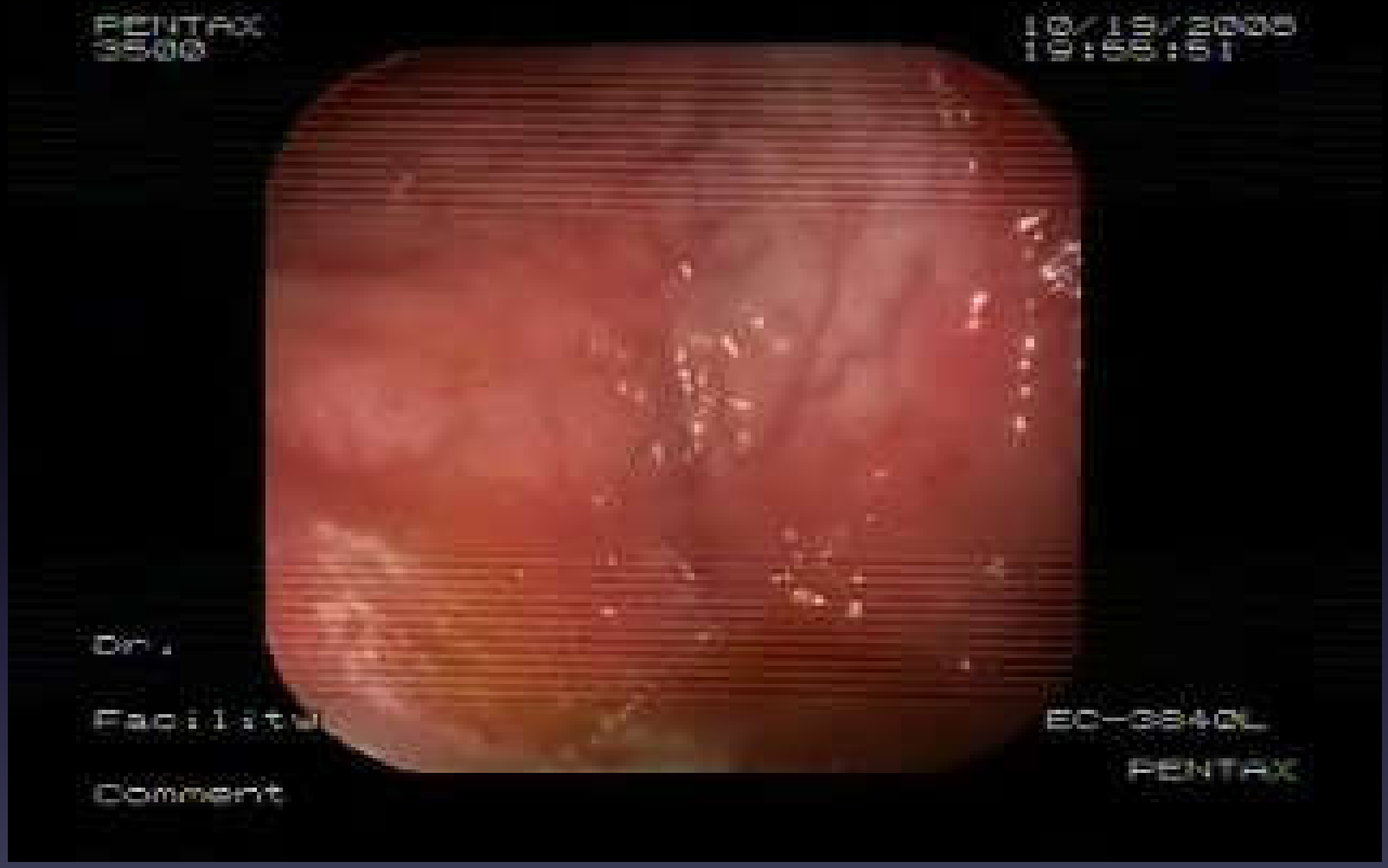
- Hyperemia, edema, and loss of vascular pattern.
- Presence of yellowish exudates on the mucosa.
- Shallow irregular ulcers.
- Relatively deep ulcers surrounded by erosions and erythematous mucosa.
- Inflammatory polyposis in extensive UC.
- No "Skip lesions" and No cobblestone appearance.
- Mucosal changes are diffuse, circumferential and continuous.



