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Inflammatory Bowel Disease of Pet Animals

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Abstract: Inflammatory bowel disease is a relatively common chronic disease affecting the intestines of both dogs and cats. In this poorly understood disease in which the cause of which is currently exactly unknown. The lining of the intestines particularly of the colon become inflamed through a process mediated by the patient's immune system. Several specific types of cells may become inflamed through this process. The most common version of inflammatory bowel disease is called lymphocytic-plasmacytic. The eosinophilic type involves the white blood cell known as the eosinophil and it is distinguished by its severity and recalcitrance in the face of treatment. The rarest form involves the class of white bloodcells that are called granulocytes. Luckily, it is rare, as it is notoriously difficult to treat.

Key words: Gastrointestinal Tract · Inflammation · Inflammatory Bowel Disease · Pets

INTRODUCTION

Inflammatory bowel disease is a collective term describing a group of disorders characterized by persistent or recurrent gastrointestinal signs, with histological evidence of intestinal inflammation on the biopsy material. Variations in the histological appearance of the inflammation suggest that idiopathic inflammatory bowel disease is not a single disease entity and nomenclature reflects the predominant cell type present [1]. Lymphocytic-plasmacytic enteritis is the most common form reported, eosinophilic enteritis is less common and granulomatous enteritis is rare. Histiocytic ulcerative colitis is a rare form, most commonly seen in boxer dogs. It is a controversial, ambiguous, condition and much remains to be understood of its aetiopathogenesis, diagnosis and optimal treatment. Numerous studies have now been published on companion animal IBD and our understanding is undoubtedly increasing. However, despite a growing knowledge base much remains to be determined and understood [2].

The disease results when cells involved in inflammation and immune response are called into the lining of the gastrointestinal tract. This infiltration thickens the bowel lining and interferes with absorption and motility (the ability of the bowel to contract and move food). With abnormal ability to contract and abnormal ability to absorb, the bowel's function is disrupted [3]. Chronic vomiting results if the infiltration is in the stomach or higher areas of the small intestine. A watery diarrhea with weight loss results if the infiltration is in the lower small intestine. A mucous diarrhea with fresh blood (colitis) results if the infiltration occurs in the large intestine. Of course, the entire tract from top to bottom may be involved [1].

Dogs develop inflammatory bowel disease, being part of the chronic enteropathies if lasting more than three weeks and are properly defined when there is histological demonstration of mucosal inflammation and all other possible causes of enteritis or infiltrates have been investigated and excluded. Enteritis is classified depending on which predominant cells infiltrate the intestinal wall and where this infiltration takes place [3]. Thus, chronic diseases of the small intestine that can be included among inflammatory bowel disease are lymphocytic-plasmacytic enteritis, eosinophilic enteritis and eosinophilic gastro-enteritis. With regard to the large intestine, four main conditions are recognized as inflammatory bowel disease in dogs are lymphocytic-plasmacytic colitis, eosinophilic colitis, histiocytic ulcerative colitis (mainly Periodic acid-Schiff positive macrophages) and regional granulomatous colitis mainly Periodic acid-Schiff negative macrophages [4].

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The term inflammatory bowel disease is often used interchangeably with other conditions including Chronic Colitis/Colitis, Lymphocytic-plasmacytic Inflammatory Bowel Disease, Regional Enteritis, Granulomatous Enteritis and Spastic Bowel Syndrome. To further confuse matters, Irritable Bowel Syndrome is often confused with the disease, but it is the disease that is caused due to stress [5]. Therefore, the aim of this review is to through the lights on the inflammatory bowel disease in pet animals.

Etiology and Risk Factors: The cause of IBD is somewhat complex and poorly understood. It appears that genetics, diet, intestinal infection and abnormalities of a dog's immune system all play a role. The intestine is responsible for processing large amounts of food and bacterial particles called antigens [4]. Antigens can be recognized by a dog's body as foreign and cause an abnormal allergic (immune-type) response. The end result is that the lining of the intestine is invaded with inflammatory cells and this inflammation interferes with the ability to digest and absorb nutrients. Common antigens in the intestine include proteins and preservatives from the food, parasites, viruses or bacteria and ingested foreign material (toys, garbage, etc). Any of these antigens can start an abnormal immune response but eventually the inflammation continues even when the antigen is no longer present. In most instances, an exact underlying cause cannot be identified and this is called idiopathic (or true) IBD [6].

