Pathology

Crohn’s Disease (Ileitis) and Ulcerative Colitis (UC) — Causes and Treatment

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Inflammatory bowel disease (IBD) is a chronic inflammatory disease of the gastrointestinal tracts and is comprised of two major disorders: ulcerative colitis (UC) and Crohn’s disease (CD). Both diseases have characteristics that may be overlapping while other characteristics may be different. Characteristics which will be discussed in detail throughout this article.

Introduction

Although the two inflammatory bowel diseases almost have the same general symptoms, they are two separate disorders because each affects different areas of the gastrointestinal tract. However, in 10—15 % of the patients it is difficult to classify them into any of the two diseases and thus they are labelled cases of indeterminate colitis.

Crohn’s disease commonly affects the terminal ileum and the start of the colon, but it can also attack any point in the GI tract, i.e. from the mouth to the anus. Ulcerative colitis specifically affects the colon. It is important to know the characteristic signs and symptoms of the two diseases for proper treatment.
Definitions of Crohn’s Disease (Ileitis) and Ulcerative Colitis (UC)

Crohn’s disease
Is characterized by transmural inflammation (entire wall thickness) with skip lesions, affecting any point along the GI tract. The particular affected area can vary among every affected individual.

The inflammation can occur as patches in the intestine, leaving un-inflammatory section (skip lesions), while, in ulcerative colitis, this is not observed.

It is also associated with the development of fistulas which are channels or open connections between two areas, such as one twist of the colon to another or colon to skin, bladder, or vagina.

**Ulcerative colitis**

Ulcerative colitis is characterized by frequent episodes of inflammation that affect the innermost layer of the rectum and colon (mucosal layer) causing ulcers and soreness in
the GI tract (no fistula formation). The combination of inflammation and ulceration can cause abdominal discomfort and frequent emptying of the colon.

Both are long-lasting and persistent when not carefully managed in their early stages. Long-term remission can be observed with treatment for these inflammatory diseases.

Risk Factors of Crohn’s Disease (Ileitis) and Ulcerative Colitis (UC)

The exact pathophysiology of inflammatory bowel disease (IBD) is unclear, but a number of risk factors are associated with their development.

<table>
<thead>
<tr>
<th>Risk factors</th>
<th>Description</th>
</tr>
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<tbody>
<tr>
<td>Age and gender</td>
<td>• Most cases of IBD start at age between 15 and 40 years.</td>
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<tr>
<td></td>
<td>• In Crohn’s disease, there is a slight female predominance which suggests hormonal factors in the disease progression.</td>
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<td>Racial and ethnicity</td>
<td>• The racial and ethnic differences are significantly dependent on environmental and lifestyle factors in addition to the underlying genetic differences.</td>
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<td></td>
<td>• IBD occurs more in the developed, urban, and northern areas rather than undeveloped, rural and southern climates.</td>
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<td>• It occurs more commonly in Jewish patients.</td>
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<td>• It is more common in Caucasians.</td>
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<tr>
<td>Genetic susceptibility</td>
<td>• IBD usually runs in the family; 25% of patients with IBD have a first degree relative (parent-children, siblings, and parent-siblings) with the disorder.</td>
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<td></td>
<td>• Genetics have a major threat of having Crohn’s disease rather than ulcerative colitis with more risks when both parents are affected.</td>
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<tr>
<td>Smoking</td>
<td>• Ulcerative colitis: Current studies suggest that smoking is not a risk factor for development of UC and, in fact, may even be protective of or reduce disease symptoms.</td>
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<tr>
<td></td>
<td>• Crohn’s disease: Smoking increases the risk of Crohn’s disease twofold. It also increases the risk of the recurrence of CD.</td>
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<tr>
<td>Diet</td>
<td>• Suggested that certain food antigens may precipitate the development of IBD and it is suggested that the Western diet (e.g. processed, fried, and sugary foods) is associated with an increased risk of Crohn’s disease, and also ulcerative colitis.</td>
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<tr>
<td>Obesity</td>
<td>• Excessive obesity may contribute in the development of IBD due to intra-abdominal accumulation of fat, leading to mucosal inflammation and disease development.</td>
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<tr>
<td>Infections</td>
<td>• The GI tract naturally contains beneficial bacteria that are harmless and help in digestion.</td>
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<tr>
<td></td>
<td>• Imbalance and/or alterations in the gut commensal microorganisms may contribute to the development of IBD.</td>
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<td></td>
<td>• It has been suggested that multiple pathogens (e.g., Shigella, Salmonella, Campylobacter, Clostridium difficile spp.) can trigger an inflammatory response which can’t be controlled by the mucosal immune system.</td>
</tr>
<tr>
<td>Antibiotics</td>
<td>• Antibiotics may alter the gut flora and increase the risk of IBD.</td>
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<tr>
<td>Oral contraceptives and Hormone Replacement Therapy</td>
<td>• Hormone therapy can have thrombotic effects on the microvasculature which predisposes for IBD. Women using OCP or HRT have an increased risk of developing IBD.</td>
</tr>
<tr>
<td>Appendectomy</td>
<td>• Several studies have shown that an appendectomy may protect patients from the occurrence of UC. The mechanism is yet unknown.</td>
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</tbody>
</table>
Psychosocial factors

