Immune Mediated Musculoskeletal Disorders of Dogs: An Overview

R.K. Jadhav[1*], S.K. Singh[1], A.A. Dar[1], R. Tiwari[2], M.C. Sharma[1]

[1]*Division of Medicine, Indian Veterinary Research Institute, Izatnagar-243 122*
[2]*Division of Extension Education, Indian Veterinary Research Institute, Izatnagar-243 122*

Abstract

Immune mediated musculoskeletal diseases are important diseases of dogs which occur due to failure of immunoregulation or to an abnormal immune response. As clinical signs of these disorders overlap with numerous other syndromes of musculoskeletal system, the confirmative diagnosis is difficult. Glucocorticoids are the basis of therapy with adjunct therapy of cytotoxic drugs, chrysotherapy which require continuous monitoring of patient. Generally there is no curative treatment in most of the disorders due to recurrence of disease after withdrawal of treatment.

Keywords: Canine, Immune mediated diseases, Musculoskeletal system

Introduction

Immune system operates as a surveillance and defense system of the animal body. It is programmed to work for the good will of the body by fighting both intracellular as well as extracellular foreign pathogens. Immune system seldom acts abnormally against the individual's body which might culminate in deleterious consequences. An individual can concede immune mediated disease either by the failure of immune-regulation or by mounting an abnormal immune response against the self body components. An abnormal consequence of the immune functions for instance autoimmunity, hypersensitivity, immunodeficiency, immunosuppression or any combination of these may culminate in immune mediated diseases (Tizard, 2009). Immune mediated musculoskeletal diseases are major ailments caused by immune system dysfunction which are responsible for abnormalities of skeleton and ambulation. They have complex clinical presentation which makes diagnosis a challenging task. The article aims to review the clinical pattern, advances in diagnostics and management of important immune mediated musculoskeletal diseases occurring commonly in dogs.

Immune mediated musculoskeletal diseases

Immune mediated arthritides/polyarthritis

Immune mediated arthritis is comprised of a group of inflammatory but non-infectious affections of joints which responds to immunosuppressive therapy (Kohn, 2007). Inflammation is either due to persistence of an antigenic material in the synovium of affected joints, possibly as sequel to previous infection, or to deposition of immune complexes in synovium, derived from inflammatory lesions elsewhere in the body. Immune mediated arthritis is typically a polyarthritis involving more than one joint. It is common in dogs and cats and is characterized by the major involvement of joints of locomotion. Idiopathic polyarthritis, systemic lupus erythematous (SLE) associated polyarthritis, drug induced polyarthritis, polyarthritis of Grey hounds, rheumatoid arthritis are some of the examples of polyarthritis most commonly reported in dogs (Thompson, 2005, Day and Bennett, 2008). Immune mediated arthritides has been categorized in to erosive and non-erosive arthritis based on radiographic changes observed in joints and bone (Bennett, 2005).

1. Erosive arthritis:

Erosive arthritis constitutes immunological process that occurs in the joint itself with acceleration of

*Corresponding author: R.K. Jadhav
Address: Indian Veterinary Research Institute, Izatnagar-243 122
E-mail address: jadhavrk11@gmail.com

pannus formation ultimately terminating in development of erosions of the margins of articular cartilage, instability or luxation of joints, or fusion of low-motion joints. Rheumatoid arthritis and Polyarthritis of Grey Hounds are important erosive arthritides frequently reported in dogs.

1. a. Rheumatoid arthritis (R.A.)

It is the most common type of canine erosive polyarthritis which typically affects small & toy breeds irrespective of sex & age (Tizard, 2009). It is a potentially deforming & crippling idiopathic, symmetrical polyarthritis of dogs & cats basically similar to human counterpart. It is mostly prevalent in small and toy breeds of dogs with no sex or age predilection (Thompson, 2005). Clinically disease is characterized by episodes of anorexia, depression & fever with generalized or shifting lameness associated with development of swelling around affected joints and eventual erosive changes in joints. It has progressive course with involvement of multiple joints (tarsal, carpal & phalangeal joints) in advanced stage of the disease which are persistently swollen & painful. Progression of disease eventually results in destruction of articular cartilage & bone. With progression of inflammation there is swelling and proliferation of synovia with outgrowths of fibrous vascular tissues (pannus) extending into the joint cavities. Protease released from panuus produces 'punched out' erosions of articular cartilage and destruction of adjacent bones (Bennett, 1987a). Radiography reveals soft tissue swellings followed by loss of bone density, collapse of the joint space, joint luxation, fibrous or bony ankylosis in advanced disease.