With the discovery of certain genes that may cause IBD, it has become apparent that there is a hereditary component to IBD. First-degree relatives of parents who have IBD are significantly more likely to also have the disease. However, the majority of parents who have IBD have no family history. So while IBD clearly does run in families, it is not the only factor to be taken into consideration when looking at the possible causes of IBD. The allergic response sets off a chain of events resulting in an excess of eosinophils (cells that try to fight the allergic response) in the body [3]. These eosinophils release four toxic compounds, three of which are found in statistically significant amounts in the stool of IBD patients. This leads some researchers to conclude that an allergic response may have a role in the development of IBD. An emerging area of research is the role that cytokines play in the development of IBD. Cells called T helper cells are a type of white blood cell that are responsible for removing foreign bodies or unhealthy bacteria from the body. In dogs having ulcerative colitis or crohn's disease, there is an imbalance of T cells that may promote inflammation in the intestine [7].

Both crohn's disease and ulcerative colitis result from an inappropriate immune response that occurs in genetically susceptible individuals as the result of a complex interaction among environmental, microbial factors and the intestinal immune system [5]. The inflammatory process leads to the mucosal damage and subsequent disturbance of the epithelial barrier function, resulting in an increased influx of bacteria into the intestinal wall. The onset and reactivation of inflammatory bowel disease triggered by the environmental factors which transiently break the mucosal barrier and alter the balance between the beneficial and pathogenic enteric bacteria [3]. Other environmental factors, which trigger inflammatory bowel disease, include several infectious agents, diet, drugs such as nonsteroidal anti-inflammatory drugs (NSAIDs) and antibiotics, stress and social status. Among above of them, atypical *Mycobacterium*, oral contraceptives and antibiotics could play a role in the pathogenesis of crohn's disease. Genetic factors seem to have a stronger influence in crohn's disease than ulcerative colitis [8].

The basic theory of IBD is an immunologic reaction to some kind of stimulation. This could include an allergy, parasites, bacteria or an immune system problem. However, usually an extensive search for the cause is not made because of expense [4]. A bacterium called Helicobacter is associated with inflammatory bowel disease. While it is not known which is the cause and which is the effect, Helicobacter infection can lead to ulceration and inflammation, compounding the problems of the IBD. Special treatment is necessary for this type of infection [9].

Several factors may be involved, such as GI lymphoid tissue (GALT), permeability defects, genetic, ischemic, biochemical and psychosomatic disorders, infectious and parasitic agents, dietary allergens and adverse drug reactions. IBD may also be immune mediated. The intestinal mucosa has a barrier function and controls exposure of antigens to GALT [10]. The latter can stimulate protective immune responses against pathogens, while remaining tolerant of harmless environmental antigens (e.g., commensal, protozoa, virus, fungi, bacteria and food). Defective immunoregulation of GALT results in exposure and adverse reaction to

antigens that normally would not evoke such a response. Although dietary allergy is an unlikely cause of IBD (except in eosinophilic gastroenteritis), it may contribute to increased mucosal permeability and food sensitivity [11].

Types of Inflammatory Bowel Disease

Lymphocytic-Plasmacytic Enteritis: This is the most common form of IBD. This disease is due to an excessive accumulation of two types of white blood cells, lymphocytes and plasma cells, in the lining of the gastrointestinal tract especially lamina propria. Excessive protein loss from the blood stream into the intestines is seen in very severe cases and is termed a protein-losing enteropathy [11]. If inflammation is persistent and untreated, fibrosis (scar tissue) can result causing irreversible tissue damage. Prognosis depends on the severity of the inflammation, presence of fibrosis, body condition and response to therapy. Severe lymphocytic-plasmacytic enteritis may be a premalignant lesion, meaning that cancer (specifically lymphoma) development may occur at a later date [12].

