Chapter 7
Clinical Features

Natalia Fabisiak

This chapter focuses on their localization, symptomatology and course of the disease. Additionally, the most frequent extraintestinal manifestations and complications associated with inflammatory bowel diseases are discussed in the section.

7.1 Localization

Crohn’s disease (CD) can affect all parts of the gastrointestinal tract, from mouth to anus. The upper part of the alimentary tract is occupied quite rarely—the lesions are observed only in 0.5–13 % of CD patients. These lesions are mostly accompanied by the inflammation in the ileum or large intestine. However, in some cases they can appear exclusively in oral cavity, esophagus, stomach or duodenum.

Frequency of oral manifestations is estimated at 5–20 % cases in adults and 40–80 % in children with CD. The lesions in oral cavity can precede occurrence of a full-blown disease.

Esophageal lesions in CD are usually related with manifestations in ileum and/or colon and exist especially at a younger age. Usually, the distal part of esophagus is involved. Different studies estimate the frequency of these lesions at 7–43 % in children and at 0.2–11 % in adults with CD.

Crohn’s disease may affect the stomach and duodenum. Gastroduodenal manifestation is present in 0.5–4.5 % of all CD patients. Gastroduonenal CD the most frequently occupies the antrum of the stomach and the second part of duodenum.

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The usual localization of Crohn’s disease is the distal part of the ileum. Ileocecal region is occupied in 40–50% of patients and that is why the disease was called ‘ileitis terminalis’ in the past. In 25–30% of cases CD is limited to the small intestine and in 30–40% of patients the inflammation is localized simultaneously in both: small and large intestine. The isolated occupation of colon is observed in 20% of cases.

Anal lesions are characteristic for CD and occur in 35–45% of patients. Fissures, fistulae or abscesses can precede lesions in intestine or occur concurrently. Lesions in the anal region are more often observed in patients with occupied large bowel, or small and large intestine than in patients with disease solely in the small intestine.

Three forms of ulcerative colitis (UC) are distinguished with regard to localization of the disease: (1) proctitis, when only the rectum is involved, (2) left-side colitis, when lesions are localized distally to the splenic flexure and (3) extensive colitis, when lesions extend proximally to the splenic flexure. Pancolitis, belonging to the extensive colitis, is inflammation of the entire colon.

### 7.2 Signs and Symptoms

Symptoms presenting in CD and UC show fundamental differences in respect of different localization of lesions in the bowel.

The most common symptom presenting in patients with colonic CD is chronic diarrhea, which lasts more than 6 weeks. The majority of patients complain of persistent abdominal pain or cramps and weight loss. Blood and/or mucus in stool occur in almost half of the patients. Palpable tumor localized in the right lower area of abdomen is present in about one third of the patients. When the disease occupies the upper part of the digestive tract, patients may complain about pain in oral cavity, swallowing difficulties (dysphagia) or pain (odynophagia), epigastric pain, nausea and vomiting. Pain in the region of the anus may indicate inflammation and the formation of fistulae and abscesses.

Chronic, bloody diarrhea, sometimes with passage of mucopurulent exudates, is the primary symptom of patients with UC. Visible blood in the stool occurs in more than 90% of patients. In the active phase of disease patient may pass up to twenty stools per day. Crampy pain in the lower left area of abdomen, relieved after defecation is reported by patients. Rectal urgency, tenesmus and nocturnal defecation is often described by patients. If lesion are bound only to the terminal part of the colon, especially to the rectum, different symptoms occur. Instead of diarrhea, patients may suffer from constipation, and rectal bleeding may be the only symptom.

Similar nonspecific general manifestation of both diseases are fatigue, tiredness, malaise, anorexia (loss of appetite) or fever.
Main differences between CD and UC involving signs and symptoms are summarized in Table 7.1. Information about a thorough medical history and examination is shown in Boxes 7.1 and 7.2.

### Table 7.1 Differences between Crohn’s disease and ulcerative colitis on the basis of signs and symptoms

<table>
<thead>
<tr>
<th>Signs and symptoms</th>
<th>Crohn’s disease</th>
<th>Ulcerative colitis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abdominal pain</td>
<td>Often, severe</td>
<td>Less increased</td>
</tr>
<tr>
<td>Hemorrhage</td>
<td>Seldom</td>
<td>Very common</td>
</tr>
<tr>
<td>Palpable tumor in abdomen</td>
<td>Common</td>
<td>Absence</td>
</tr>
<tr>
<td>Fistulae</td>
<td>Common</td>
<td>Seldom</td>
</tr>
<tr>
<td>Stenosis lesions</td>
<td>Common</td>
<td>Seldom</td>
</tr>
<tr>
<td>Perianal changes</td>
<td>Common</td>
<td>Seldom</td>
</tr>
<tr>
<td>Rectum occupation</td>
<td>Seldom</td>
<td>Very common</td>
</tr>
<tr>
<td>Distribution of lesions</td>
<td>Continuous</td>
<td>Discontinuous</td>
</tr>
<tr>
<td>Toxic megacolon</td>
<td>Seldom</td>
<td>Common</td>
</tr>
<tr>
<td>Perforation</td>
<td>Seldom</td>
<td>Common</td>
</tr>
<tr>
<td>Pseudopolyps</td>
<td>Quite common</td>
<td>Seldom</td>
</tr>
</tbody>
</table>

