Severe acute colitis

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Definitions

Â Colitis
   ï **Inflammatory and/or ischemic** focal or diffuse lesions of the colonic wall

Â Acute
   ï **Within the six weeks** following the onset of symptoms
   ï Not necessarily sudden

Â Severe
   ï **May lead to death**
     Â **(Multi)organ failure** secondary to
     ï Septicaemia (initial pathogen or translocation)
     ï Cytokine release (*Clostridium difficile*)
     Â **Mechanical complication of colitis** (perforation, severe bleeding (hematochesis))
     Â **Complication of acute undernutrition** (opportunistic infection, pulmonary embolism, etc.)
Main contexts and causes (1)
No pre-existing chronic inflammatory disease

Å Acute intestinal infection
   • Usual bacterial pathogens (*Salmonella, Shigella, Campylobacter, Entero-haemorrhagic E. coli (including 0157:H7)*)
   • *Clostridium difficile* (developed countries++)
   • Amebiasis, (tuberculosis) (developing countries++)
   • Cytomegalovirus (underlying immunodeficiency, AIDS++)

Å First flare of IBD (ulcerative colitis++)
   • May be triggered or associated with intestinal infection (including *Clostridium difficile*)

Å Pure ischemic colitis
   • Special contexts: Aortic surgery, crack or cocaine abuse
Main contexts and causes (2)
Pre-existing chronic inflammatory disease

Å IBD +++
   • Severe attack of Ulcerative colitis
     Å 15% of the patients
     Å May be transposed to severe attack of Crohn’s colitis
     • May be triggered or worsened at any moment by intestinal infection (including Clostridium difficile AND Cytomegalovirus)

Å Vasculitis
   • Periarteritis nodosa, lupus, cholesterol embolisms)
   • Very rare
   • Ischemic mechanism++
Management of severe acute colitis
Universal initial approach (1)

Â Integrated **medical and surgical** approach

Â Clinical monitoring
   ï Palpation of the abdomen twice daily

Â Routine biology
   ï Leukocyte and neutrophil count
   ï Renal function, serum electrolyte levels, hemostasis parameters
   ï Three major parameters for assessing global severity of colitis and evolution under treatment
      Â Blood **Haemoglobin** level
      Â Serum **CRP** level
      Â **Albuminemia** (validated severity marker in CD-associated colitis)
Management of severe acute colitis
Special interest of Hb, CRP and albuminemia

Â Haemoglobin monitoring
   ï Blood transfusion according to the context (age, active bleeding or not)

Â CRP monitoring
   ï Almost always elevated initially
   ï A dramatic drop in serum CRP level within the first 48h of a given therapeutic strategy is usually associated with subsequent favourable anatomoclinical evolution: excellent surrogate marker

Â Severe acute hypoalbuminemia
   ï Severe exsudation (short-term) and decreased synthesis (mid-term)
   ï Good global marker of severity (especially in CD-colitis, with a good correlation with ascîtis)
Management of severe acute colitis
Universal initial approach (2)

Â Imaging
  ï At least plain X-ray of the abdomen
    Â Pneumoperitoneum
    Â Toxic megacolon (>6cm, transverse colon)
  ï If possible, abdominal CT-scan
    Â Extent and severity of lesions of the colonic wall
    Â Ascitis
    Â Extra-intestinal gas (definite indication for surgery), abscess

Â Endoscopy
  ï Contra-indicated in case of pneumoperitoneum/peritonitis
  ï Standard (or bedside in ICU) rectosigmoidoscopy
  ï Biopsies for pathology and microbiology
Severe acute colitis
Yield of CT-scan
Severe acute colitis
Superficial ulcerations at sigmoidoscopy
Severe acute colitis
Deep ulcerations at sigmoidoscopy
Management of severe acute colitis
Universal initial approach (3)

Å Microbiology
  • Blood culture (elevated fever)
  • Feces
    Å Stool culture for Salmonella, Shigella, Campylobacter (E. coli O157:H7, Mycobacterium tuberculosis)
    Å Search for CD and toxins A and B (antibiotic-associated colitis, nosocomial colitis, IBD)
    Å Search for vegetative forms of Entamoeba histolytica
  • Culture from colonic biopsies (improves the yield of microbiology work-up)