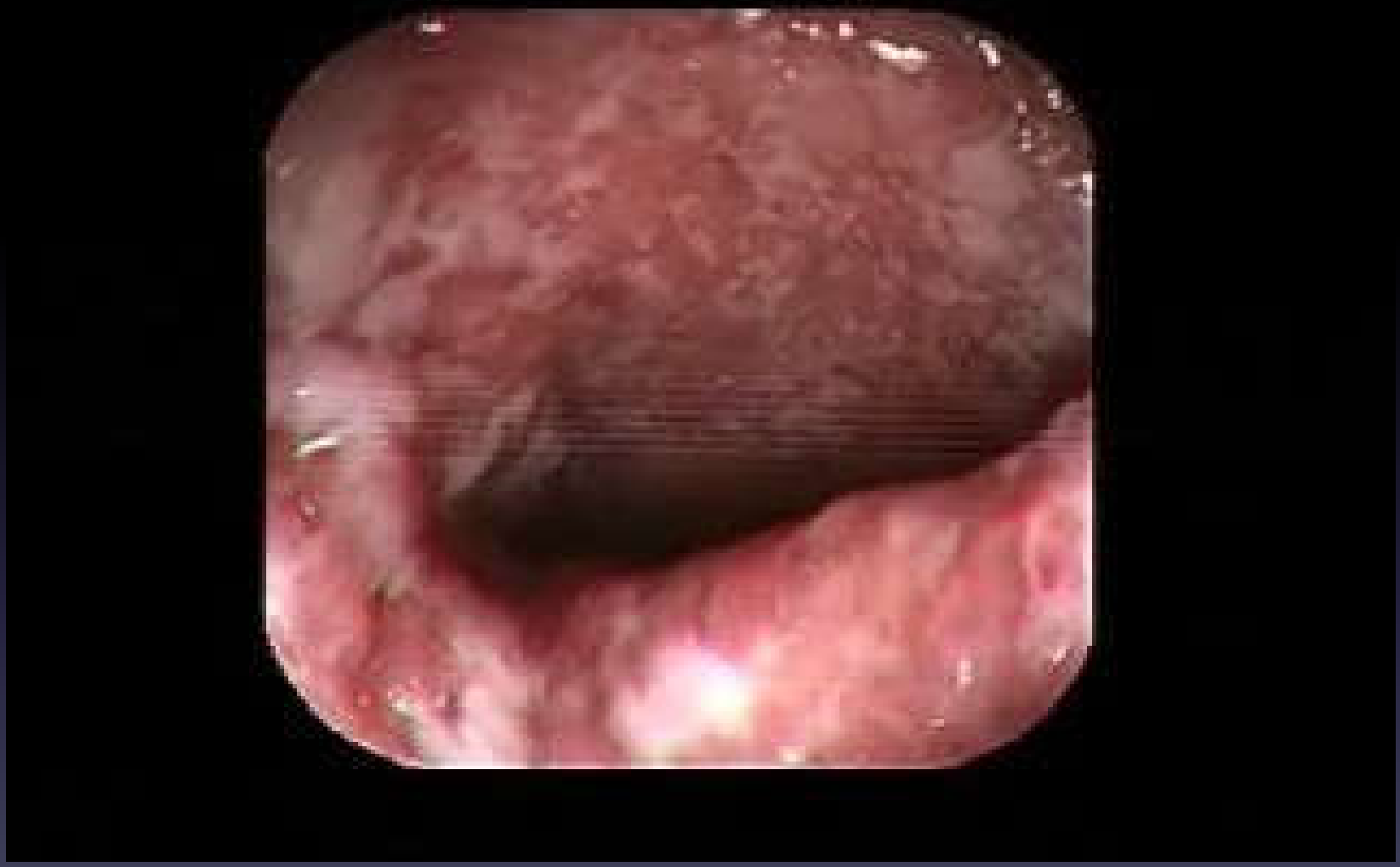
Colonoscopic examination shows normal mucosa



