American Academy of Nurse Practitioners

PRACTICE

Clinical review of Crohn's disease

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Keywords
Crohn's disease; inflammatory bowel disease; ulcerative colitis.

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Received: March 2006;
accepted: January 2007

doi:10.1111/j.1745-7599.2007.00242.x

Abstract

Purpose: This clinical review presents proposed theories regarding the etiology of Crohn's disease (CD), the pathophysiology of the disorder, and current diagnostic methods.
Data sources: Pertinent publications in the literature, the Crohn's and Colitis Foundation web page, and relevant texts regarding pathophysiology of the gastrointestinal system.
Conclusions: CD can be a devastating disease and difficult to diagnose. The advanced practice nurse (APRN) should be aware of the etiology, pathophysiology, diagnostic methods, and current treatment options of this disorder.
Implications for practice: In collaboration with a gastroenterologist, APRNs can provide much needed information to the patient with CD. Practice recommendations include patient education, pain management, and support for quality of life issues.

Introduction

Crohn's disease (CD) is a chronic inflammatory process of the gastrointestinal system. It is categorized under a broader group of illnesses known as inflammatory bowel disease (IBD). It can involve any portion of the alimentary tract from mouth to anus but primarily targets the ileum of the small intestine. CD can affect all layers of the bowel and often leads to multiple comorbidities. The onset of the disease is often insidious and can present in a similar fashion to ulcerative colitis (UC), which is another form of IBD. Unlike CD, UC only affects the large colon and rectum and is limited to the mucosal layer of the bowel (Stenson, 1999). At times, it may be difficult to establish a diagnosis of CD because of the overlapping symptoms of these disorders. The term indeterminate colitis is used in about 2%–16% of IBD cases when neither UC nor CD can be accurately distinguished (Matsui et al., 2003). Not only is CD physically debilitating but the episodic relapses and remissions of the disease can have a substantially negative impact on the quality of life for the affected individual. It is important for advanced practice nurses (APRNs) to be aware of this disease in order to assist patients in understanding their disease as well as provide therapeutic treatment options. This article will provide a clinical review of the incidence, pathophysiology, clinical presentation, diagnostic methods, and treatment of CD.

Incidence

IBD affects approximately 1.5 million people in the United States and more than 2 million in Europe. The incidence continues to rise in Asia and in other developing countries. This number is almost equally divided between CD and UC. CD can occur at any age, but the diagnosis is often made between the teenage years and early adulthood with a smaller incidence occurring between the fifth and seventh decades of life. The disorder appears to affect women and men equally; however, some studies show a higher incidence in females than in males (Loftus, 2004). CD appears to involve certain ethnic groups more than others. For instance, it is more common in Jewish than in non-Jewish persons and in white people more than African Americans.

Last, the disease has a higher incidence among smokers than nonsmokers. Individuals who smoke and have a diagnosis of CD are at higher risk of a complicated clinical course and increased frequency of exacerbations. On the other hand, there seems to be an inverse association between

Journal of the American Academy of Nurse Practitioners *19* (2007) 392–397

smoking and UC. Current smokers have a decreased risk for UC, whereas ex-smokers have 70% likelihood of developing UC. There are numerous studies confirming this unusual finding, but the exact relationship remains unclear (Loftus, 2004).

Pathophysiology and etiology of CD

To better understand the pathophysiology of CD, one should have a basic understanding and appreciation of the anatomy and normal function of the digestive system. The digestive tract consists of a continuous tube that runs from the mouth to the anus and has four layers throughout most of its length. The four layers from the innermost lumen of the tract outward are as follows: mucosa, submucosa, muscularis externa, and serosa. Throughout much of the digestive tract, the serosa is continuous with the mesentery, which suspends the digestive organs from the wall of the abdominal cavity. The basic processes of the gastrointestinal system include motility, secretion, digestion, and absorption. The small intestine is the primary site for digestion of food and absorption of nutrients, while the large intestine is responsible for absorption of salt and water and converting contents into stool (Sherwood, 2004).

It is important to note that although CD can affect any portion of the digestive tract, it does favor the small intestine in most cases. The ileum and cecum are affected in 40% of cases, the small intestine in 30% of cases, and the colon in 25% of cases (Stenson, 1999). With such a large percentage of presentations being in the small intestine, this disease can be detrimental to a patient's nutritional status.