Various infectious agents have been implicated for R.A. but none have direct involvement. Indirect involvements through generation of immune complexes or induction of autoimmunity by molecular mimicry are possible mechanisms (Thompson, 2005). Irrespective of etiology, the deposition of immune complexes in articular structures is central to the pathology followed by complement activation terminating in joint tissue injury. The autoantigen involved in R.A. is still not well defined but three major autoantigens, viz., Rheumatoid Factor (RF), collagen and glycosaminoglycans may be implicated in the development of disease (Thompson, 2005). Rheumatoid Factors are the autoantibodies of IgM, IgG and IgA subclass directed

against altered host IgG (Tizard, 2009). These can be detected in synovial fluid & sometimes in serum of the affected dogs. RF's can be also detected in dogs with systemic lupus erythematosus (SLE) and other diseases involving extensive immune complex generation. Serum anti-type II collagen antibodies determined by ELISA have been demonstrated in R.A. positive dogs with correlation between levels of anti-collagen type II antibodies and total IgG in the immune complexes (Bari *et al.*, 1989). Antigens of canine distemper have been demonstrated in synovial fluid of dogs with R.A. which suggest possible role of natural infection or vaccination in R.A. (Bell *et al.*, 1991). The diagnostic criteria's for R.A. in dog are adapted from those defined for human by American Rheumatism Association (Thompson, 2005, Day and Bennett, 2008). In dogs these includes, stiffness, pain on manipulation of at least one joint, signs of arthritis for at least 3 months, periarticular soft tissue swelling, typical radiographic changes, subchondral bone destruction, irregularity of the articular surface or punched out erosions, demineralization of the epiphysis, calcification of soft tissue around joint, changes in joint space, finally extensive bone destruction with gross joint deformity, inflammatory synovial fluid, characteristic symmetrical deformations of the distal joints, detection of rheumatoid factor in serum, characteristic histopathological changes in synovial membrane, and extra articular symptoms (tendosynovitis, lymphadenopathy). The presence of at least 5 of above criteria suggests disease while dogs positive for 7 or more criteria are declared positive for rheumatoid arthritis. Radiography and detection of RF in synovial fluid or sometimes in serum is also helpful in diagnosis (Bennett, 2005). The synovial effusion contains large number of polymorphonuclear cells and there is massive infiltration of lymphocytes in synovial membrane with formation of germinal centers (Bennett, 1987a, b, Newton *et al.*, 1976). Increased levels of matrix metalloproteinases 9 with high gelatinolytic activity in synovial fluid has been reported in dogs with R.A. but its significance in non-erosive arthritis is still unknown (Coughlan *et al.*, 1998).

Treatment commonly started with Non Steroidal Anti-inflammatory Drugs (NSAIDs) & antibiotic particularly Doxycycline until the availability of confirmative diagnosis (Kohn, 2007). Treatment of R.A. with drugs is likely to be disappointing and

disease carries poor prognosis (Day and Bennett, 2008). After ruling out infectious etiology & diagnostic confirmation of disease, treatment should be sidetracked to immunosuppressive drugs like corticosteroids e.g. Prednisone, Prednisolone at 2-4 mg/kg PO orally in divided doses for at least 2 weeks with gradual tapering of the dose over next 6-8 weeks with improvement in clinical signs. But use of corticosteroids is controversial as it delays healing and known to promote articular degeneration (Gorman and Werner, 1986b). If corticosteroid treatment fails to contain relapse then regimen should be shifted to cytotoxic drugs like Cyclophosphamide at 1.5-2.5 mg/kg orally for 4 consecutive days every week for 2-4 months with low dose prednisolone (0.25-0.5 mg/kg) daily to control pain. Prolonged therapy with cyclophosphamide causes sterile hemorrhagic cystitis as well as bone marrow suppression, so monitoring of hematological parameters as well as regular examination of urine at interval of 7-14 days should be done to rule out drug toxicity (Peterson *et al.*, 1992; Day and Bennett, 2008). Use of gold preparations (chrysotherapy) which have been categorized as slow-acting anti-rheumatic drugs (SAARD) like aurothiomalate and auranofine has been limited by high cost and adverse effects on different organ systems (Kohn, 2007, Day and Bennett, 2008). Surgical arthrodesis has been indicated in advanced cases of R.A. to restore the joint mobility (Gorman and Werner, 1986b). In human cases of R.A. immunomodulatory therapies that either induce or block cytokines have been used like monoclonal antibodies to TNF-α (Infliximab), CD4, thymocytes or IL-2R have shown significant anti-inflammatory activity along with inhibition of matrix metalloproteinase production (Ferraro-Peyret *et al.*, 2004, Chung *et al.*, 2007). But these anti-cytokine therapies are not developed for canine R.A to the date.