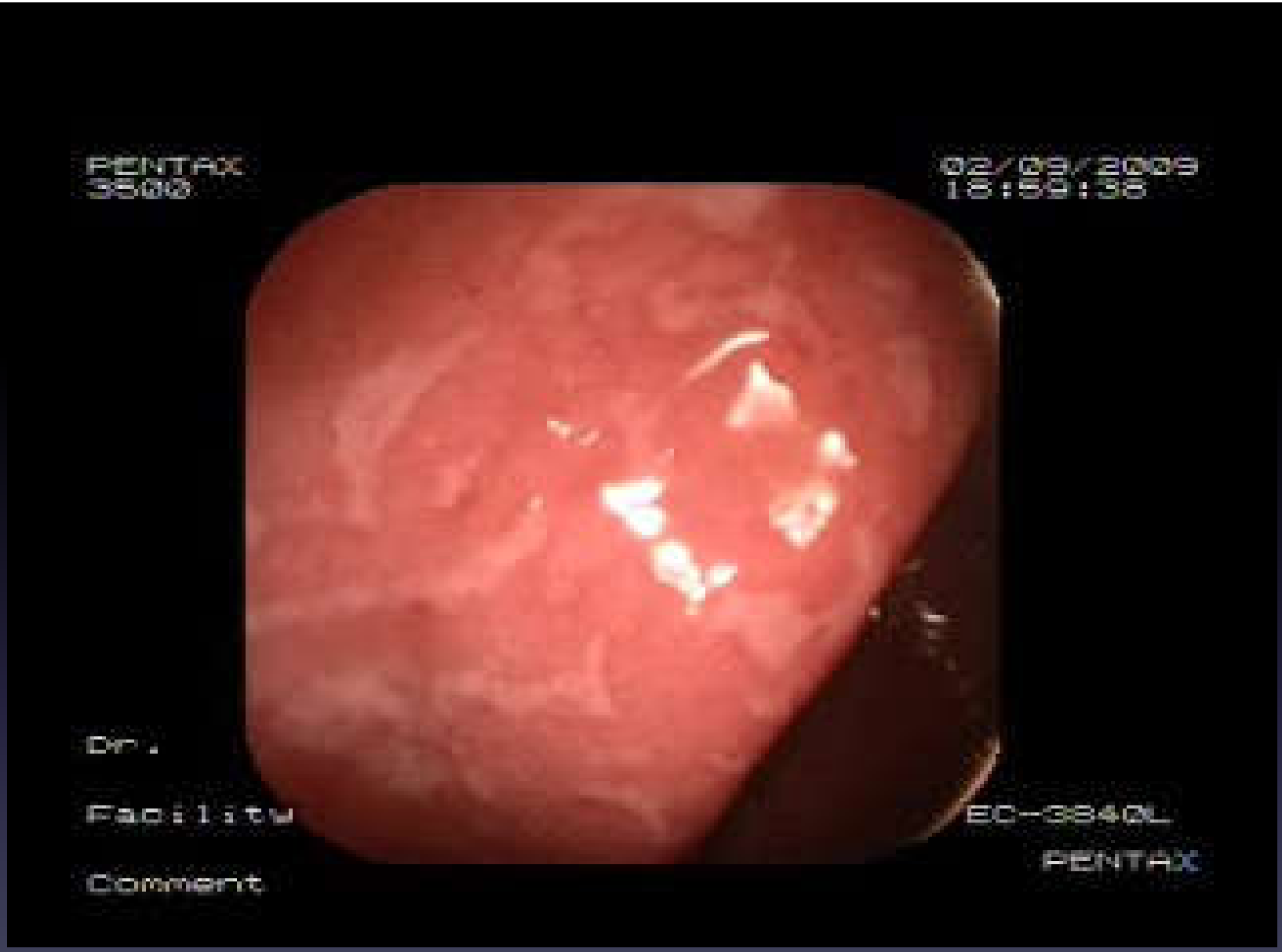
Colonoscopic examination of patient with active UC



Colonoscopic examination of patient with active UC shows a clear demarcation between involved and uninvolved mucosa.



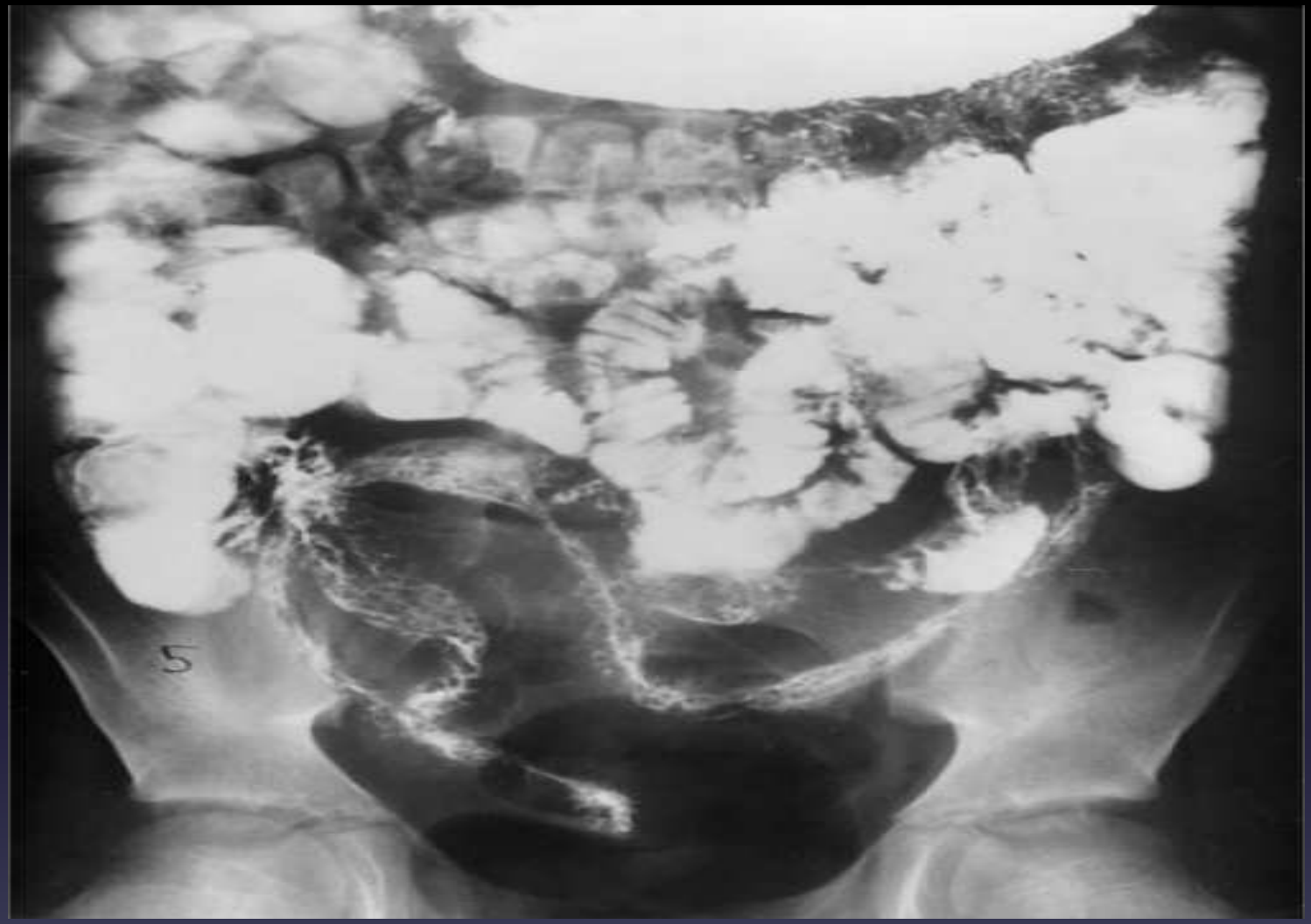
Colonoscopic examination of patient with sever extensive ulcerative colitis