Lymphocytic-plasmacytic enteritis has been associated with giardiasis, food allergy and overgrowth of intestinal bacteria. Lymphocytes and plasma cells are the target cells seen on biopsy. Certain breeds are predisposed, suggesting a genetic influence. They are the Basenji, Soft Coated Wheaten Terrier, German Shepherd Dog and Chinese Shar-Pei. In the Basenji, the disease is known to be related to an autoimmune disorder [10]. While signs can show up in younger dogs, most dogs are middle-aged when diarrhea starts. Lymphocytic-plasmacytic enterocolitis produces a small bowel type of diarrhea. Vomiting is common. Involvement of the colon produces signs of colitis. This is an illness for which the realistic goal is control, not cure. Hypoallergenic diets bring about partial or complete resolution of symptoms in some dogs. Antibiotics are used to treat bacterial overgrowth and giardiasis. Immunosuppressant drugs such as azathioprine and prednisone are used if other treatments are not successful [13].

Neutrophilic Enterocolitis: This inflammatory bowel disease produces acute and chronic large bowel diarrhea. The inflammatory infiltrate is composed of mature white cells, neutrophils, in the tissues and blood vessels. Diagnosis is based on a colon biopsy and stool cultures to exclude bacterial infection. Antibiotics and corticosteroids are used to control the disease [14].

Eosinophilic Enterocolitis: This is a relatively uncommon form of inflammatory bowel disease in dogs. On biopsy, eosinophils may be found in the stomach, small intestine, or colon and the eosinophil count in the blood may be elevated [10]. Some cases are thought to be associated with food allergy or the tissue migration of roundworms and hookworms. High-dose corticosteroids are used to treat this disease. They are tapered off as symptoms diminish. The dog should be tested for intestinal parasites and placed on a hypoallergenic diet [15]. This appears to be an allergic reaction to a dietary protein. A strict elimination diet in conjunction with medical therapy is often needed to resolve the signs. Prognosis is variable since some animals are unusually sensitive to many foods and are difficult to control [12].

Granulomatous (Regional) Enteritis: This is a rare disease, similar to Crohn's disease in humans. There is thickening and narrowing of the terminal small bowel due to inflammation of surrounding fat and lymph nodes. Macrophages, which are cells found in tissues that fight infections, are found on biopsy of the colon [3]. The diarrhea is the chronic large bowel type, containing mucus and blood. Biopsies are processed with special stains to exclude histoplasmosis and intestinal tuberculosis. The use of corticosteroids and immunosuppressive drugs reduce inflammation and scarring. A course of metronidazole may be of benefit. A strictured bowel requires surgery [16].

Epidemiology: Inflammatory bowel disease can occur in pets of any age, but tends to affect pets in their middle to later years of life (8 years of age and older) [17]. There are some clear trends in the epidemiology of IBD that may point to one or more environmental causes. IBD tends to occur most often in developed countries and amongst those with higher socioeconomic status [11]. IBD also tends to occur more often in the urban areas of developed countries. These factors have led researchers to think that there may be some connection between IBD and the lifestyles or environment of people living in developed countries, although no one knows yet what this could be [10].

Pathogenesis: In pet animals, the development of IBD is thought to originate as a consequence of a deregulation of mucosal immunity in predisposed animals. The loss of tolerance to antigens (food and intestinal bacteria) is one of the most studied mechanisms that could justify the development of chronic intestinal inflammation [18].

The immune mediated basis of the disease can be inferred by the response to the administration of immune modulator drugs; the presence of increased IgE positive cells in diseased dogs compared to healthy dogs is a further aspect that also suggests the involvement of hypersensitivity reactions in the pathogenesis of canine IBD [19], as well as the increased concentration of eosinophils and mast cells in many dogs with EGE [13]. Interruption of the mucosal barrier, independently of the primary cause (bacterial, chemical, etc.), can also lead to further antigen exposure, allowing the process to become chronic and is enforced by decreased apoptosis of lymphocytes, as demonstrated in dogs with IBD compared to control dogs [20]. Homeostasis inside the digestive tract is maintained by the equilibrium between the reactions to pathogens and to commensal bacteria or other inoffensive luminal antigens (tolerance) that are mediated by different molecules [14].