Although the etiology of CD has yet to be determined, current research has proposed several theories. These theories suggest that CD may result from genetic predisposition, environmental agents, immune system dysfunction, or a combination of these factors. The most firmly established risk factor for development of CD or IBD in general is genetics. Approximately 15% of patients with IBD have a first-degree relative with the disease. The incidence of CD is higher among first-degree relatives than in UC. There is no clear-cut pattern of inheritance, but patients with CD and their relatives with CD often present with a similar disease course (Stenson, 1999). There are several detailed studies describing specific genes, which have been linked to the development of CD, and a full account of these studies is beyond the scope of this review.

Clinical presentation

CD encompasses a spectrum of clinical and pathologic patterns and can be "manifested by focal, asymmetric, transmural, and, occasionally, granulomatous inflammation affecting the gastrointestinal tract with the potential for systemic or extraintestinal complications" (Hanauer, Sandborn, & The Practice Parameters Committee of the American College of Gastroenterology, 2001, p. 635). Patients with CD may complain for months, even years, of vague abdominal pain and diarrhea before a diagnosis is ever made. Physical findings can vary depending on the activity of the disease. When the disease is active, the patient may present with weakness, pallor, fever, fatigue, and can appear chronically ill. Predominant symptoms of the disease include abdominal pain, diarrhea, and weight loss.

Abdominal pain is the hallmark of CD and is dependent upon anatomic location (Stenson, 1999). For example, cramping over the right lower quadrant is indicative of ileocolonic disease. This pain may be related to partial obstruction secondary to a narrow lumen of bowel affected by the disease. Pain can occur after eating as the bowel wall proximal to the obstruction stretches, attempting to push contents through the narrowed space. Patients with CD may also experience visceral pain, which is related to inflammation of the serosa and is often seen in transmural disease. Frequently, abdominal distention, nausea, and vomiting may be present with the pain. The abdomen may be tender to palpation over the area of active disease, and rebound tenderness is common.

Diarrhea is present in almost all cases, but again, the severity is dependent upon the anatomic location of the disease process. Because the majority of cases present in the small intestine, the stools are of large volume and are usually not associated with urgency or tenesmus. However, diarrhea secondary to colonic disease, especially with rectal involvement, may be of small volume and associated with both urgency and tenesmus. Colonic disease is usually associated with rectal bleeding and perianal disease, including induration, redness, tenderness near the anus, fissures, and fistulous openings (Stenson, 1999). All of these conditions are aggravated by diarrhea.

Weight loss can occur in almost all the patients with CD. This is usually a result of malabsorption but can also be related to diminished intake; however, more than a 20% loss of weight is uncommon (Stenson, 1999). Patients with small bowel disease may avoid eating as this can bring about pain or diarrhea.

CD may be associated with a variety of extraintestinal complications involving the joints, eyes, liver, and skin. Patients may present with one or several of these extraintestinal manifestations with or without existing gastrointestinal involvement. Occasionally, the extraintestinal complications may be more bothersome to the patient than the bowel disease. It is imperative for the clinician to be able to accurately identify these features and to be aware of their association with CD.

One of the most common extraintestinal manifestations is arthritis. The two types of joint involvement often seen with IBD include peripheral arthritis and ankylosing spondylitis. Peripheral arthritis affects the large joints such as knees, ankles, elbows, and hips. Ankylosing spondylitis affects the spine and may present with morning stiffness, stooped posture, and low back pain (Stenson, 1999).

Ocular complications may result from the inflammatory process itself or may occur secondarily to treatment of the disease with corticosteroids. Clinical presentation could include uveitis, episcleritis, keratopathy, and dry eyes. Inflammation can also occur in the retina or the optic nerve. Early detection and treatment of these complications will decrease the chance of blindness (Crohn's and Colitis Foundation of America [CCFA], 2004).

Liver manifestations such as sclerosing cholangitis occurs in 1%–4% of persons with UC and less frequently in those with CD. Sclerosing cholangitis is a chronic cholestatic liver disease that affects the intrahepatic and extrahepatic bile ducts causing strictures to occur. Patients presenting with sclerosing cholangitis and no other bowel symptoms should have a colonoscopy to rule out IBD because the prevalence of IBD is high in the presence of sclerosing cholangitis (Stenson, 1999).