Colonoscopic examination of patient with active UC shows superficial ulcers and inflamed mucosa

Diagnosis-CD

- **Radiography**
- Contrast studies/ air contrast barium enema may show
  - ❖ Presence of aphthous ulcers.
  - ❖ Nodular appearance on radiographs.
  - ❖ Presence of fistulas.
  - ❖ Thickening of the bowel wall.
  - ❖ Decreased luminal diameter and stricture formation.
  - ❖ Small bowel can be evaluated by bowel follow-through.
- CT and US are useful in identifying abscesses, fluid collections and bowel wall thickness.

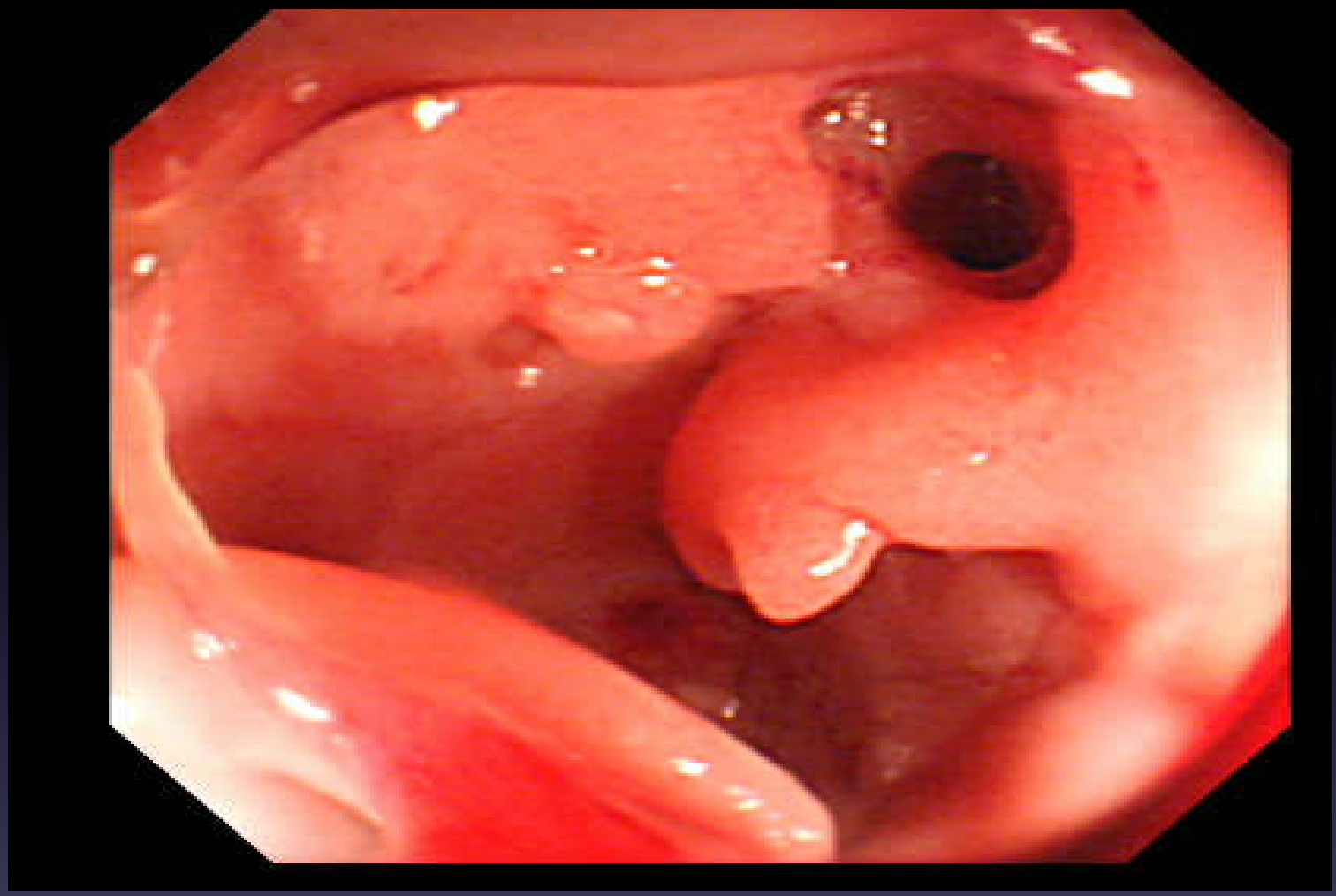


Small bowel follow-through in a patient with Crohn's disease of the ileum. Luminal narrowing, mucosal ulceration, and separation of the barium-filled loops because of thickening of the bowel wall