Å Others
  • Search for CMV colitis (systemic PCR, search for inclusions in colonic biopsies) in case of immunodeficiency
  • (Search for tuberculosis (PPD, Chest X-ray (CT-scan), Quantiferon®) in case of suggestive context)

Barbut F et al., Clin Infect Dis 1999; 29:356-60
Management of severe acute colitis
Initial treatment (1)

Â Integrated **medical and surgical** approach

Â **Empirical antibiotics**
  ï Metronidazole (amebiasis (1.5 g/day for 7 days), also covers putative infection with *C. difficile*)
  ï Quinolones (ex: ofloxacin 200 mg twice daily for 5 days)

Â **(Intravenous steroids)**
  ï IBD previously diagnosed (24 to 36 h after antibiotic initiation)
  ï Specific IBD histological features on biopsies (crypt distorsion and or malformations)
  ï IBD suspected (no improvement after 36 to 48h of empirical antibiotics)
Management of severe acute colitis
Initial treatment (2)

Â Supportive therapy
- Fluid and electrolytes replacement
- Parenteral nutrition
- (Blood transfusion, albumin infusion)

Â Special contexts
- Overt or suspected immunodeficiency (ex: AIDS with <100 CD4/mm³, cancer and chemotherapy, post-transplant)
  - Add empirical gancyclovir 5mg/kg IV twice daily until the diagnosis is ruled out
- Suspected tuberculosis: antituberculous treatment
Treatment of toxic megacolon

- **Treatment of the cause of colitis**
  - Intestinal infection and/or
  - Severe flare IBD flare

- **Endoscopic treatment of colonic dilatation**
  - Perendoscopic colonic decompression
  - Placement of an intracolonic fenestrated tube over a colonoscopically inserted guide wire for preventing recurrence

- Colectomy if failure of the combined two previous approaches

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1Beaugerie L et al., Gastroenterology 1994;107:858-63
Endoscopic treatment of colonic dilatation

Figure 1. (A) Radiograph of the abdomen of patient 6 in the supine position at the time of the diagnosis of toxic megacolon, showing a marked dilatation of the colon. (B) Radiograph of the abdomen of patient 6 in the upright position 12 hours after colonoscopic insertion of a fenestrated tube.

Beaugerie L et al., Gastroenterology 1994;107:858-63
Management of severe acute colitis
Emergency **subtotal colectomy**
with ileostomy and colostomy

- **Indications**
  - Colonic perforation
  - Untractable haemorrhage
  - Failure of medical treatment

- **Prognosis**
  - 50% postoperative mortality
  - 100% mortality if wrongly delayed or undone
Severe acute ischemic colitis

Â Particular contexts
   ï Aortic surgery
   ï Vasculitis
   ï Cocain, crack, amphetamine abuse

Â Transmural ischemic necrosis of the colonic wall
   ï Suggestive mucosal endoscopic aspect in the first hours
   ï Unusual involvement of the rectum

Â Treatment
   ï Surgery
      Â Mandatory if perforation,
      Â To be discussed if irreversible shock or organ failure
   ï Supportive therapy in all cases
Severe acute colitis
*Clostridium difficile*

- **Non invasive** Gram+ anaerobic bacterium
- Intestinal lesions are due to combined cytotoxicity of **toxins A and B** on cytoskeleton (**no colitis in non toxin-producing strains**)
- **Expanding epidemiology** and impact in developed countries:
  - x4 in Olmstedt county between 1995 and 2005
  - 3393 deaths in UK in 2006
- **Emergence of a virulent New Variant strain** (US-Europe)
  - mutation of *tcdC* (loss of down-regulation of toxins A and B)
  - *cdtA* and *ctdB* genes encoding fo 2 cytotoxic binary toxines
CD-colitis
Long-standing established clinical contexts

Å Antibiotic-associated colitis
  ï High risk
    Å Ampicillin, cephalosporins, clindamycin
    Å Quinolones (new)
  ï Intermediate
    Å Tetracyclins, sulfamides
    Å Macrolides

Å Nosocomial
  ï Antibiotics (not necessarily)
  ï Elderly
  ï Long stay
  ï Promiscuity
CD-colitis
Emerging contexts

Å Antibiotic-associated colitis in the community

Å Patients under antineoplastic chemotheray

Å Surinfection in IBD ++
  ï 50% without underlying antibiotic treatment
  ï Often developed in an ambulatory setting in patients under immunosuppressive therapy
  ï Endoscopic lesions identical to those encountered in IBD alone
Diagnosis of *Clostridium difficile* infections