Last, cutaneous manifestations such as erythema nodosum, pyoderma gangrenosum, and oral ulcerations are commonly associated with CD. Erythema nodosum is characterized by painful, indurated, purple–red nodules that are usually seen over extensor surfaces. Pyoderma gangrenosum is characterized by painful, purulent ulcerations that often occur with extensive disease. Canker sores occur in the mouth and are usually small in diameter and can be exquisitely tender. Oral ulcers can occur in persons without any form of IBD, but patients with numerous, almost constant ulcerations should be evaluated for IBD. All of these cutaneous manifestations usually parallel intestinal inflammation and resolve when the underlying inflammatory process is treated (Jorizzo, Sherertz, & Bennett, 1999).

Diagnostic methods

CD can be difficult to diagnose because of the insidious onset and overlapping features with other types of colitis. Differential diagnosis may include acute appendicitis, small bowel obstruction, UC, infectious colitis, *Clostridium difficile*, and diverticular disease. A diagnosis of CD should be considered in any person who presents with abdominal pain, diarrhea, weight loss, or any of the extraintestinal complications previously listed.

When choosing a diagnostic method, an upper or lower endoscopy is considered hallmark. This is used to confirm the disease location and to obtain tissue biopsy for pathologic evaluation (Hanauer et al., 2001). Aphthous ulcers are frequently seen with endoscopic evaluation. These ulcers can become large in nature and appear in a cobblestone fashion along the mucosa of the bowel (Stenson, 1999).

Diagnosis can also be achieved with the use of contrast radiography. A small bowel follow-through can assist with confirmation of anatomic location of the disease, as well as identification of internal fistulas, which are common in small bowel disease. Computed tomography and ultrasonography can identify abscesses and determine the thickness of the bowel wall (Stenson, 1999).

Laboratory values alone do not provide a definitive diagnosis and may or may not reflect the patient's clinical presentation. Nevertheless, a thorough lab work up can support other key diagnostic information and help the clinician with assessing overall patient health. Obtaining a complete blood count is useful when CD is suspected. The white blood cell count may be elevated in the presence of active infection or abscess formation. Anemia might be noted because of mucosal blood loss or malabsorption of vitamin B12 secondary to inflammation of the small intestine. An elevated erythrocyte sedimentation rate or C-reactive protein may be present if the patient is experiencing active inflammation (McQuaid, 2004). Last, a stool specimen should be collected and tested for the presence of fecal leukocytes that can confirm intestinal inflammation. The specimen should also be tested for enteric pathogens, parasites, and *C. difficile* (Hanauer et al., 2001).

Antibody testing may be helpful in distinguishing CD from UC. The two types of antibodies used to differentiate these diseases are called perinuclear antineutrophil cytoplasmic antibody and anti-*Saccharomyces cerevisiae* antibody (ASCA). This type of testing cannot be used independently as many patients may not have either antibody but may still have the disease. The ASCA cannot be used as a discriminating marker for CD as it has been shown to have a low sensitivity for patients with IBD (Matsui et al., 2003).

Medical management

Medical management of CD is based on the location, severity, and presenting complications of the disease. Treatment of CD has two goals: to treat acute flare-ups and to maintain remission (Knutson, Greenberg, & Cornau, 2003). Working definitions have been published in regards to CD activity and are helpful for the clinician in determining the severity of the disease and treatment options. CD is categorized into mild to moderate disease, moderate to severe disease, severe-fulminant disease, and remission (Hanauer et al., 2001). The patient with mild to moderate disease is ambulatory and is able to take oral nutrition. A patient with this form of the disease does not

present with fever, abdominal tenderness or masses, obstruction, or weight loss of greater than 10%. Moderate to severe disease includes the patient who has failed treatment for mild to moderate disease or has pronounced symptoms, including significant weight loss, fever, occasional nausea and vomiting, and significant anemia. Severe-fulminant disease is defined as persistent symptoms despite therapy with steroids or presentation of a high fever, persistent vomiting, evidence of obstruction or abscess, and cachexia. Remission is said to occur when the patient is asymptomatic or without extraintestinal complications (Hanauer et al.).

