

A REVIEW of INFLAMMATORY BOWEL DISEASE in CATS and DOGS

Kedi ve Köpeklerdeki Inflammatory Bowel Disease Hakkında Bir Derleme

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SUMMARY

The term inflammatory bowel disease (IBD) in cats and dogs denotes a group of chronic intestinal disorders characterised by diffuse infiltration of the mucosa by various populations of inflammatory cells, including lymphocytes, plasma cells, eosinophils and neutrophils (1,2). Although Giardia or Campylobacter infections can cause a mixed inflammatory cell infiltration in the lamina propria, inflammatory bowel disease describes a chronic disorder in which no definitive causative agent can be identified (3). IBD is well recognised as one of the most common causes of chronic vomiting and diarrhoea in cats and dogs, however, there is very little information about the pathogenesis of IBD in this species (4). The clinical features, natural history and complications of IBD are poorly defined (5). In this review, it has been given some informations about its aetiology, clinical signs, clinical pathology and histopathological findings, diagnosis and treatment.

Key Words: IBD, Chronical intestinal disorder, Diarrhoea, Vomiting.

ÖZET

Kedi ve köpeklerde inflammatory bowel disease (IBD), lenfosit, eozinofil ve nötrofillerin dahil olduğu çeşitli yangı hücreleri tarafından mukozanın yaygın infiltrasyonu ile karakterize olan bir grup kronik bağırsak hastalığını tanımlamaktadır (1,2). Giardia ve Campylobacter infeksiyonları lamina propriyadaki yangısal hücre infiltrasyonuna dahil olmakla beraber, IBD kesin sebebi bilinmeyen kronik bir hastalıktır (3). IBD kedi ve köpekte kronik kusma ve ishalin en yaygın sebeplerinden biri olarak bilinmektedir. Bununla birlikte bu türlerde IBD hakkında sınırlı bilgiler bulunmaktadır (4). Bulgular, hastalığın doğal oluşumu ve komplikasyonları çok iyi tanımlanmamıştır (5). Bu derleme hastalığın etiolojisi, klinik bulguları, klinik patoloji ve histopatolojik bulguları, tanı ve tedavi hakkında bilgi vermektedir.

Anahtar Sözcükler: IBD, Kronik bağırsak hastalığı, İshal, Kusma.

INFLAMMATORY BOWEL DISEASE IN CATS

The cause of IBD in cats is unknown but it is suspected to have an immune-mediated basis (6). Current theories for IBD are based on the suggestion that a chronic antigenic challenge occurs with the subsequent development of a cytopathic immunological response (7).

Other factors which may have a role in IBD in cats include defective immunoregulation of the gut associated lymphoid tissue (GALT), genetic, infectious or parasitic agents, permeability defects or dietary allergies (8,9).

It is generally thought that the pathogenesis of IBD involves hypersensitivity responses to antigens in the bowel lumen or mucosa (7).

In bacterial overgrowth in cats, the most commonly isolated anaerobes were Bacteriodes, Eubacterium and Fusobacterium spp, while Pasteurella spp, were the most common aerobes (10). Increased numbers of bacteria in the small intestine were found to be related to feline IBD (11).

Vomiting is one of the most common clinical signs observed with idiopathic small intestinal IBD in cats (1). In IBD, vomiting is most often recognised as an intermittent occurrence for weeks, months or years. Vomiting episodes usually associated with retching, are non-projectile and may lead to the production of clear fluid, bile or foam. Vomiting of food

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which is either fresh or partially digested is sometimes observed. Blood is rarely present in the vomitus. Vomiting in IBD can occur at variable times after eating. The vomiting and associated non-specific signs may be cyclical in nature (2,9).

The second most common sign observed in feline IBD is diarrhoea. Diarrhoea may be the sole clinical sign or may occur in conjunction with intermittent vomiting. Diarrhoea may be acute or chronic but most cases involve chronic diarrhoea which is often characterised by large quantities of soft-formed, bulky or watery stool. The diarrhoea associated with IBD has a complex pathogenesis. Sometimes, an inflammatory process of the small bowel results in increase of fluid and electrolytes. The accumulated inflammatory cells result in a diffusion barrier, and as a consequence of released Mediators, vilus damage and atrophy can occur. These changes lead to malabsorption of nutrients. Bacterial overgrowth resulting from intestinal hypomotility, malabsorption or partial obstruction may contribute to the diarrhoea (2). The cause of the hypomotility is not clear, but it may result either from a direct effect of mediators such as prostaglandin E₂ (PGE₂) or leukotrienes on smooth muscle function, or an indirect effect of these mediators on the enteric nervous system. Food in the small intestine will be degraded by increased bacteria. Therefore clinical manifestations are frequent defecation and tenesmus with small quantities of pasty stool.