1. b. Polyarthritis of Greyhounds

An erosive polyarthritis has been described in Greyhounds in Australia, U.K. and USA. It affects both sexes and characterized by mild to severe lameness, joint swelling affecting the gait due to involvement of limb joints (Thompson, 2005). No infectious agent has been confirmed yet for polyarthritis of Greyhounds. It causes a non-suppurative inflammation of synovium frequently with concurrent destruction of articular cartilage in limb joints (Huxtable and Davis, 1976).

2. Non-erosive arthritis:

The primary disease is located somewhere else in the body and products of immune process are delivered to the capillary bed of synovium of affected joints. Here the primary disease may be transient, cyclic, or responsive to treatment, and is not centered in joint. So, the products of immune response that initiates the synovitis can be cleared periodically or permanently from joint. Thus, there is no chronic stimulation of pannus or destruction of articular surfaces (Gorman and Werner, 1986b, Thompson, 2005). Non-erosive arthritis includes idiopathic polyarthritis, drug-induced arthritis, polyarthritis/polymyositis syndrome, lymphocytic /plasmacytic arthritis and Systemic Lupus Erythematosus (SLE).

2. a. Idiopathic polyarthritis (IPA)

It is by far the most common of all the immune-mediated arthropathies in dog. The "idiopathic" type is again categorized into 4 subcategories (Bennett, 1987c, Bennett, 2005, Kohn 2007). Type I (uncomplicated) IPA accounts for approximately 50% of all the "idiopathic" cases in which underlying disease or trigger usually untraceable. Type II (reactive) IPA is associated with infectious disease outside the joints which might provide a source of antigen for immune mediated injury (approximately 25% of all IPA cases). Infections of the respiratory tract, urogenital tract, teeth, ears or skin, leishmaniasis, ehrlichiosis, anaplasmosis, borreliosis, and bacterial endocarditis have been reported to have association with type II IPA (Roush *et al.*, 1989, Thilagar *et al.*, 1990, Spreng, 1993). Type III (enteropathic/hepatopathic) IPA is associated with gastrointestinal diseases. The diseased gut may cause increase in permeability to potential antigens which might stimulate the production of immune complexes. Type IV (paraneoplastic) IPA occurs in association with neoplasia outside the joints, e.g. squamous cell carcinoma, leiomyoma, mammary carcinoma, and lymphoma. Formation of circulating immune complexes might occur by activation of immune system by neoplastic conditions. Weight of evidence suggests that the synovitis is secondary to deposition of circulating immune

complexes in the synovial capillary bed (Bennett, 1987c, Kohn, 2007).

An immune-based polyarthritis can follow vaccinations, either after the first injection or after booster vaccinations have been reported in dogs (Bell, *et al*., 1991). The lameness is often only transient, lasting for several days. More severe form has been described in Weimaraner and Akita Inu puppies up on vaccination with modified live canine distemper vaccine (Day and Bennett, 2008). IPA generally affects male dogs with around half of the cases in young dogs in the age group of 1-3.5 years (Tizard, 2009). Disease is characterized by overt lameness or stiffness after rest or exercise, stiff gait, reluctance to move, lethargy, inappetance, fever, and shifting leg lameness. The disease is diagnosed by examination of synovial fluid. The changes like increase in volume, turbidity, discoloration, decreased viscosity and clot formation are detected in synovial fluid from affected joints. Total protein and nucleated cell count also used to incline towards higher side.

