GI Bacterial Infections (part-2)

Mohammed Abdulla Mehdi
FIBMS (internal medicine), FIBMS (G&H)

Clostridium difficile infection

- *C. difficile* is the most commonly diagnosed cause of antibiotic-associated diarrhea, and is an occasional constituent of the normal intestinal flora.

- *C. difficile* is capable of producing two toxins (A and B). Infection usually follows antibiotic therapy, which alters the composition of the GI flora permitting colonization with *C. difficile* if the patient is exposed to *C. difficile* spores.

- Toxin production and environmentally stable spores accounts for the symptoms and transmissibility of infection.

### Clinical features of C. difficile infection

- Symptoms range from mild watery diarrhea to life-threatening pseudomembranous colitis.

- Around 80% of cases occur in people over 65 years of age, many of whom are frail with comorbid diseases.

- Symptoms usually begin in the first week of antibiotic therapy but can occur at any time up to 6 weeks after treatment has finished.

- The onset is often insidious, with lower abdominal pain and watery diarrhea. The presentation may <u>resemble</u> acute ulcerative colitis with bloody diarrhea, fever and even toxic dilatation, ileus and perforation.

Investigations

- Stool culture (less useful):
    - 30% of patients with antibiotic-associated diarrhea
    - >90% of those with pseudomembranous colitis
    - ~5% of healthy adults and up to 20% of elderly patients in residential care.
- *Stool C. difficile* toxin assay (more reliable):
    - Enzyme-linked immunosorbent assay (ELISA)
    - Tissue culture cytotoxicity assay
- Stool glutamate dehydrogenase level (an enzyme produced by *C. difficile*), or stool *C. difficile* nucleic acid (e.g. by PCR); can be used as initial screen to select patients for definite toxin assay testing.
- Endoscopy (colonoscopy/sigmoidoscopy):
    - Erythema, white plaques or an adherent pseudomembrane.
    - Appearance may also resemble that of ulcerative colitis.
    - Occasionally rectal sparing with only proximal colitis is seen.

- Abdominal and Chest X-rays:

    - Patients who are seriously ill may require abdominal and erect chest X-rays to exclude perforation or toxic dilatation.

- Abdominal CT scan:

    - Useful when the diagnosis is in doubt.
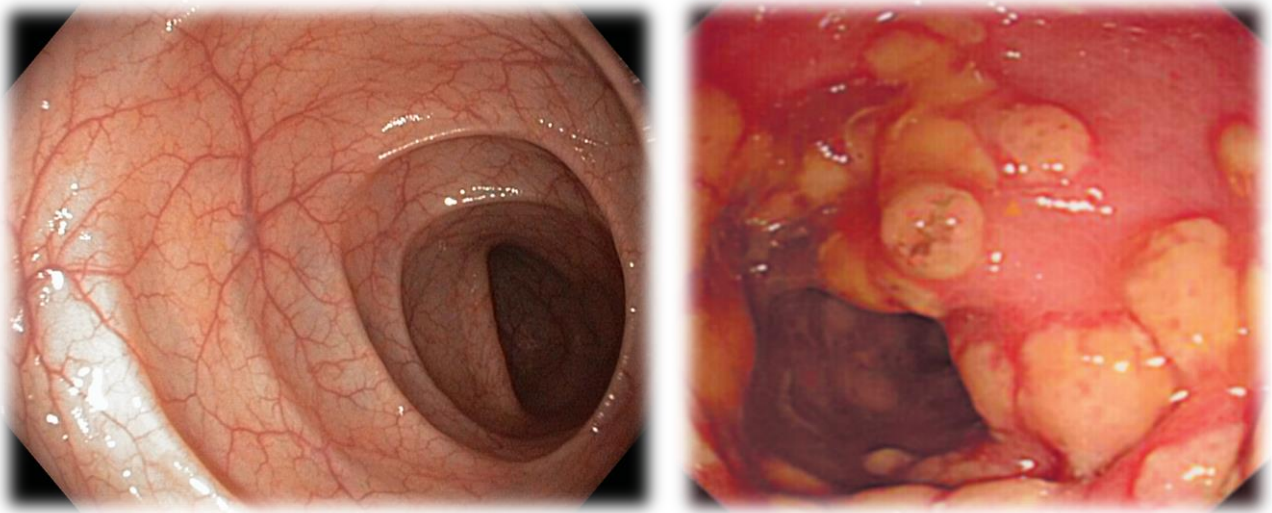
Management

- Precipitating antibiotic stopped and the patient contact-isolated.