Steatorrhea may be evident and more chronic cases are often accompanied by weight loss and listlessness. Appetite changes in cats with IBD range from an increased appetite to complete anorexia which seems to occur more commonly in cats with IBD during exacerbations of clinical signs. Findings on physical examination of affected cats may vary widely depending on the stage and severity of illness during which the cat is examined. Patients with early or mild disease may appear apparently normal (6,7,12).

Physical changes are not diagnostic, although diffusely thickened and firm intestinal loops may be palpated (2,13). Mesenteric lymphadenopathy is rarely present in idiopathic IBD (1). Non-specific signs of sickness such as dehydration and unkempt appearance may be evi-

dent. Abdominal radiographs of cats with IBD are usually unremarkable (1).

INFLAMMATORY BOWEL DISEASE IN DOGS

The term IBD in dogs refers to a group of chronic gastrointestinal disorders characterised by idiopathic infiltration of the gastrointestinal tract by inflammatory cells. These cellular infiltrates include various populations of lymphocytes, plasma cells, eosinophils and neutrophils present within the lamina propria. Infiltrative lesions may involve stomach, small intestine or colon. Histological forms of IBD include lymphocytic-plasmacytic, eosinophilic and granulomatous (19,20,21). Lymphocytic-plasmacytic infiltrates are the predominant lesion observed in the lamina propria of biopsy specimens from dogs (22). The cause and pathogenesis of IBD in dogs remain unknown. It has been proposed that recruitment of inflammatory cells represents a non-specific immunologically mediated response to various dietary or microbial antigens (7,12). In the dog, several experimental studies have demonstrated that sensitising a dog to dietary antigens (e.g. egg albumin) can produce chronic colitis (23). Chlamydia particles have been observed in the cytoplasm of macrophages of boxer dogs with histiocytic colitis (24). Gluten sensitivity in Irish setter dogs is also well documented and extensively studied. This naturally occurring enteropathy is characterised by partial vilus atrophy, intraepithelial lymphocyte infiltration, and specific biochemical abnormalities (25).

Small intestinal bacterial overgrowth was considered as an underlying cause of lymphocytic-plasmacytic enteritis in the dog (26). Small intestinal bacterial overgrowth was diagnosed by quantitative bacterial culture of duodenal juice samples obtained from dogs that had histological evidence of mild to moderate lymphocytic or eosinophilic infiltrates. Small intestinal bacterial overgrowth associated with lymphocytic-plasmacytic enteritis in dogs was treated with orally administered prednisolone (27). Small intestinal bacterial overgrowth was observed in dogs with enteropathy, and this overgrowth frequently was of the normal flora (28).

It has been suggested that beagles may have small intestinal bacterial overgrowth in the absence of clinical signs with normal gut histology, although an increase in gut permeability was found using sugar absorption tests. Some dogs can have bacterial overgrowth in the proximal portion of the small intestine, which is associated with enhanced intestinal permeability and may not be suspected by clinical examination or routine histological examination of the mucosa (29). It was shown in the dog intestine, that sensitisation to bacterial flora would exacerbate mild bowel inflammation and cause granulomatous inflammation induced by different antigens (30). Dietary changes could modify the intestinal flora and lead to the presence of large numbers of bacteria in the small intestine (10). Small intestinal bacterial overgrowth have been observed in idiopathic inflammatory bowel disease associated with intestinal ulceration in dogs and cats (31). Permeability tests may therefore help detect and assess the severity of mucosal damage in bacterial overgrowth, but an abnormal result needs to be repeated following antibiotic therapy to assess whether such changes are primarily due to an overgrowth of flora (32).

The observed clinical signs vary according to the site of gastrointestinal involvement and the extent of cellular infiltrates, but most frequently include chronic diarrhoea, vomiting, weight loss or alteration in appetite. Mucosal lesions may be visualised endoscopically in dogs and include xerithema, granularity and the presence of erosions or ulcers. Diagnosis requires intestinal mucosal biopsy because there are no radiographic or clinical pathological changes which are pathognomic (7,19).