- Psychosocial factors (e.g. stress) may have a role in exacerbations of symptoms in patients with IBD, possibly though stimulating the enteric nervous system and the release of proinflammatory cytokines.

Classification of Crohn’s Disease (Ileitis) and Ulcerative Colitis (UC)

Crohn’s disease classification

The classification of Crohn’s disease is based on the inflammation (clinical behaviour), anatomical distribution (location) and operative history (age). There are generally two types which hold different values for the mentioned features:

- Vienna class
- Montreal class

Vienna class

This was an older staging system which was arrived at as a report of the working party of the world congress of gastroenterology in 1998. It classifies patients based on three major parameters as:

Age at diagnosis

- A1- less than 40 years
- A2- more than or equal to 40 years
- Location of the disease
  - L1- terminal ileum
  - L2-colon
  - L3-ileocolon
  - L4-upper gastro-intestinal

Behavior of the disease

- B1-non-stricturing non-penetrating
- B2- stricturing
- B3 -penetrating

Montreal class

The classification of the disease has undergone tremendous changes to try and establish a classification that is easy and thus widely used by clinicians. An updated classification of the Vienna classification was released which did not make changes of the three main characteristics of the classification but on the subclassification of the disease category.

Age at presentation:

Recognition of the diseases early in life lead to the subclassification into:

- A1- less than 16 years
- A2- 17- 40 years
- A3- greater than or equal to 40 years

Location of the disease:

With the advent of upper gastrointestinal endoscopy more cases of upper gastrointestinal
tract disease were identified leading to the classification as:

- L1- terminal ileum
- L2-colon
- L3-ileocolon
- L4-upper gastro-intestinal

**Behavior of the disease:**

Rectal disease was considered a different entity and an extra group added

- B1-non-stricturing non-penetrating
- B2- stricturing
- B3 -penetrating
- P-type perianal disease

**Ulcerative colitis classification**

![Image: “Gross photograph of ulcerative colitis. Diffuse erythema, edema, and many inflammatory polyps are noted in the rectum, left colon, transverse colon, and hepatic flexure. The right colon and terminal ileum are normal.” by openi. License: CC BY 3.0]

This specific type of IBD is classified by considering the area of colon affected, along with its severity:

- Class I/S1– Mild UC
- Class II/S2 – Moderate UC
- Class III/S3 – Severe UC

**Class I/S1 - Mild UC**

Passing up to four stools per day, together with blood and normal inflammatory markers (ESR) with absence of any systemic illness. The affected area is restricted to rectum (ulcerative proctitis).

**Class II/S2 - Moderate UC**

Passing four or more stools per day and has negligible signs of systemic noxiousness.

**Class III/S3 - Severe UC**

Passing six or more blood-containing stools regularly, a pulse rate of >90 bpm, a temperature of >37.5°C, blood haemoglobin <10.5 g/100 ml, and elevated ESR >30 mm/h. Youngsters below 16 years of age having prolonged ulcerative colitis are inclined to have severe symptoms. ESR is a terminology used for erythrocyte sedimentation rate.
Clinical Features of Crohn’s Disease (Ileitis) and Ulcerative Colitis (UC)

IBDs, when symptomatic, have nearly the same presentation. The affected area is the main key way of distinguishing Crohn's disease from ulcerative colitis. The signs and symptoms of inflammatory bowel disease usually range from mild to severe conditions. Symptoms may develop suddenly.