Once the disease category is determined, the clinician can decide on the appropriate therapy. Medical management includes pharmacotherapy and, if needed, surgical intervention. Currently, patients with mild to moderate disease can be treated with an oral amino salicylic acid (5-ASA) formulation such as sulfasalazine. This works well for colonic or ileocolonic disease. Mesalamine, another oral 5-ASA drug, works well for patients with ileitis or ileocolitis because of the higher levels of drug availability in the ileum. One disadvantage to using 5-ASA drugs is that a clinical response may not be seen for 3–4 weeks (Stenson, 1999).

Use of antibiotics is an acceptable form of therapy in mild to moderate CD if 5-ASA drugs are ineffective. Two of the most common antibiotics used in the treatment of CD are ciprofloxacin and metronidazole. Most patients report a clinical improvement with the use of metronidazole in a dosage of 10–20 mg/kg/day (Knutson et al., 2003). Ciprofloxacin 1 g/day is equal to the use of mesalamine and has been effective in achieving clinical remission. The combination of metronidazole and ciprofloxacin has been reported to provide superior results than using either antibiotic alone (Hanauer et al., 2001).

For patients with moderate to severe disease, the use of corticosteroids can be beneficial. Oral prednisone 40–60 mg/day is generally administered for acute flare-ups and is given for 2–3 weeks until improvement is noted; the steroids should then be slowly tapered and discontinued. Use of steroids on a long-term basis should be avoided secondary to the many complications of these drugs. For example, corticosteroids have the potential to cause osteoporosis, cataracts, diabetes, hypertension, and a multitude of unpleasant side effects (McQuaid, 2004).

If a flare-up of the disease occurs with tapering of steroids, a trial of immunomodulatory drugs such as Azathioprine 2–2.5 mg/kg and mercaptopurine (6-MP) can be initiated. Usually, oral steroids are continued for 3–4 months after beginning an immunomodulatory drug because a clinical response may not be seen for about 6 weeks. These drugs have been proven effective in long-term treatment of CD and can provide effective disease management, which often leads to remission (Stenson, 1999). It is important for the clinician to monitor blood counts as a risk for leukopenia may occur with increased dosage of immunomodulatory drugs.

One of the latest treatments available to CD patients is an infusion of infliximab. Infliximab has proven effective and may be an alternative to immunomodulatory drugs and/or steroid treatment. Clinical improvement has been seen in 80% of patients within 4 weeks of therapy and more than 50% achieved remission; however, continued treatments may be necessary to prevent relapse (Hanauer et al., 2001).

Individuals with severe-fulminant disease who continue to have persistent symptoms despite treatment with oral steroids or infliximab, or those who present with high fever, evidence of obstruction or abscess should be hospitalized. Surgical consultation may be indicated for refractory disease, intestinal obstruction, or the formation of an abscess or fistula (Hanauer et al., 2001). Approximately 60% of patients with CD will require surgery. A complete cure of CD is not possible with surgery, and a conservative approach is essential to preserve as much bowel as possible. Many patients who have surgery for small intestine involvement will likely require additional surgeries for recurrence of the disease (Stenson, 1999).

APRN perspective on management

CD is a complex chronic disease that requires collaborative management with a gastroenterologist. Addressing quality of life needs and providing patient education in regards to nutrition, pain relief, cessation of smoking, and medication side effects are just a few ways the APRNs can collaborate in the care of the patient with CD. It is imperative to remember that CD is a lifelong chronic disease condition and the patient should be supported at all levels of the disease. Patients with chronic disorders such as CD can benefit by knowing detailed information about their disease process. Of particular interest to patients are the areas of diagnosis, therapy, and diet (Verma, Tsai, & Giaffer, 2001). The APRN should take time to explain the etiologic theories and current medical management of CD to the patient. This gives the patient an opportunity to express concerns and fears that may arise from the diagnosis of this disorder.

Quality of life issues are of utmost importance to the patient. Individuals with CD may face numerous emotional, social, and financial issues. There is an increased incidence of neuroses and depression in individuals with CD. For persons suffering with CD, social interactions and sexual relationships can be difficult. They often experience a lack of desire to socialize or interact at a deeper level of intimacy. Women often express concerns regarding fertility and pregnancy (Leshem, 2003, p. 248). Financial

problems are also common because of absenteeism from work secondary to disease flare-ups or hospitalizations. The cost of medications might also place a financial burden on some individuals. It is imperative for the APRN to be sensitive to these issues and obtain a thorough history when evaluating a patient with CD. Generally, patient education, relaxation techniques, and low-impact exercise programs may be helpful in reducing stress and increasing quality of life. Patients may also benefit emotionally and socially from a recommendation to a local support group or referral to organizations such as the CCFA (Knutson et al., 2003).