Treatment starts with analgesics like Meloxicam at 0.1 mg/kg or Carprofen at 2-4 mg/kg are used to control pain, fever and inflammation in type I IPA or vaccine induced arthritis. Immunosuppressive therapy is initiated with corticosteroids (Prednisolone at 2-4 mg/kg q24hr for 2 weeks with gradual tapering of dose with clinical improvement over next 3-4 months). Dogs respond well to corticosteroid treatment with better prognosis than other forms of immune arthritis (Tizard, 2009). Always avoid simultaneous use of glucocorticoids and NSAIDs which might end in life threatening gastrointestinal ulceration (Kohn, 2007, Bolten, 2010). If there is no improvement in signs, cytotoxic drugs like cyclophosphamide at1.5 mg/kg (dogs with > 30 kg BW), 2 mg/kg (dogs with 15-30 kg BW) and 2.5 mg/kg (dogs with <15 kg BW) every four consecutive days per week for 3-4 months with low dose prednisolone (0.25-0.5 mg/kg po q24hr) is successful regimen (Kohn, 2007). Azathioprine at 2 mg/kg with low dose prednisolone could be used both on alternate days with regular hematological monitoring.

2. b. Drug induced arthritis

Drug induced arthritis is also considered to be immune mediated which is observed in a small proportion of dogs. Dobermans are generally more susceptible when treated with potentiated sulfonamides (Sulfadiazine-Trimethoprim) are usually responsible through development of drug-antibody complex leading to type III hypersensitivity mediated injury (Little and Carmichael, 1990, Cribb, 1989). The drugs may act directly as an antigen or as a hapten in combination with host proteins. The disease is clinically characterized by polyarthritis, fever, and occasionally lymphadenopathy, anemia, leukopenia, and thrombocytopenia which develop after 8-20 days of treatment with predisposed drugs (Thompson, 2005). Most common drugs responsible for drug induced arthritis include antimicrobials like lincomycin, erythromycin, penicillin's, cephalosporins, and sulfonamides (Kohn, 2007). Diagnosis is based on the worsening of the symptoms up on continuation of therapy. Line of treatment includes immediate withdrawal of responsible drug. Clinical signs usually regress within 2-5 days of drug withdrawal. Immunosuppressive doses of corticosteroids like prednisolone (1-2 mg/kg PO q24hr) could be used (Day and Bennett, 2008).

2. c. Polyarthritis/Polymyositis syndrome

Polyarthritis/Polymyositis is most prevalent in Spaniel breed and is clinically characterized by development of marked stiffness, poor exercise tolerance with crouched stance, muscle swelling and pain in the early stages of disease (Bennett and Kelly, 1987). There might be atrophy of muscle with contracture leading to reduced mobility of joints in affected areas. Serum biochemistry illustrates increased levels of muscle enzymes like Creatinine Kinase (CK), Aspartate Aminotransferase (AST) and Aldolase (Day and Bennett, 2008). For diagnosis of disease, muscle biopsy from at least 6 different areas should be taken for histopathology, of which at least two samples should be positive for inflammatory changes. Aggressive therapy with cytotoxic drugs (cyclophosphamide, azathioprine, and cyclosporine) is preferred to control the disease in combination with low dose prednisolone. The syndrome can also be treated with prednisolone at 1-2 mg/kg PO q 24 hours till improvement in the clinical signs followed by gradual tapering of dose over next 2-3 months.

2. d. Lymphocytic/Plasmacytic arthritis

It is an insidious syndrome affecting mainly

small to medium size dogs with propensity for stifle joint. The disease may be accompanied by joint laxity, partial or complete rupture of cranial cruciate ligament without any order in occurrence of lesions. The probable etiology of might be an exaggerated immune response to mediators or antigens released following ligament damage, surgical correction or as a result of an ensuing degenerative joint disease (Thompson, 2005). Grossly synovial membrane shows edematous thickening with red/yellow discoloration. Microscopic examination is characterized by marked diffuse and/or nodular infiltration of plasma cells or lymphocytes in the synovium and hypertrophy of synovial cells. Mononuclear cell infiltration (lymphocytes and plasma cells) is also reported in the synovial fluid. There is no clear cut evidence to show the immunological cause as a primary etiological agent in the disease (Day and Bennett, 2008). Management of disease is done with immunosuppressive doses of prednisolone.