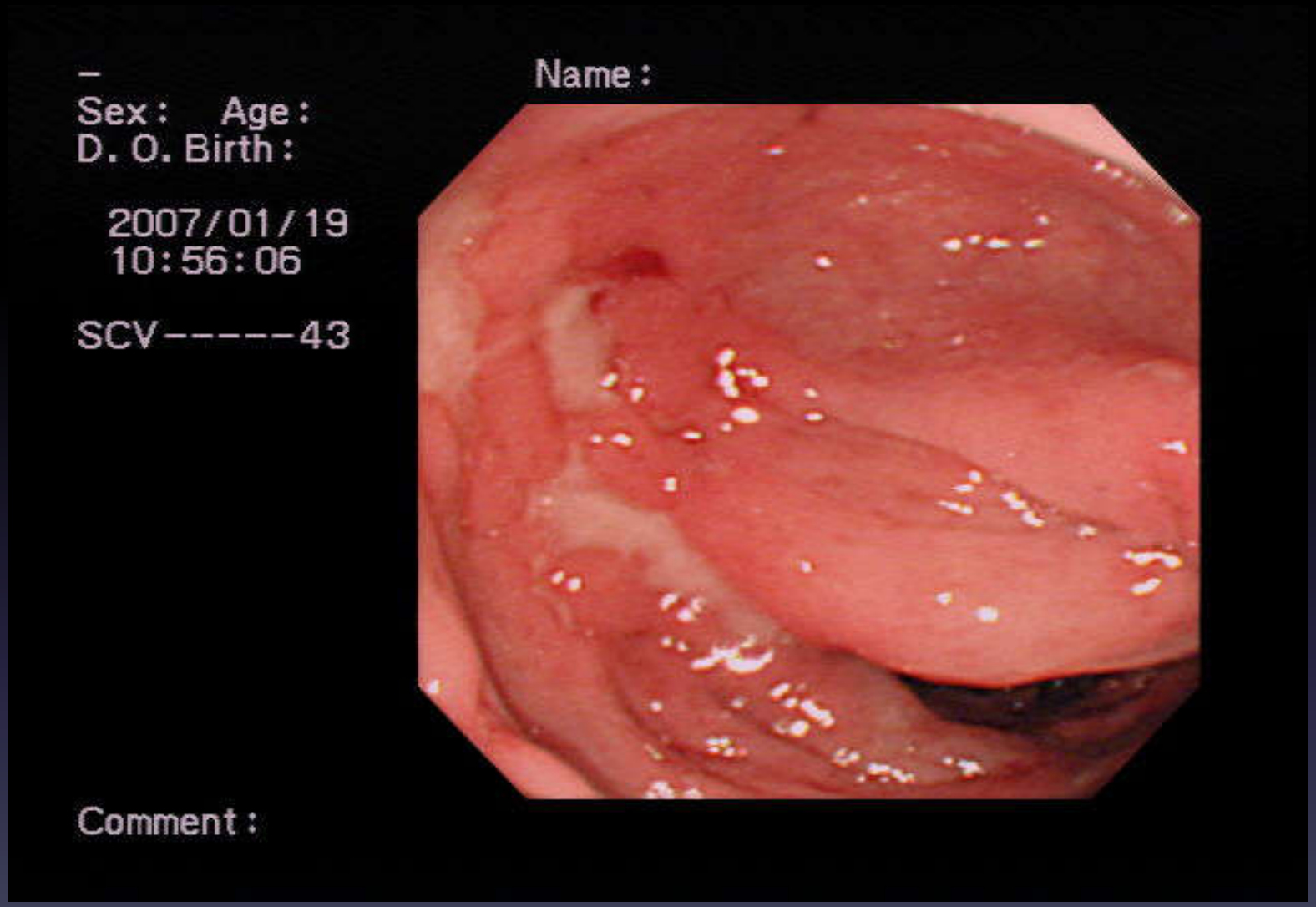
Diagnosis-CD

GIT endoscopy and mucosla biopsy
Endoscopic features include

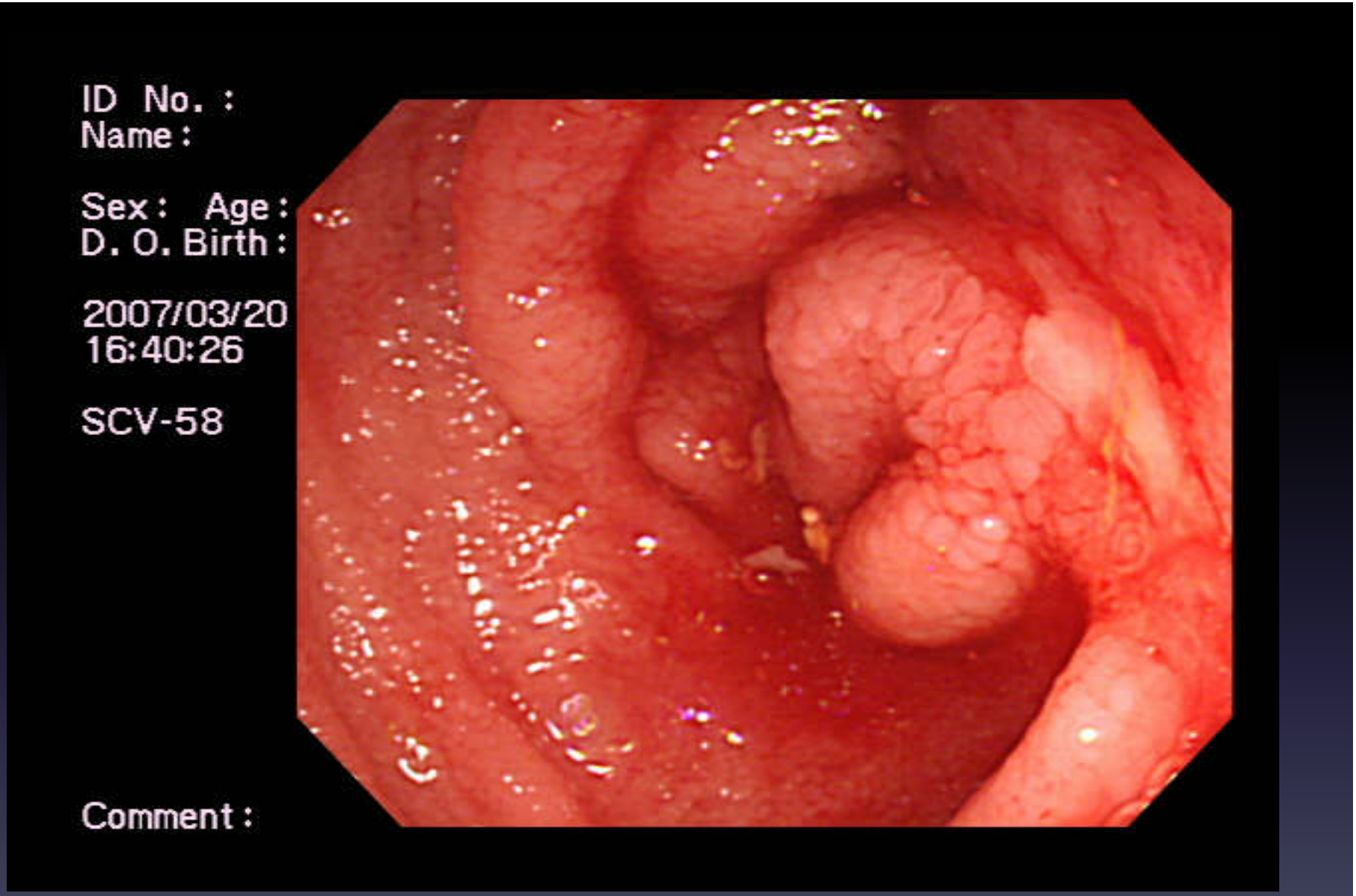
- Aphthous ulcer
- Longitudinal and transverse ulcers.
- Large, deep, penetrating ulcers can be surrounded by areas of normal-appearing mucosa
- "Skip lesions"
- Presence of fistula.
- Cobblestone appearance.
- Narrowing of the lumen.
- The rectum may or may not be involved.
- Hyperemia, edema, and loss of vascular pattern.