Providing detailed information regarding diet is valuable to the patient. As stated earlier, 85% of patients experience diarrhea. This can be detrimental to the patient in regards to weight loss and malnutrition. Antidiarrheal medication such as loperamide 2–4 mg can help to relieve symptoms; however, this medication should be closely monitored and not given to a patient with active severe colitis because of the risk for toxic megacolon. Before using loperamide, it is essential to rule out an infectious cause of the diarrhea (McQuaid, 2004).

Diet recommendations are dependent upon location and severity of the disease. Overall, people diagnosed with CD should eat a well-balanced diet with as few restrictions as possible. Patients with mainly large intestine involvement may benefit from a high-fiber diet or fiber supplementation. On the other hand, patients with obstructive disease should be placed on a low-fiber and low-fat diet. Vitamin B12 is often needed for patients with ileal involvement or for those who have had an ileal resection (McQuaid, 2004). The APRN can suggest keeping a food diary to note the foods that increase discomfort and those that are well tolerated. Encouraging the patient to eat foods that are well tolerated can help maintain and possibly improve nutritional status. Supporting the patient with nutritional information may have the potential to decrease the risk of exacerbations and prevent overburdening the bowel.

Fluid intake is another important aspect of diet. Because of the high rate of diarrhea, patients may become dehydrated. Depending on the amount of output, the patient should be counseled to drink at least 1–2 L of fluid per day. If the patient continues to experience diarrhea, the APRN should ensure replacement fluid if needed and closely monitor electrolyte values, especially potassium and magnesium.

Pain relief and management of medication regimens and side effects are crucial in the treatment of patients with CD. Because patients with CD may experience chronic pain, the APRN should educate the patient on the distinguishing characteristics of bowel obstruction, which include abdominal distention, fever, and bloody diarrhea. It is important to assess the frequency, location, characteristics, aggravating symptoms, and duration of the patient's pain. Pain is often best controlled by measures that reduce the inflammatory process in the bowel. For example, the use of 5-ASA drugs can help reduce inflammation, thereby reducing pain. Use of narcotics may not be helpful as they may induce megacolon or lead to dependency. Occasionally, tricyclic antidepressants can be useful as an adjunct to pain management even if the patient does not present with signs or symptoms of clinical depression (Stenson, 1999).

It is important for the APRN to remember that medications that reduce inflammation and pain can cause numerous offensive side effects. Corticosteroids may cause side effects such as acne, weight gain, moonfacies, and osteoporosis. Either tapering down the dosage of steroids or changing to an immunomodulator can result in less offensive side effects. If the patient is to remain on steroids, the clinician should consider prescribing a multivitamin with vitamin D and calcium supplements to help prevent osteoporosis. Routine bone density testing should also be done (McQuaid, 2004). Last, the clinician should schedule routine follow-up appointments to ensure therapeutic benefits of treatment. Close monitoring and supportive counseling are the mainstays of CD management.

Conclusions

In review, CD is a chronic IBD that causes considerable morbidity. The etiology of CD remains unclear, and further research is necessary to pinpoint the causative agent(s). Making a definitive diagnosis of this disease can be difficult because of the overlapping symptoms with other gastrointestinal disorders. To aid in a complete and accurate diagnosis, the clinician should review all of the presenting symptoms, physical findings, pertinent laboratory values, and results of radiographic and endoscopic testing. Medical management includes a variety of pharmacological regimens and surgical intervention if needed. Individuals affected by CD face both physical and emotional challenges that can seem overwhelming and frightening. The APRN is in a unique position to help the patient cope with quality of life issues and nutritional needs. Assisting the patient with medication regimens and side effects are especially important. The diligent care of APRNs can assist these patients in leading healthy and productive lives.

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Conflict of interest disclosure

No relationship exists between the author and any commercial entity or product mentioned in this article that might represent a conflict of interest. No inducements have been made by any commercial entity to submit the manuscript for publication.