Å **Rapid antigenic test (glutamate dehydrogenase)**
   - Negative predictive value ~ 100%

Å **Immunoenzymatic tests for toxins A and B**
   - Sensitivity and specificity > 70-90%

Å **Stool culture**
Severe *Clostridium difficile* infections

Å Criteria
- At least 2 of the following criteria: age > 60, fever > 38.4°C, leukocytes count > 15 G/L, albuminemia < 25 g/L, creatinin blood level > 200 µmol/L
- And/or septic shock
- And/or ascitis or colonic dilatation
- And/or pseudomembranes or deep ulcers at endoscopy

Å Severe acute colitis
Endoscopic aspect of *Clostridium difficile*-associated Pseudomembranous colitis
Medical treatment of *Clostridium difficile* infections

![Bar chart showing the response rates for mild and severe infections with Vancomycin and Metronidazole.]

- **Mild Infection**
  - Vancomycin: 98%
  - Metronidazole: 90%

- **Severe Infection**
  - Vancomycin: 97%
  - Metronidazole: 76%

*Clin Infect Dis 2007;45:302*
Treatment of severe *Clostridium difficile* acute colitis
Rapid step-up approach

- Empirical metronidazole 4x250mg/day orally on a 10-day basis

- When CD infection is confirmed, switch for or add vancomycin 125mgx4/day orally for 10 days

- (If no improvement (CRP, clinical condition) within 48-72h, consider rescue infusion of polyvalent immunoglobulins 300 mg/kg)

- If no improvement within 48-72h, consider subtotal colectomy
Severe CD-colitis
Rescue immunoglobulin infusion

Vancomycine
Metronidazole

MBP (mm Hg)

CF (b.p.m.)
MBP (mm Hg)
Noadrenaline (μg per 10 kg per min)

IVIg

Time (h)

Sokol H et al., Am J Gastroenterol 2009;104:2649-50
Severe acute colitis
Ulcerative colitis
Severe acute colitis
Ulcerative colitis
Definition

\[ \geq 6 \text{ bloody stools per day} \] and at least one of the following criteria:

- Cardiac frequency > 90 beats/min
- Evening temperature > 37.5°C
- Erythrocyte sedimentation rate > 30 mm
- Haemoglobinemia < 10 g/dL

Severe acute colitis
Ulcerative colitis
Lichtiger score

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General well-being

- Perfect: 0
- Very good: 1
- Good: 2
- Average: 3
- Poor: 4
- Terrible: 5

Abdominal tenderness

- None: 0
- Mild and localized: 1
- Mild to moderate and diffuse: 2
- Severe or rebound: 3

Need for antidiarrheal drugs

- No: 0
- Yes: 1

Maximal score 21
SAC > 10
Response to treatment < 10 2 consecutive days

Severe acute colitis in IC
Principles of specific management

Â In case of first attack of UC or sudden worsening of an established UC
  ï Search and empirical antibiotics for usual pathogens
  ï Delayed (at least 24-48h) initiation of immunosuppressive therapy

Â Include repeated search for surinfection by C. difficile (stool tests) and CMV (blood PCR, search for inclusions)
  ï At admission
  ï At each step of immunosuppressive therapy (indicated for failure of the previous one)
  ï When the patient condition worsens without any change in the treatment

Â Emergency subtotal colectomy is indicated at any time in case of mechanical complication
Treatment of acute severe colitis in Ulcerative Colitis
Rapid step-up approach

Â Methylprednisolone IV 0.8 mg/kg/day + bowel rest + steroid enemas + anticoagulation for five days

Â If no improvement, consider to add cyclosporin IV 2 mg/kg/day

Â (If no improvement and if the general condition of the patient is not too altered, consider one shot of infliximab 5mg/kg in expert tertiary centres)

Â If no improvement within a week, subtotal colectomy is indicated
Management of severe acute colitis

Key-points

• Medical and surgical approach

• Importance of initial work-up immediately followed by empirical antibiotics

• Rigorous rapid step-up approach in the specific treatment of *C. difficile* infection and severe attacks of Ulcerative Colitis

• Usefulness of biological monitoring

• Emergency subtotal colectomy may be indicated at any time