The presence of mucosal tolerance to harmless antigens is very important, because depending on its absence the subsequent inflammatory response can be exaggerated and even detrimental. Such tolerance is probably based on the fact that the antigen is presented or not, contextually to other danger signals [18]. The difference between tolerance and reaction is also based on pattern recognition receptors (PRRs) [21], which are able to recognize micro-flora according to their pathogen-associated molecular patterns or microbe-associated molecular patterns [22]. Similar to humans, the study of IBD in affected dogs has led to the hypothesis that genetic factors and enteric bacteria can play a pivotal role in the pathogenesis of these disorders, owing to the abnormal intestinal response to commensal micro-flora [23]. Once stimulated, PRRs such as Toll-like receptors (TLRs) start their pro-inflammatory activity and a recent study showed that three TLRs stimulated by bacteria are up-regulated in dogs with IBD [24].

These results are similar to those following the activation of TLR4 which has been demonstrated in humans suffering from IBD [25]. In these patients, both genetic predisposition and environmental factors are considered important elements in the development of the disease. Moreover, as already well known in humans a recent study showed that in IBD dogs, small intestinal bacteria are different from those found in healthy dogs, (strengthening the idea of a correlation between microflora and IBD [26]. Thus, even in small animals and similar to that in man, intestinal lymphocyte subset distribution and major histocompatibility complex class II antigens, as well as cytokine gene expression and other markers, have yielded interesting and sometimes overlapping results [27]. For instance, one study showed that dogs with IBD display a larger number of IgE positive cells than healthy dogs, in a manner similar to that for interleukin 4 (IL-4) expressions in man with IBD [28]. In addition, the modulation of the expression of intestinal lamina propria lymphocytes P-glycoprotein seems to play a similar role in both human and dog IBD [5].

In fact, in IBD patients scarcely responsive to steroid treatment, P-glycoptrotein is highly expressed and in dogs showing a good response to treatment this protein is modestly represented [11]. As previously documented in humans, in IBD dogs the investigation of specific subsets of cell populations led to the demonstration of decreased numbers of mast cells (MCs) and of an increase in both CD3+ cells and IgG+ plasma cells. In veterinary medicine, encouraging results also originate from the study of nuclear receptors such as peroxisome proliferators-associated receptor á (PPARá) and especially of NR target genes such as multi-drug-resistancegene-1, multiple drug resistance-associated proteins, cytochrome P450 and phenol sulfating phenol sulfo-transferase [29].

Pathophysiology: There is an involvement of hypersensitivity reactions to antigens (e.g., food, bacteria, mucus, epithelial cells) in the intestinal lumen or mucosa. More than one type of hypersensitivity reaction is involved in IBD [30]. For example, type I hypersensitivity is involved in eosinophilic gastroenteritis, whereas type IV hypersensitivity is likely involved in granulomatous enteritis. The hypersensitivity reaction incites the involvement of inflammatory cells, resulting in mucosal inflammation that impairs the mucosal barrier, in turn facilitating increased intestinal permeability to additional antigens. Persistent inflammation may result in fibrosis [12].

The proposed pathophysiology of IBD questions whether the disease is due either to an appropriate or excessive response to a foreign antigen or an inappropriate response to a normal antigen. Possible antigens include bacterial, dietary and/or parasitic antigens [23]. Increased GI tract permeability, which enables larger peptides to access and stimulate the immune system, may also play a role. It is unclear whether the increased GI tract permeability is a cause or an effect of IBD, or possibly both. Presently the role of cytokines and immune modulation is being investigated, as well as possible roles of genetic predisposition via the major histocompatibility complex and IgA deficiency (failure to bind antigens in the GI lumen) [30].