**Signs and symptoms include:**

- Abdominal pain due to inflammation and ulceration
- Bloody stool
- Ongoing diarrhea that causes intensified intestine cramping
- Diarrhea that sustains sleeplessness
- Low grade fever lasting more than a day
- Mouth sores
- Fatigue and stress
- Nausea and vomiting
- Severe abdominal/pelvic pain
- Abnormal eating habits and difficulty in absorption and digestion

**Characteristic Crohn’s disease symptoms:**

- Perianal disease with fistula formation
- Delayed growth
- Skin and joint inflammation
- Liver inflammation

**Particular ulcerative colitis symptoms**

- Rectal pain
- Rectal bleeding with mucous and pus
- Perseverance to defecate
- Incapability to have a bowel movement despite urgency

**Diagnosis of Crohn’s Disease (Ileitis) and Ulcerative Colitis (UC)**

When Crohn’s disease or ulcerative colitis is suspected, diagnosis is confirmed with biopsy and radiological exams. There is no specific test for IBDs, besides biopsy, and one has to go through multiple options for the investigations.

**Blood tests**

**Hemoglobin**

Patients are usually anemic and the efficiency of red blood cells is inadequate for transmission of oxygen to the tissues. Also, the early signs of infections can be interpreted.

**Stool tests**
Identifying fecal occult will help in investigating the root cause behind these deadly diseases.

Other Diagnostic Tests

**Colonoscopy**

This specific procedure is performed with the help of an endoscope. A few tissue samples can be taken out during the procedure for histological analysis. Groups of inflammatory cells known as granulomas are associated with Crohn’s.

**Flexible sigmoidoscopy**

The sigmoid is the last segment of the colon and is examined with an endoscope known as a slender.

**X-ray**

An erect abdominal e-ray is recommended for the diagnosis of a perforated colon. It is a severe complication.

**Computerized tomography (CT)**

It is a focused X-ray to show the more detailed X-ray analysis. This scan can be performed for abdomen and pelvis inflammation. This is equally helpful in ulcerative colitis, as well as Crohn’s disease.

**Magnetic resonance imaging (MRI)**

Magnetic field, together with radio waves, is created in this procedure for a detailed analysis of tissues and organs. MRI is predominantly valuable for assessing a fistula near the anal area and it is termed as pelvic MRI; a CT scan does this too.

**Investigations of Crohn’s disease**

**Capsule endoscopy**

In this particular procedure, you swallow a capsule consisting of a small camera to take
pictures that are transmitted to a computer belt. After the procedure, the camera expels out of the body with the stool.

**Investigations for ulcerative colitis**

**CT enterography combined with magnetic resonance (MR) enterography.**

Unlike conventional imaging procedures, ulcerative colitis is diagnosed with more precision by using a combination of CT and MR enterography revealing soreness in the bowel. MR enterography is a substitute source. Soreness is the patch making a pattern caused by the ulcerative colitis.

**Chromoendoscopy**

Ulcerative colitis with colorectal cancer can be examined by chromoendoscopy in which a technician uses a spray dye to spot abnormal tissue variations.

**Differential Diagnosis of Crohn’s Disease (Ileitis) and Ulcerative Colitis (UC)**

The following comparison may help in distinguishing between both diseases:

<table>
<thead>
<tr>
<th>Clinical</th>
<th>Ulcerative Colitis</th>
<th>Crohn’s Disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gross blood in stool</td>
<td>Yes</td>
<td>Occasionally</td>
</tr>
<tr>
<td>Mucus</td>
<td>Yes</td>
<td>Occasionally</td>
</tr>
<tr>
<td>Systemic symptoms</td>
<td>Occasionally</td>
<td>Frequently</td>
</tr>
<tr>
<td>Pain</td>
<td>Occasionally</td>
<td>Frequently</td>
</tr>
<tr>
<td>Abdominal mass</td>
<td>Rarely</td>
<td>Yes</td>
</tr>
<tr>
<td>Significant perineal disease</td>
<td>No</td>
<td>Frequently</td>
</tr>
<tr>
<td>Fistulas</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Small intestinal obstruction</td>
<td>No</td>
<td>Frequently</td>
</tr>
<tr>
<td>Colonic obstruction</td>
<td>Rarely</td>
<td>Frequently</td>
</tr>
<tr>
<td>Response to antibiotics</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Recurrence after surgery</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>ANCA-positive</td>
<td>Frequently</td>
<td>Rarely</td>
</tr>
<tr>
<td>ASCA-positive</td>
<td>Rarely</td>
<td>Frequently</td>
</tr>
</tbody>
</table>