There are several therapeutic options for treating IBD in dogs. Dietary therapy is often useful and when inadequate by itself, may make drug therapy more likely to be effective. The clinical signs of some dogs with chronic colitis or cats with eosinophilic gastro-enteritis, will resolve if the patients are placed on a controlled diet (33,34). Corticosteroids, azathioprine, azulfidine and metronidazole are useful drugs for treatment of IBD in dogs (12).

CLINICAL PATHOLOGY AND HISTOPATHOLOGICAL FINDINGS IN IBD

In cats and dogs, haematological abnormalities are uncommon in IBD. Routine haematological studies often yield normal results, but may show non-specific changes such as mild normocytic, normochromic anaemia or leukocytosis (1,12). Biochemistry profiles usually yield normal results. Mild increases in serum liver enzymes such as alanine aminotransferase (ALT) and alkaline phosphatase (ALP), hypoalbuminaemia, and hyperglobulinaemia have been observed in some cats (1). Tests for feline leukaemia-virus antigen and feline immunodeficiency-virus antibody are negative in most cats (12).

Inflammatory cells including small lymphocytes and plasma cells with occasional eosinophils infiltrate the mucosa, submucosa, and muscularis mucosa in cats with IBD (6). Disruption of normal architecture, villous atrophy and fibrosis can be observed in the intestine of cats with IBD (2). Despite the presence of significant infiltrative disease, the serosal surface of the intestine usually appears normal at laparotomy (6).

Lesions of lymphoplasmacytic enteritis are graded as mild, moderate or severe on the basis of the degree of cellular infiltrate and the degree of changes in the epithelium, mucosa and villus architecture. A mild grade consists of mild to moderate, diffuse infiltration of lymphocytes and plasma cells with normal epithelium, no fibrosis or oedema of the mucosa, and normal villus structure. A moderate grade consists of moderate, diffuse infiltration of lymphocytes and plasma cells, mild to moderate oedema or fibrosis of the mucosa, slight blunting of villi with irregular crypts. A severe grade consists of severe, diffuse infiltration of lymphocytes and plasma cells, variable epithelial flattening and erosion, moderate to severe oedema and fibrosis, and flattening of villi (14). Sometimes feline lymphocytic-plasmacytic enteritis (LPE) may be difficult to differentiate histologically from lymphoma (15).

The clinical management of cats and dogs with IBD is usually based on a combination of a controlled diet and medication. Dietary

therapy is a very important part of treatment. The ideal diet is highly digestible, low in lactose, moderately low in fat, hypoallergenic, not markedly hypertonic and contains generous doses of potassium, water-soluble and fat-soluble vitamins (16). Diets of high digestibility provide bowel rest and reduce the allergenicity of the diet, by decreasing the amount of dietary protein absorbed intact by the mucosa and the number of bacteria and bacterial products in the bowel. In small bowel disease, it is traditional to use low fibre diets because high dietary fibre content reduces the digestibility of many dietary components (16). Choice of the protein included in the diet should be based on the cat's dietary history. It is best to avoid any proteins the cat has been eating for the last 4-6 months (6). Good nutritional balance and changes in diet which are summarised above reduce the number of antigens presented to the gut-associated lymphoid tissue, minimising the probability of hypersensitivity reactions (9,16).

Corticosteroids are the first line of treatment for feline and canine IBD. Cats and dogs with inflammatory changes characterised as mild to moderate by biopsy, usually have a good response to prednisolone given at 2-4 mg/kg/day. If there is a good response to prednisolone the initial dose is usually decreased until alternate day therapy is achieved. This dose should be maintained for a further three months and if the animal requires further treatment, lower dose therapy should be adequate (9,13).

In severe cases a combination of prednisolone and azathioprine has been used. Azathioprine is an immunosuppressive drug and the recommended dose is 0.3 mg/kg on alternate days (1,2).

Metronidazole administration is often used in during therapy. Metronidazole has an anti-protozoal effect against *Giardia*, and an anti-bacterial activity against anaerobic bacteria in addition to inhibition of cell-mediated immune responses (17,18).

The majority of cases of feline and canine IBD are manageable, but not always curable. Some cases of chronic IBD fail to respond to medical treatment. Failures may be related to reliance on drugs alone for managing the

problem, inadequate client education and non-compliance of owners.

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