### Box 7.1 A full medical history of IBD should include answers to the following questions:

- When did the disease begin? When were the first symptoms?
- Are there recurrent episodes of rectal bleeding or bloody diarrhea?
- Does abdominal pain occur?
- Have you had any problems with stools (tenesmus/incontinence/nocturnal diarrhea)?
- Have you travelled recently?
- Have you got food intolerance?
- Does anyone in your family suffer from inflammatory bowel diseases?
- Have you ever had appendectomy?
- Do you take any medicines, especially antibiotics or non-steroidal anti-inflammatory drugs?
- Do you smoke?
- Have you had any contact with enteric infectious illness recently?
- Have you ever had any problems with your skin, eyes, joints?
- Have you ever had any changes in your mouth or anal area?
7.3 The Course of Disease

Crohn’s disease is a chronic, longstanding condition with alternating periods of remission and exacerbation as characteristic features. Longstanding persistent remission after first episode of the disease occurs only in 10–20% of patients. Progression of the disease proceeds to the fibrosis, formation of stenoses and fistulae. A risk of fistulae formation is estimated at 20–40% of patients during the overall duration of CD. Young age during onset of the disease, presence of perianal changes and an early beginning of aggressive treatment are negative prognostic factors.

Ulcerative colitis proceeds with periods of exacerbation and remissions. However, in 5% of patients permanent exacerbation without remission occurs. Another 5% of patients have one episode of acute symptoms with longstanding period of remission. Remission is defined as a complete reversal of symptoms and lack of changes in endoscopy. In clinical practice, remission is characterized by a reduction in a number of stools without blood and rectal urgency (3 stool per day or less). Presence of bleeding, increased number of stools and intensity change in endoscopic activity indicate relapse of UC.

7.4 Extraintestinal Manifestations

The frequency of extraintestinal manifestations (EIMs) in patients with IBD ranges from 6 to 47%; more than one EIM is observed in 25% of patients. Inflammatory involvement of joints, liver, skin and eyes are considered primary manifestations, with two major groups distinguished: (1) extraintestinal immune-related manifestations in IBD, which are associated with intestinal inflammatory activity e.g. arthritis, erythema nodosum, pyoderma gangrenosum, aphthous stomatitis, iritis,
uveitis and (2) autoimmune disorders associated with IBD but not correlating with disease activity e.g. insulin-dependent diabetes mellitus, pancreatitis, primary biliary cirrhosis, primary sclerosis cholangitis, Raynaud phenomena, thyroid autoimmune disease and others.

7.4.1 Musculoskeletal Involvement in IBD

Joint manifestations are the most common extraintestinal manifestations in patients with IBD. The inflammatory involvement of joints occurs in 7–25 % of cases and affects equally both: males and females. Arthritis occurs more frequently in patients with colonic disease than small-bowel disease. Peripheral or axial articular involvement can precede, be simultaneous or begin afterward the diagnosis of IBD. Peripheral arthritis is observed in 5–10 % of patients with UC and 10–20 % in cases of CD. It is associated with the skin, mouth and ocular manifestations. Two types of peripheral arthritis are known: (1) pauciarticular arthritis—involves less than five large joints and is strongly related to IBD activity; acute and self-limiting swelling occur and persist for 5–10 weeks; (2) polyarticular arthritis - affects symmetrical five or more small joints and is not associated with the disease activity. Arthritis may last month or years.

Axial arthropathies occur less frequently than peripheral articular involvement in IBD patients and more often affect males than females. Axial arthropathies are not related to intestinal IBD activity and can be grouped into ankylosing spondylitis and sacroiliitis. The prevalence of ankylosis spondylitis in patients with IBD occurs in around 5–10 % of patients. Severe onset of back pain at a younger age is often characterized. Patients may complain of morning stiffness or pain exacerbation by periods of rest. Prevalence of sacroiliitis is observed in up to 25 % of cases. Symptoms are usually absent and the disease is diagnosed radiographically.