**Endoscopic**

| Rectal sparing                    | Rarely             | Frequently      |
| Continuous disease                | Yes                | Occasionally    |
| “Cobblestoning”                   | No                 | Yes             |
| Granuloma on biopsy               | No                 | Occasionally    |

**Radiographic**

| Small bowel significantly abnormal| No                 | Yes             |
| Abnormal terminal ileum           | No                 | Yes             |
| Segmental colitis                 | No                 | Yes             |
| Asymmetric colitis                | No                 | Yes             |
| Stricture                         | Occasionally       | Frequently      |
Treatment of Crohn’s Disease (Ileitis) and Ulcerative Colitis (UC)

Treatment of IBD can be divided into:

- Pharmacological treatment
- Surgical treatment

The goals of treatment of the disease include:

1. Achieve remission
2. Avoid flares of inflammation

Pharmacological treatment

It involves a stepwise approach that progresses as follows:

1. Antibiotics and anti-inflammatory medications such as amino salicylates
2. Steroids
3. Immunomodulators

Anti-inflammatory medications

5-aminosalicylates

5-ASA agents, such as sulfasalazine, are effective in inducing and maintaining remission in UC, with a limited role in inducing and maintaining remission in CD. This is most useful for the treatment of active Crohn’s disease involving the colon.

Corticosteroids

Corticosteroids are effective in the treatment of moderately severe UC or CD. Corticosteroids don’t play any role in maintaining remission of either UC or CD. They can be given orally as prednisone (40–60 mg/d) or parenterally as hydrocortisone (300 mg/d) or methylprednisolone (40–60 mg/d). Because of the systemic side effects of standard corticosteroids, another medication called budesonide (9 mg/day), which is used for 2–3 months, has the same potent effect of prednisone, but with fewer side effects.

Immunosuppressors

Azathioprine and 6- Mercaptopurine

They are purine analogs that are used mainly in the treatment of corticosteroids-dependent IBD and used as glucocorticoid-sparing agents in UC & CD.

Methotrexate

It is effective in inducing and maintaining remission in active CD, and allows the reducing of the dosage of glucocorticoids.

Biological therapies

The first approved biological therapy in the treatment of Crohn’s disease refractory to previous regimens or moderate to severe active ulcerative colitis.
Antibiotics

Antibiotics can lessen the quantity of drainage and occasionally dissolve fistulas in patients with Crohn’s disease. Regularly recommended antibiotics include Metronidazole and Ciprofloxacin depending on the severity.

Anti-diarrheals

A fibrous supplement including psyllium powder or methylcellulose help relieve moderate diarrhea by adding fiber bulk to the stool. Loperamide is effective for severe diarrhea.

Supplements

Iron and vitamin supplements taken on a daily basis will overcome iron deficiency and vitamin B-12 will fulfill the body’s needs and will encourage regular growth and development. Calcium supplements can reduce the risk of osteoporosis that occurs in Crohn’s disease.

Surgery

Indications and the preferred type of surgery vary with the specific disease.

Ulcerative colitis

Here surgery is curative, and it is only indicated when:

- there is persistent inflammation
- Medical therapy has failed
- There is a concurrent malignancy or anaplastic process

Procedures of choice include:

a. Proctocolectomy with stoma fashioning
b. Proctocolectomy with ileoanal anastomosis which is the most common procedure although it has associated complications of pouch formation.

Crohn’s disease

The disease may involve any part of the gastrointestinal tract and thus surgery is not curative. It is only indicated when there are complications such as strictures or fistula formation.

Due to the imminent risk of recurrence the smallest possible resection is done to allow for future resections and minimize onset of surgery related complications.

Procedures of choice include strictureplasty in which the impaired section is separated from the small intestine.

Review Questions

The correct answers can be found below the references.

1. **Which area of the body is affected in ulcerative colitis?**
   
   A. Ileum
B. Colon
C. Anus
D. Vagina

2. Which part of the GI tract is removed during surgery in Crohn’s disease?
   A. Rectum
   B. Colon (large intestine)
   C. Ileum (small intestine)
   D. Mouth

3. What are the main causes of Crohn’s disease?
   A. Genetics
   B. Environment
   C. Immunity
   D. All of the above

References


Correct answers: 1B, 2C, 3D

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