Clinical Signs and Symptoms: Clinical signs vary, depending upon the location of the immune response. Pets with disease of the stomach and upper intestinal tract (small intestines) typically have vomiting, whereas those with immune lesions in their lower intestinal tract (colon) usually have diarrhea [20]. The diarrhea causes loose feces that may or may not contain mucus and variable amounts of bright red blood. Some pets with IBD manifest as chronic weight loss. It's important for owners to understand that pets can have any combination of vomiting, diarrhea and weight loss, or may only have 1 or 2 signs [31]. Clinical manifestations of IBD in dogs are numerous and nonspecific; the most common clinical signs are weight loss, persistent or recurrent vomiting and/or diarrhea, frequently associated with symptoms that are an expression of eventual complications, such as ascites (if hypo-albuminemia is present) or pallor of mucous membranes in the case of chronic gastrointestinal bleeding [32].

Stomach inflammation (called gastritis) typically causes loss of appetite and vomiting. Vomit may contain undigested food, partially digested food, clear or brownish liquid or even a small amount of blood. Inflammation of the small intestine (called enteritis) often causes vomiting, diarrhea and weight loss. Vomit may be clear liquid, yellow or green bile, foam or food [30]. Diarrhea is usually soft to watery, large volume and occurs one to three times daily. Affected dogs will frequently exhibit weight loss, lethargy and general unthriftiness. Colon inflammation (called colitis) most often causes diarrhea. The diarrhea is usually of small volume and very frequent (up to ten or more times per day). Dogs with colitis often strain to defecate and have blood or mucus in the stool. These dogs usually remain active, have a healthy appetite and do not lose weight [15].

The signs seen with IBD vary with the severity of the disease and the location affected. Animals with gastrointestinal (stomach and small intestine) IBD usually present with chronic vomiting, weight loss, diarrhea. Those with large intestinal IBD present with diarrhea with or without blood and mucous present, straining to defecate, increased urgency to defecate and occasionally vomiting [32]. The cardinal symptom of ulcerative colitis is bloody diarrhea, whereas patients with Crohn's disease usually present with non-bloody diarrhea. Other associated symptoms include colicky abdominal pain and tenesmus. As the inflammation increases, systemic symptoms including low-grade fever, malaise and anorexia develop. A severe presentation of ulcerative colitis carries a high mortality and morbidity. Symptoms of Crohn's disease are more heterogeneous, but typically include abdominal pain, diarrhea and weight loss [5].

Systemic symptoms are more common with Crohn's disease than ulcerative colitis. Crohn's disease may cause intestinal obstruction due to strictures, fistulae or abscesses. Both types of inflammatory bowel disease are associated with an increased risk of colonic carcinoma. The clinical course of inflammatory bowel disease is marked by exacerbation and remission. Weight loss is more common in Crohn's disease than in ulcerative colitis because of the associated malabsorption [3]. Both ulcerative colitis and Crohn's disease are associated with extra intestinal manifestations such as delayed growth and sexual maturation in children mucocutaneous lesions arthralgia and arthritis hepatobiliary disease ophthalmologic complications renal disease. Clinical signs may come and go and sometimes the entire gastrointestinal tract is affected. A dog may also lose his appetite, seem melancholy, run a fever or lose weight [14, 18].

IBD is probably the most common cause of chronic intestinal clinical signs and would be the likely condition to pursue first. Chronic vomiting is a common sign if the inflammation is affecting a dog's stomach and/or upper intestine. Long-term diarrhea that may contain blood or mucus may be due to inflammation of the colon [15, 22]. Occasional vomiting and diarrhea that occur over weeks to years are the most common signs of IBD in dogs. These symptoms may be responsive to brief changes in diet or short courses of antibiotics, but eventually return. The signs are usually slowly progressive but can be severe and sudden in onset in advanced stages of the disease. A combination of symptoms is most common in dogs with IBD as the stomach, small intestine and colon may be involved [31].

Diagnosis

History Taking: The history of long-standing diarrhea and/or vomiting, weight loss, increased mucous in the stool and possibly blood in the stool would lead a veterinarian to consider IBD as a possible cause [14, 17, 21].

Physical Examination: The dog may appear thin on physical examination. In some animals, veterinarians may palpate (feel) thickened intestines. The physical examination can be normal. Abnormal findings may include weight loss, cachexia, "gassy" or thickened bowel loops (the latter primarily in cats) and generalized poor condition [12].