- Supportive therapy (iv fluids and electrolytes with bowel rest).

- Antibiotics:

    - metronidazole (500 mg orally 3 times daily for 10 days) or vancomycin (125 mg orally 4 times daily for 7–10 days).

    - Fidaxomicin (new drug with lower relapse rate than vancomycin).

- Iv immunoglobulin &/or corticosteroids (severe or refractory cases)

- Fecal transplantation (for frequently relapsing patients)

- Surgical intervention is sometimes needed and needs to be considered early in severe cases.

Yersinia enterocolitica infection

- Commonly found in pork.

- Causes mild to moderate gastroenteritis.

- Can produce significant mesenteric adenitis.

- Incubation period is 3–7 days.

- Mainly affects children but adult cases can also occur.

- The illness resolves slowly, with 10-30% of cases complicated by persistent arthritis or Reiter's syndrome.

Cholera

- Cholera, caused by *Vibrio cholerae* serotype O1, is the classical toxin-mediated bacterial cause of acute watery diarrhea.

- The enterotoxin activates adenylate cyclase in the intestinal epithelium, inducing net secretion of chloride and water.

- *V. cholerae* O1 has two biotypes, classical and El Tor, and each of these has two distinct serotypes, Inaba and Ogawa.

- Large epidemics have occurred, often in association with large religious festivals or flooding.

- El Tor is more resistant to commonly used antimicrobials than classical *Vibrio*, and causes prolonged carriage in 5% of cases.

- Infection spreads via the stools or vomit of symptomatic patients or of the much larger number of subclinical cases.

- Organisms survive for up to 2 weeks in fresh water and 8 weeks in salt water. Transmission is normally through infected drinking water, shellfish and food contaminated by flies, or on the hands of carriers.

Clinical features

- Severe diarrhea without pain or colic begins suddenly and is followed by vomiting.

- Following the evacuation of normal gut fecal contents, typical 'rice water' material is passed, consisting of clear fluid with flecks of mucus.

- Classical cholera produces enormous loss of fluid and electrolytes, leading to intense dehydration with muscular cramps. Shock and oliguria develop but mental clarity remains.

- Death from acute circulatory failure may occur rapidly unless fluid and electrolytes are replaced. Improvement is rapid with proper treatment.

- The majority of infections, however, cause mild illness with slight diarrhea.

- Occasionally, a very intense illness, 'cholera sicca', occurs, with loss of fluid into dilated bowel, killing the patient before typical gastrointestinal symptoms appear. The disease is more dangerous in children.

Diagnosis

- During an epidemic, cholera is a clinical diagnosis.

- Otherwise, diagnosis is based on high clinical suspicion, together with:

- Culture (stool or rectal swab) or

- Dark- field microscopy of stool (comma- shaped organisms are seen moving around, which stop moving when diluted O1 antisera is added).

Management

- Fluids (oral and iv):

  - Maintenance of circulation by replacement of water and electrolytes is vital. Ringer-Lactate is the best fluid for intravenous replacement.

  - Vomiting usually stops once the patient is rehydrated, and fluids should then be given orally.

  - Early intervention with oral rehydration solutions (ORS) that include resistant starch, based on either rice or cereal, shortens the duration of diarrhea and improves prognosis.

  - Total fluid requirements may exceed 50 L over a period of 2–5 days and accurate fluid records are greatly facilitated by the use of a 'cholera bed'.

