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Etiopathogenesis and Clinical Management of Inflammatory Bowel Disease

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ABSTRACT

Inflammatory bowel disease, which includes Crohn's disease and ulcerative colitis, is a relapsing and remitting condition characterized by chronic inflammation at various sites in the GI tract, which results in diarrhea and abdominal pain. This review summarizes the types, epidemiology, aetiology, risk factors, pathogenesis, clinical signs and symptoms, complications, diagnosis and recent advances in clinical management of inflammatory bowel disease.

Keywords: Inflammatory Bowel Disease, Ulcerative Colitis, Crohn's Disease, Immunomodulating drugs.

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INTRODUCTION

Inflammatory bowel disease (IBD) is an idiopathic and chronic intestinal inflammation [1]. inflammatory bowel disease (IBD), which includes Crohn's disease (CD) and ulcerative colitis (UC), is a relapsing and remitting condition characterized by chronic inflammation at various sites in the GI tract, which results in diarrhea and abdominal pain. Although Crohn's disease and UC are similar, they can be distinguished in most cases:

Crohn's Disease (CD)

Small bowel is involved in 80% of cases. Recto sigmoid is often spared; colonic involvement is usually right-sided. Gross rectal bleeding is rare, except in 75 to 85% of cases of Crohn's colitis. Fistula, mass, and abscess development is common. Perianal lesions are significant in 25 to 35% of cases. On x-ray, bowel wall is affected asymmetrically and segmentally, with "skip areas" between diseased segments. Endoscopic appearance is patchy, with discrete ulcerations separated by segments of normal-appearing mucosa. Microscopic inflammation and fissuring extend transmurally; lesions are often highly focal in distribution. Epithelioid (sarcoid-like) granulomas are detected in bowel wall or lymph nodes in 25 to 50% of cases (pathognomonic).

Ulcerative Colitis (UC)

Disease is confined to the colon. Rectosigmoid is invariably involved; colonic involvement is usually left-sided. Gross rectal bleeding is always present. Fistulas do not occur. Significant perianal lesions never occur. Bowel wall is affected symmetrically and uninterruptedly from rectum proximally. Inflammation is uniform and diffuse. Inflammation is confined to mucosa except in severe cases. Typical epithelioid granulomas do not occur.

Epidemiology

IBD affects people of all ages but usually begins before age 30, with peak incidence from 14 to 24. IBD may have a second smaller peak between ages 50 and 70; however, this later peak may include some cases of ischemic colitis [2]. IBD is most common among people of Northern European and Anglo-Saxon origin and is 2 to 4 times more common among Ashkenazi Jews than in non-Jewish whites. The incidence is lower in central and southern Europe and lower still in South America, Asia, and Africa. However, the incidence is increasing among blacks and Latin Americans living in North America. Both sexes are equally affected. First-degree relatives of patients with IBD have a 4- to 20 fold increased risk; their absolute risk may be as high as 7%. Familial tendency is much higher in Crohn's disease than in UC. Several gene mutations conferring a higher risk of Crohn's disease (and some possibly related to UC) have been identified. Cigarette smoking seems to contribute to development or exacerbation of Crohn's disease but decreases risk of UC. NSAIDs may exacerbate IBD.

Aetiology

Although IBD has been described as a clinical entity for over 100 years, its aetiology and pathogenesis have not been definitively elaborated. An unknown factor or agent (or a

combination of factors) triggers the body's immune system to produce an inflammatory reaction in the intestinal tract that continues without control. As a result of the inflammatory reaction, the intestinal wall is damaged leading to bloody diarrhea and abdominal pain. Genetic, infectious, immunological and psychological factors have all been implicated in influencing the development of IBD [3]. Mutations in a gene called NOD2 tend to occur more frequently in people with CD [4].

Risk factors

I) Modifiable: Smoking – CD, higher socioeconomic class, white colour jobs, psychological factors, NSAIDS, oral contraceptives, diet.
II) Unmodifiable: Genetic- Ist degree relative, ethnic, age and gender.

Pathogenesis

Exogenous factors such as infectious agents (*Mycobacterium paratuberculosis, Paramyxovirus, Helicobacter species*); psychosocial factors such as illness or death in family, divorce or separation, interpersonal conflict, acute daily stress and inflammatory cascade results in T cell activation that causes acute immune inflammatory response which releases inflammatory cytokines, such as Interleukin - 1 (IL-1), as Interleukin - 6 (IL-6) and tumor necrosis factor (TNF) that promotes fibrogenesis, collagen production, activation of tissue metalloproteinases, production of other inflammatory mediators that results in inflammation (i.e. due to imbalance between pro-inflammatory and anti-inflammatory mediators [5,6].

Clinical signs and symptoms

Abdominal pain, vomiting, diarrhoea, rectal bleeding, weight loss and various associated complaints or diseases like arthritis, pyoderma gangrenosum and primary sclerosing cholangitis [7].

Complications

Profuse bleeding from the ulcers, perforation (rupture) of the bowel, strictures and obstruction, fistulae (abnormal passage) and perianal disease – more common in person's with CD, toxic megacolon, malignancy (i.e. colon cancer) and arthritis.

Diagnosis

History and physical examination are the first steps and may reveal risk factors. Blood tests may help establish the diagnosis and are also routinely used to identify anaemia and nutritional deficiencies. In some cases, stool cultures may be used to identify bacterial infections that can trigger the disease. Abdominal X–ray and CT scan can aid in diagnosis, rule out other diseases, and evaluate for complications, including bowel obstruction and abscess. Colonoscopy with biopsy is usually recommended to diagnose and observe the extent of disease, and rule out other diseases that may appear similar to IBD, such as cancer

and haemorrhoids. However, colonoscopy should be avoided in patients with severe disease because it increases the risk of colon perforation.

Treatment

Treatment involves medications in mild to moderate cases, or surgery in severe and recurrent cases. Common medications include sulfasalazine, corticosteroids (e.g., prednisone), azathioprine, and cyclosporine. In addition, antibiotics (e.g., ciprofloxacin, metronidazole, and ampicillin) are often used when infection is a concern. Additional medications are used for symptomatic relief, including antidiarrheals (e.g., loperamide), iron supplements, and vitamin B12 supplements. Surgery to address complications of the disease, such as abscess formation, or to remove all or part of the colon may be necessary for severe disease. However, it usually will not cure the disease. Lifestyle factors may affect the disease. Limited evidence indicates that stress reduction reduces symptoms in patients with Crohn's disease, and results in less pain and decreased need for anti–inflammatory medication in patients with ulcerative colitis. However, additional clinical trials are necessary to learn more about the psychological aspects [8-11].

CONCLUSION

Because inflammatory bowel disease (IBD) is a chronic, often lifelong disease that is frequently diagnosed in young adulthood, increasing patient knowledge improves medical compliance and assists in the management of symptoms.

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