Endoscopic Examination: Endoscopy involves the use of a skinny tubular instrument (an endoscope) which has a tiny fiber optic or video camera at the end [4]. The endoscope is inserted down the throat, into the stomach and into the small intestine where small pinches of tissue are obtained via tiny biting forceps. If the large intestine is to be viewed, a series of enemas is needed prior to the procedure as well as a relatively long fast. The endoscope is inserted rectally and again tissue samples are harvested [12]. The advantage of this procedure over surgery is that it is not as invasive as surgery. Patients typically go home the same day. Disadvantages are expense (often referral to a specialist is necessary) and the fact that the rest of the abdomen cannot be viewed. Growths that are seen via endoscopy cannot be removed at that time and a second procedure typically must be planned whereas, if surgical exploration is used to obtain the biopsy, any growths can also be excised at that time [33].

Laboratory Examination: In most cases, the chemistry panel of a dog with inflammatory bowel disease is normal. If the inflammation of the intestines is severe, the neighboring liver and pancreas may also become inflamed. This results in an elevation of liver enzymes and/or pancreatic lipase immunoreactivity [25, 28]. Lipase is produced by the pancreas and if the pancreas is inflamed the values are increased. There may be a decreased amount of protein in the blood and if the vomiting is significant the electrolytes (especially potassium) may be at abnormal levels. In most cases, the complete blood count (CBC) is normal. Some animals will demonstrate an increase in the number of eosinophils in the blood. Blood Panel and Urinalysis is used to rule out other problems, such as liver or kidney disease. These tests are usually normal, but they may show a general inflammatory response in the blood, or a loss of blood proteins albumin (an important blood protein) may leak from the intestine into the bowel [16].

Radiography (X-Rays) and Ultrasound: There is no consistent radiological finding in dogs with inflammatory bowel disease. The intestines may appear thickened and there may be more gas than normal in the intestines, but these signs can occur in many conditions. Radiographs (X-rays) are to rule out growths in the abdomen or tumors [34].

Biopsy: The only definitive way to diagnose inflammatory bowel disease is through a biopsy. The biopsy will demonstrate increased numbers of inflammatory cells in the intestinal wall. The types of cells which are present will denote what type of inflammatory bowel disease is present. Biopsies can be obtained through use of an endoscope or exploratory surgery [13, 14]. The intestines may appear normal to the naked eye, but microscopically the changes can be seen. In other cases, the lesions of the gastrointestinal tract are quite apparent. Inflammatory bowel disease is easily diagnosed by endoscopic biopsy. In this procedure, a sedative or light anesthetic is given to the pet. The doctor introduces a tube called an endoscope into the pet's gastrointestinal tract and removes tiny pieces of tissue for a microscopic examination [29]. Surgical exploration may also be used to obtain samples. The recovery afterwards is typically a couple of days though some patients bounce back immediately. With surgery, other organs can also be sampled and abnormal sections of tissue can be removed. Surgery tends to be more expensive than endoscopy but this depends on the recovery period. Tissue samples obtained are processed by a laboratory and analyzed. The infiltration of inflammatory cells is graded as mild, moderate, or severe and the type of cells involved in the inflammation are identified [35].

Broad Spectrum Deworming: Fecal testing and broad spectrum deworming is often performed at this time to rule out parasitism as a cause of the chronic inflammation. If the patient is young or has been housed with multiple animals, more obscure parasites may be afoot and often special fecal testing is submitted to the laboratory for PCR testing. Typical organisms screened by this kind of testing include Giardia, Cryptosporidium, Salmonella, Tritrichomonas and Clostridium perfringens. Younger dogs are also tested for Salmonella and Campylobacter [35]. Since in dogs the diagnosis of IBD is by exclusion, it is obvious that many tests performed during the diagnostic titer (for example blood, urine and fecal examinations) are necessary to exclude other causes of inflammation and are rarely specific for IBD, thus, not overestimating the incidence of such a diagnosis [36].