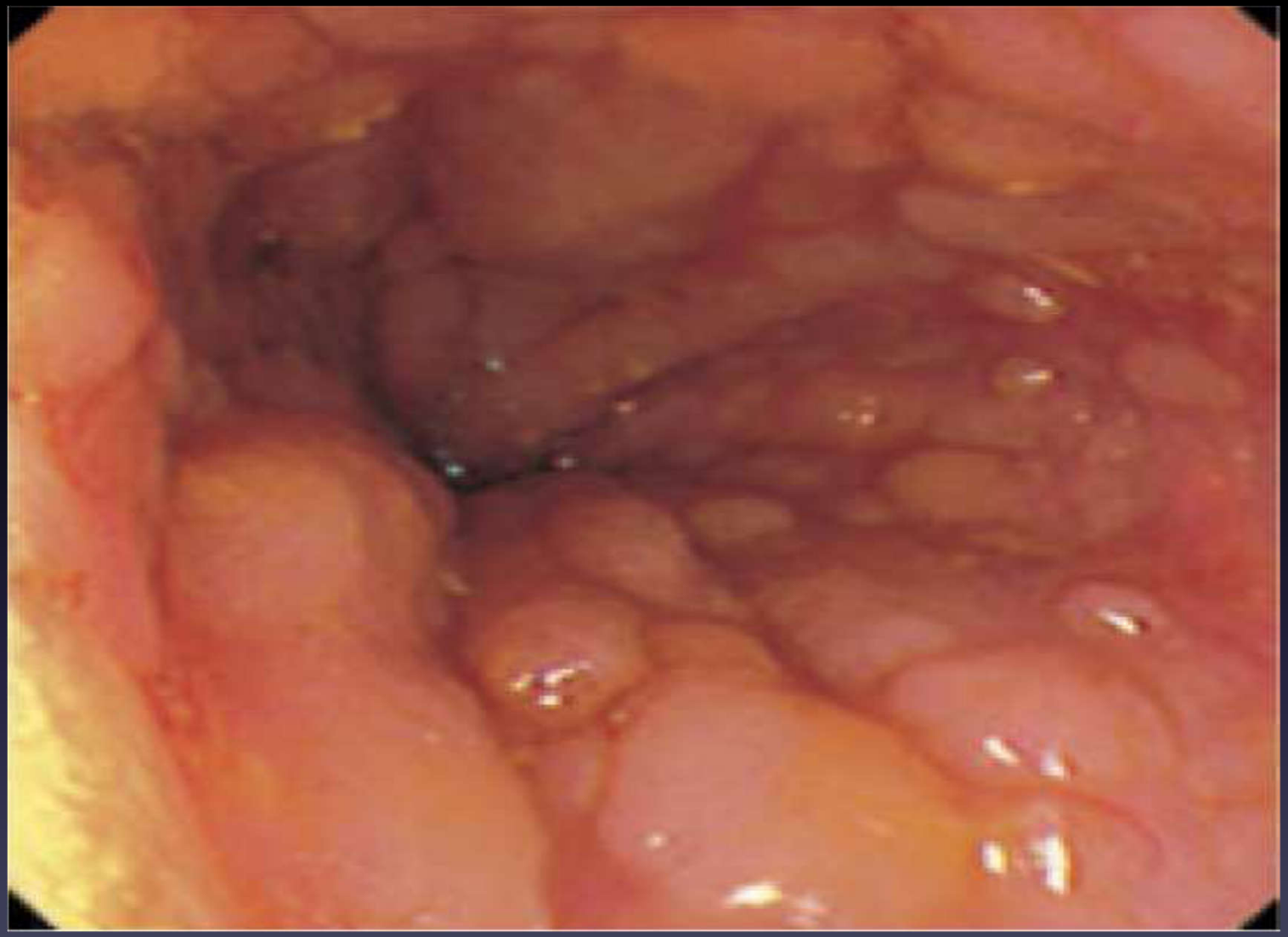
Female patient, 23 year with active Crohn's disease. Colonoscopic examination revealed colonic fistula



Colonoscopic examination revealed longitudinal ulcers



Crohn's disease.
Longitudinal ulcer in terminal ileum



Crohn's disease of the colon shows “cobblestone” appearance

Diagnosis

Differential diagnosis-UC

- Crohn's disease
- Infections
  - Infections with Shigella, Amoeba, Giardia, and *Escherichia* coli, can give bloody diarrhea and endoscopic picture identical to UC
  - Diarrhea has limited to a period of days to a few weeks.
  - Stool cultures for pathogens and Serologic tests.

- Pseudomembranous colitis
  - The presence of small membranous plaques adherent to the mucosa on sigmoidoscopy is pathognomonic.
  - Check the stool for Clostridium difficile toxin

Diagnosis

- **Differential diagnosis-CD**

❑ Ulcerative colitis

❑ Infections

Infections with Shigella, Amoeba, Giardia. Diarrhea has limited to a period of days to a few weeks. Stool cultures for pathogens and Serologic tests.

❑ Pseudomembranous colitis.

❑ Collagenous colitis.

❑ TB in terminal ileum.

❑ Diverticulitis.

❑ Intestinal lymphoma.

Medical Therapy-UC

- **Proctitis**
  For active ulcerative proctitis ;
  - ➢ Nightly administration of 5-ASA retention enemas or suppositories, often supplemented with an oral aminosalicylate.
  - ➢ Corticosteroid enemas can also be used.
  - ➢ Another approach to proctitis or distal colitis is an oral aminosalicylate, although a response may not be evident for 3 to 4 weeks.