Management

- Antibiotics:

  - Antibiotics can reduce the duration of excretion of *V. cholerae* and the total volume of fluid needed for replacement.

  - Options for adult patients include:

    - Tetracycline 250 mg 4 times daily for 3 days.

    - Doxycycline 300 mg as a single dose.

    - Ciprofloxacin 1 g as a single dose.

Oral rehydration solution (ORS)

- ORS has been a key resource in the treatment of acute diarrhea in the developing world since the 1970s.

- The initial solution, referred to as the WHO-ORS, was iso-osmolar and provided glucose-mediated Na (& fluid) absorption in the small intestine via a cyclic AMP-independent process. It was later demonstrated that hypo-osmolar solutions performed better than the initial iso-osmolar solution.

- Despite proven efficacy of ORS in limiting dehydration and metabolic acidosis in acute diarrhea, the use of ORS has been somewhat limited due, in part, to its inability to reduce stool output significantly.

- Efforts to introduce a new ORS began after the demonstration that short-chain fatty acids (SCFA) stimulate colonic Na and fluid absorption by a cyclic AMP-independent mechanism.

- The addition of high-amylose maize starch (HAMS), an intestinal amylase-resistant starch, to ORS results in delivery of non-absorbed carbohydrate to the colon where it is fermented to SCFA which in turn stimulates colonic Na and fluid absorption.

- Recent studies with a HAMS-ORS in India have shown a substantial decrease in diarrheal stool duration and volume in both adults and children hospitalized for acute diarrhea.

Prevention of cholera

- Strict personal hygiene is vital.

- Drinking water should come from a clean piped supply or be boiled and flies must be denied access to food.

- In epidemics, public education and control of water sources and population movement are vital.

- Mass single-dose vaccination and treatment with tetracycline are valuable.

- Disinfection of discharges and soiled clothing, and scrupulous hand-washing by medical attendants reduce the spread of infection within health care facilities.

- Parenteral and oral vaccines are available but are of limited efficacy.

WHO-7-points-plan for diarrhea control:

Treatment package	Fluid replacement
	Zinc treatment
Prevention package	Rotavirus and measles vaccination
	Promotion of early and exclusive breast-feeding and vitamin A supplementation
	Promotion of handwashing with soap
	Improved water supply quantity and quality, including treatment and safe storage of household water
	Community-wide sanitation promotion

Bacillary dysentery (shigellosis)

- Diarrhea illness caused by strains of invasive forms of *Shigella* or invasive *Escherichia coli* comprises bacillary dysentery.

- The genus *Shigella* is divided into four species: *S. dysenteriae, S. flexneri, S. boydii*, and *S. sonnei*, based on serology and biochemical reactions.

- The organisms cause bacillary dysentery by an invasive mechanism identical to enteroinvasive *E. coli* (EIEC).

- DNA hybridization studies show that *E. coli* and *Shigella* are a single genetic species.

Clinical features

- Disease severity varies:

    - *Sh. sonnei* infections are mild and may escape detection.

    - *Sh. Flexneri* infections can be moderate to severe.

    - *Sh. dysenteriae* may be fulminating and may cause death within 48 hours.

- In a moderately severe illness, the patient complains of:

    - Diarrhea, colicky abdominal pain and tenesmus.

    - Stools are small, and after a few evacuations contain blood and purulent exudate with little fecal material.

    - Fever, dehydration and weakness occur, with tenderness over the lower abdomen.

- Arthritis or iritis may complicate illness in HLA-B27 positive patients (Reiter's syndrome).

Management and prevention

- Fluid and electrolytes replacement:
  - Oral rehydration therapy or, if diarrhea is severe, iv replacement of water and electrolyte loss is necessary.
- Antibiotic therapy:
  - Ciprofloxacin 500 mg twice daily for 3 days is effective in known shigellosis and appropriate in epidemics.
- Use of antidiarrheal medications should be avoided.
- The prevention of fecal contamination of food and water and the isolation of cases is critical. Hand-washing is very important.