After having excluded the most common causes of chronic enteropathies, intestinal biopsies, obtained surgically or endoscopically depending on circumstances (endoscopy is less invasive, but sampling is limited in terms of site of execution and/or of dimension), can allow the diagnosis of IBD. However, it is important to stress that biopsy samples are not unequivocally interpretable, even though recent work helped in clarifying such interpretation by providing a histopathological score for mucosal changes in dogs [37]. In dogs, a trypsin-like immunoreactivity (TLI) test would be performed to rule

out pancreatic exocrine insufficiency, a deficiency of digestive enzymes. Typically this test is run in combination with a vitamin B-12 level and a folate level. When intestinal bacterial populations alter, folate levels rise and B-12 levels drop. Antibiotics are likely indicated in this situation as well as vitamin B12 injections [35].

Differential Diagnosis: Diseases that can be confused with IBD include parasites (usually easily diagnosed and treated) and food allergy which is actually very rare in pets. Despite what some veterinarians say, no pet should simply be diagnosed with a sensitive stomach. There are too many pets suffered and die with IBD when owners were told that their breeds of pets had sensitive stomachs and were improperly treated [35]. Other causes of diarrhea and or cellular infiltrates must be ruled out. Therefore, in a complete work-up, a fecal exam would be performed to rule out parasites such as *Giardia, Crytospoidium* and *Trichomona* [35]. Bacterial cultures would be obtained to rule out e.g., Salmonella and Campylobacter and further blood tests to rule out other concurrent diseases such as liver disease would be conducted [15].

In dogs, a condition called Addison's disease is able to create chronic waxing and waning intestinal disease, among numerous other possible manifestations. This condition, more correctly termed hypoadrenocorticism, is often referred to as the Great Imitator as it can mimic many other diseases besides IBD. This condition revolves around a deficiency in cortisol, a crucial hormone in adaptation to stress [3, 7]. Treatment is relatively straightforward so it is important not to forget to screen for this condition. This is done with a screening test called baseline cortisol blood level or with a longer test called an ACTH stimulation test, which is a more definitive test that requires an hour or two in the hospital [16].

Treatment: A food trial using hypoallergenic diets is usually one of the first steps in the initial treatment and is used to verify the diagnosis. The key is to use a protein source and carbohydrate source the animal has never eaten before, such as duck and potato, or to use a diet consisting of hydrolyzed proteins. The dog must eat nothing else, including treats. If a diet change will help, it will generally start to do so in two weeks [38]. If a hypoallergenic diet does not improve the condition, other diets may be tried. Diets low in fats is generally better tolerated in dogs with IBD. Some dogs do better on a low fiber diet, while others, especially those with disease of the colon, may tend to do better on diets higher in fiber. Homemade diets are sometimes used; however, they must be developed by a veterinary nutritionist to assure they are complete and balanced. Multiple diets may have to be tried before one sees improvement in the dog's condition. This takes a lot of patience on the part of the owner [9].

Medication: The cornerstone of treatment for IBD is suppressing the inflammation. In milder cases of large intestinal IBD, the immunomodulating properties of metronidazole might be adequate for control but usually prednisone or its cousin prednisolone is needed. Prednisolone will work on IBD in any area of the intestinal tract. In more severe cases, stronger immune suppression is needed (as with cyclosporine, chlorambucil, or azathioprine) [39]. Higher doses are usually used in treatment at first and tapered down after control of symptoms has been gained [40].

Some animals are able to eventually discontinue treatment or only require treatment during flare-ups. Others require some medication at all times. Long-term use of prednisone should be accompanied by appropriate periodic monitoring tests due to the immune suppressive nature of this treatment [14]. Corticosteroids (like steroids, cortisone and prednisolone) are the mainstay of therapy for IBD. Corticosteroids inhibit the inflammatory process and reduce the inflammation within the intestine. As steroids have potentially severe side effects, the goal of therapy is to gradually adjust the dose to the lowest possible amount that controls symptoms. Over time, many dogs can be weaned off steroids completely and be maintained on diet alone. Treatments for IBD are aimed at decreasing inflammation in the intestines and preventing symptoms through a combination of suppressing the immune system, slowing down intestinal motility coating and protecting the lining of the intestine killing bacteria and limiting specific diet ingredients that may cause irritation [9].