Medical Therapy-UC

Extensive colitis

- In patients with colitis of mild to moderate activity and extension proximal to the sigmoid colon, the initial drug of choice is an oral aminosalicylate; efficacy increases with increasing doses.
- Even with more extensive disease, supplementation of oral aminosalicylates with aminosalicylate enemas or suppositories may help reduce the symptoms.
- In patients with more active disease (more than five or six bowel movements per day), patients in whom a more rapid response is desired, or those who have not responded to 3 to 4 weeks of aminosalicylates, the treatment of choice is oral prednisone.

Medical Therapy-UC

Extensive colitis cont.

- For steroid refractory patients or severe colitis;
  - Immunomodulator (azathioprine or 6-MP),
  - Biological therapy with either an anti-TNF agent (infliximab, adalimumab or golimumab) or an anti-integrin therapy (vedolizumab).
  - Surgical treatment.

Medical Therapy-UC

- **Severe active ulcerative colitis**
  - Hospitalization and bed rest.
  - Evaluation for toxic megacolon.
  - Intravenous corticosteroids.
  - Intravenous fluids for rehydration.
  - Total parenteral nutrition may be necessary.
  - Parenteral antibiotics if there are signs of infection.
  - Anticholinergics are contraindicated.
  - Antidiarrheal agents are contraindicated.
  - Patients with no improvement in 7-10 days should be considered for either colectomy or trial of intravenous cyclosporine.

Medical Therapy-UC

Maintenance Therapy

- Maintenance therapy with aminosalicylates has been recommended for those brought into remission with corticosteroids
- Maintenance with 6-MP or azathioprine is recommended for patients brought into remission with these drugs or who were corticosteroid dependent and then converted to these drugs.
- No role for corticosteroids as maintenance therapy.

Surgical Therapy-UC

Colectomy may be required in

- ❑ Fulminant acute attack
  - • Failure of medical treatment
  - • Toxic dilatation
  - • Haemorrhage
  - • Imminent perforation
- ❑ Chronic disease
  - • Incomplete response to medical treatment/steroid-dependent
  - • Dysplasia on surveillance colonoscopy

Complications-UC

Toxic megacolon

- The most severe complication of ulcerative colitis toxic megacolon, or dilation of the colon to a diameter greater than 6 cm associated with worsening of the patient's clinical condition and the development of fever, tachycardia, and leukocytosis.
- Physical examination may reveal postural hypotension, tenderness over the distribution of the colon, and absent or hypoactive bowel sounds.
- Antispasmodics and antidiarrheal agents are likely to initiate or exacerbate toxic megacolon.
- If there are no signs of clinical improvement during the first 24 to 48 hours of medical therapy, the risk for perforation increases markedly, and surgical intervention is indicated.

Treatment

- **Follow-Up**

- Patients with extensive UC have a markedly increased risk for colon cancer beginning 8 to 10 years after diagnosis and increasing with time.
- Surveillance colonoscopy with random biopsies in patients with long-standing UC beginning 8 to 10 years after the onset of disease and repeated every 1 to 2 years.

Medical Management-CD

- **Active disease**

- For colonic Crohn's disease oral corticosteroids are first-line therapies.
- In patients with small bowel Crohn's disease, either prednisone or budesonide are appropriate.
- After the symptoms are controlled, prednisone can be gradually tapered until fully withdrawn from it
- 5-ASA preparation chould be added in patients with ileocolonic CD.
- Before corticosteroids are given to a patient with abdominal pain, fever, and a high leukocyte count, an abdominal CT should be obtained to exclude an abscess.

Medical Management-CD

- **Active disease-cont.**

- For corticosteroid-dependent patients, trial of an immunomodulator (6-MP , Methotrexate or azathioprine) should be considered.
- Biological therapy with either an anti-TNF agent (infliximab, adalimumab or certolizumab) or an anti-integrin therapy (vedolizumab) or IL-12/23 (Ustekinumab).
- The approach to severe Crohn's disease is similar to the approach to severe ulcerative colitis.
- Patients with severe CD who do not respond to parenteral corticosteroids within a week should be considered for surgery

Medical Management-CD

- **Active disease-cont.**
  - ➢Perianal/fistulizing disease:

  1- Drainage of abscesses.

  2- Anti-TNF

  3- Azathioprine

  4- Metronidazole/ ciprofloxacin

  5-Tacrolimus

Medical Management-CD

Maintenance Therapy

Maintenance with 6-MP or azathioprine is recommended for

-Patients brought into remission with these drugs or by surgery.

-Corticosteroid dependent and then converted to these drugs.

Maintenance with biologics with an immunomodulator.

- No role for corticosteroids as maintenance therapy.

Surgical Therapy-CD

- Surgical resection is not curative of Crohn's disease and recurrences are likely.
- Therefore the approach is more conservative in terms of the amount of tissue removed
- Failure of medical management is a common cause for resection in patients with Crohn's disease.
- Complications (e.g., obstruction, fistula, abscess) are often indications for resection/ surgical therapy.

Treatment-CD

- **Follow-Up**
- The risk for colon cancer in Crohn's colitis is less than in ulcerative colitis.
- The utility of surveillance in Crohn's colitis is unproven.

Thank you