7.4.2 Hepatobiliary Manifestation

Hepatobiliary EIMs are common in IBD patients. The most frequent hepatobiliary disease is primary sclerosing cholangitis (PSC). It is a chronic inflammatory disorder of the biliary tree, whose etiology remains unknown. Inflammation, stricture and fibrosis of intra- and extrahepatic bile ducts are characterized by PSC. PSC occurs in 5 % of patients with UC and 2 % of patients with CD. However, 75 % patients with PSC also suffer from ulcerative colitis and 5–10 % of PSC patients have Crohn’s disease. The disease more frequently occurs in male than female, especially at the age 30–59. Patients with PSC experience a few suggestive symptoms, e.g. fatigue, pruritus, jaundice and abdominal discomfort; however, 15–70 % of patients are asymptomatic.
7.4.3 Dermatologic Involvements

Erythema nodosum, pyoderma gangrenosum and oral ulceration are the most common skin manifestations in IBD, usually related to its activity. Erythema nodosum affects up to 15% of patients with CD and 10% of patients with UC. The disease more frequently occurs in women than in men. It is commonly related with the involvement of eye and joint, isolated colonic manifestation and pyoderma gangrenosum. Patients usually present risen, tender, red or violet inflammatory subcutaneous nodules of typically 1–5 cm in diameter. Erythema nodosum is usually localized on the anterior exterior surface of the lower extremities. It may rarely occur on the face and trunk.

Pyoderma gangrenosum is more severe, very debilitating and fortunately much rarer EIM, appearing more frequently in UC than CD. This chronic skin disorder occurs in about 1–2% of IBD patients. Conversely, up to 50% of patients with pyoderma gangrenosum suffer from IBD. Pyoderma gangrenosum is more common in female than male. It is associated with a familial history of UC, initial pancolitis, black African origin, permanent stoma, eye manifestations and erythema nodosum. Lesion usually begins as an erythromatous papule, pustule or nodule evolving quickly into ulcer with irregular, violet borders. The ulcers can be solitary or multiple, unilateral or bilateral and can occupy from several centimeters to an entire limb. Although pyoderma gangrenosum is localized most commonly in the legs, ulcers can appear on any part of the body. New lesions of pyoderma gangrenosum can develop after any type of trauma (pathergy phenomenon).

Prevalence of oral aphthous ulcers (aphthous stomatitis) is at least 10% of patients with UC and 20–30% of patients with CD. Ulcerations resolve quickly, when remission is achieved. Aphthous lesions typically occur on the labial and buccal mucosa but may also be located on the tongue and oropharynx. One of the more common lesions in CD is Sutton’s aphthous stomatitis. These are circular or oval ulcerations of a bigger size (1–2 cm of diameter), which can occur in every area of oral mucous membrane, most frequently in cheek and velum or in vicinity of the small salivary glands. Routinely they are single, but they can appear in groups. The ulcerations are healed during a few weeks and often recur. They are very painful and hinder eating and drinking.

7.4.4 Ocular Manifestations

Involvement of the eyes occur in 0.3–5% of IBD patients, more frequently in patients with CD than UC and are often presented with other extraintestinal manifestations, especially peripheral arthritis and erythema nodosum. Three main types of ocular manifestations are distinguished: episcleritis, scleritis and uveitis. Episcleritis is the most common ocular manifestation, defined as painless
hyperemia of conjunctiva and sclera. It often parallels intestinal activity. Acute hyperemia, irritation, burning and tenderness to palpation are characteristic symptoms of the disease.

Scleritis is suspected when above symptoms occur with impairment of vision. Inflammation of the middle chamber of the eyes is called uveitis. Uveitis is less common and occurs independently of disease activity, more frequently in women than man. It is characterized by the ocular pain, visual blurring, photophobia and headache. Uveitis may precede the diagnosis of IBD.

7.5 Extraintestinal Complications

7.5.1 Anemia

About two-third of patients with IBD have anemia, which significantly impairs the quality of life. Iron deficiency anemia and anemia of chronic disease are the most common types of anemia and often the two types overlap. Iron deficiency anemia is the most frequent anemia occurring in IBD which prevalence ranges from 36 to 76 % of patients. The latter type of anemia appears as a result of immune system activation or changes in iron metabolism occurring in patients with any chronic process of active inflammation.

7.5.2 Thromboembolic Events

Patients with IBD have increased risk of developing thromboembolic complications, which are a major cause of morbidity and mortality in IBD. In patients with IBD thrombotic accidents as deep vein thrombosis or pulmonary thromboembolism occur in earlier age than in patients without IBD. Episodes of thrombosis are more frequent in active or complicated IBD and occur mainly in veins.

7.5.3 Osteopathy and Osteoporosis

Inflammatory bowel diseases are related to an increased risk of developing osteopenia and osteoporosis. The prevalence of osteoporosis ranges from 2 to 30 %. Osteopenia occurs in up to 50 % of patients. Osteoporosis in IBD is a multifactorial process. The use of corticosteroids, malabsorption of vitamin D and calcium, low body mass index and the grade of disease activity are important pathogenic factors in IBD.