The administration of immunosuppressives is often required for patients who fail the dietary trials described, for patients with moderate to severe infiltrates and for patients that develop a condition called hypoproteinemia, a deficiency of protein in the blood due to protein leakage from the gut [34]. Oral prednisone alone is then initial drug of choice. It is usually administered at an immunosuppressive dose for two to three weeks, then decreased by 50 percent every two to three weeks and eventually continued on an alternate day basis for two to three months. The antibiotic tylosin is frequently administered at the same time. If clinical response is poor or if the adverse effects of corticosteroids are troublesome, further immunosuppression can be achieved by adding azathioprine (Imuran) to the regimen

[17]. In dogs, azathioprine is usually given every five days and then on a schedule that alternates it with prednisone. Cats are more sensitive to azathioprine and require a reduced dose. The veterinarian will want to monitor the pet's complete blood count every two to four weeks when azathioprine is given. Another drug, metronidazole, can also be used in conjunction with steroids and has effects on bacteria and the immune system [41].

Successful treatment is accompanied by a decrease in diarrhea and vomiting followed by weight gain and an increase in plasma proteins. Once a patient has had from two to three months of remission of clinical signs it may be possible to gradually withdraw the immunosuppressive therapy [38]. If signs recur, however, daily medication is continued until they resolve, then the medication is gradually reduced. In patients that respond poorly to therapy or go into relapse after an initial response, the veterinarian may want to reassess the patient and consider taking additional intestinal biopsies to rule out the presence of alimentary lymphosarcoma, a malignant tumor of the lymphoid tissue. There has been progress in developing new drugs to treat inflammatory bowel disease and related problems in humans, but unfortunately few of these new drugs are available or practical for use in dogs and cats [42].

Cyclosporine, the extraordinary immunosuppressant that made organ transplantation a lifesaver for thousands of humans, has had moderate success as a treatment for human bowel disease (in this case, Crohn's disease). The drug has serious side effects and is costly, factors that make its use in pets unlikely [37]. The antihypertensive drug clonidine has been used with success in humans, but there is no report of its use in dogs or cats. Finally, the use of the acid found in fish oil for skin diseases in dogs and cats has led to the speculation that fish oil might also benefit pets with inflammatory bowel disease. Although there is a fish oil drug available for humans with inflammatory bowel disease, the drug has not been evaluated in dogs or cats [14].

Prognosis: IBD can be controlled, but not cured. All patients with IBD will require a strict diet and possibly anti-inflammatory medication to manage their disease. Most dogs with IBD do well for many years while others require alterations in therapy every few months to treat flare-ups and recurrent symptoms. Unfortunately, a few dogs will fail to respond to treatment and some severe forms of IBD can progress to intestinal cancer [12, 15]. The owner of a dog or cat with lymphoplasmacytic enteritis should understand that the prognosis for recovery depends on the severity of the condition. Prognosis is also quite variable with many patients requiring prolonged treatment with glucocorticoid and diet modification. In the absence of accurate criteria for predicting response, veterinarians tend to give a guarded prognosis when treating the disease [43].

Control and Prevention: All patients with IBD will require a strict diet and possibly anti-inflammatory medication to manage their disease. Most dogs with IBD do well for many years while others require alterations in therapy every few months to treat flare-ups and recurrent symptoms. Unfortunately, a few dogs will fail to respond to treatment and some severe forms of IBD can progress to intestinal cancer [4, 44].

CONCLUSION

Inflammatory bowel disease is one of the disease that affecting gastrointestinal system of small animals including dogs and cats. It is caused due to genetics, diet, intestinal infection, abnormalities and various other causing factors. It has various types and show many clinical signs including vomiting, diarrhea, ascites, chronic gastrointestinal bleeding , loss of appetite, fever, malaise and anorexia. It is somewhat difficult to treat bthe disease but correcting management of dogs is very important.

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