2. e. Systemic Lupus Erythematosus (SLE)

It is a basically polysystemic autoimmune disorder of human, and also prevalent in other primates, horses, dogs, cats and laboratory animals. However, polyarthritis is the most consistent clinical finding of SLE in dogs and is the most cited example of non-erosive polyarthritis in canines (Day and Bennett, 2008). Male dogs are more predisposed to SLE with Collies, Shetland Sheepdogs, German shepherd dogs being most commonly affected breeds. It is a classical example of failed immunoregulation (Tizard, 2009). The imbalances in populations of T-cell subsets results in B cell hyperactivity through altered immunoregulation leading to general failure of immune system culminating in the production of antibodies against variety of membrane and soluble antigens like, antinuclear antibodies (dsDNA, histones), extractable nuclear antigens (Sm, RNP) and anti-phospholipids antibodies (Tizard, 2009). These auto antibodies are responsible for type III hypersensitivity mediated organ-specific and non-organ specific damages through immune complex medicated injury (Ginn *et al.*, 2005).

The exact cause of SLE is not clear. However, most researchers cite a combination of predisposing factors including genetic, environmental, drug induced, hormonal, and viral influences, that alter

suppressor T cell function allowing the expansion of autoreactive Th cell (helper T cell) and B cell clones with the production of auto-antibodies (Gorman and Werner, 1986a).

Clinical signs of the disease are categorized in two classes based on frequency of occurrence, viz., Major and minor signs which are as follows (Gorman and Werner, 1986a),

Neither major nor minor signs are truly specific for SLE. Rather a combination of these signs together with serological tests establishes disease diagnosis.

Major signs	Minor signs
Polyarthritis	Fever
Proteinuria (Glomerulonephritis)	Pleuritis
Dermatosis	Oral ulcers
Anemia (Coombs positive)	Neurological disease
Leukopenia	Myocarditis/Pericarditis
Thrombocytopenia	Lymphadenopathy

Classic SLE:

The diagnosis applies to cases presenting with two major signs and positive serological evidence or with one major and two minor signs together with positive serology.

Probable SLE:

If one major sign is present with positive serology or when two major signs are present without positive serology.

Fournel *et al.* (1992) studied 75 cases of SLE positive dogs and reported polyarthritis as a most common clinical finding followed by renal, mucocutaneous disorders and hemolytic anemia with greater predisposition of male German shepherd dogs. Central to diagnosis of SLE is demonstration of significant titers of antinuclear antibody (ANA) by indirect immunofluorescence and lupus cell test (Fournel *et al.*, 1992, Day and Bennett, 2008).

The prognosis of SLE is guarded due to multisystemic involvement, so needs institution of aggressive immunosuppressive therapy. Supportive care along with tapering doses of glucocorticoids alone or with cytotoxic drugs is the general line of treatment. Combination therapy using prednisolone and azathioprine has proved to be effective in re-

fractory cases or cases in which the maintenance dose of prednisolone produces unacceptable side effects (Stone, 2005). Induction doses of prednisolone at 2-4 mg/kg should be used reducing to an every other day maintenance dose of 0.5-1 mg/kg. Azathioprine can be given at 1-2 mg/kg daily reducing to 1 mg/kg every other day (prednisolone can be given on alternate days to the azathioprine). Novel therapeutic combination of prednisolone at 1-2 mg/kg daily orally (for 2 months) along with Levamisole at 2-5 mg/kg orally every alternate day continued for 4 months have shown encouraging recovery in dogs (Stone, 2005, Fournel *et al*., 1992). In face of relapse only levamisole therapy should be repeated for four more months (Day, 2008, Chabanne *et al*., 1995). An attempt to stop therapy may be made in dogs remaining disease free for six months. The most common causes of death in SLE patients are renal failure and infections like bronchopneumonia and septicemia.

Immune mediated muscular diseases

a) Myasthenia gravis

It may be either acquired or congenital disorder reported in human, dogs and cats. Disease is characterized by ineffective neuromuscular transmission secondary to the reduction in nicotinic acetyl choline (ACh) receptors on postsynaptic muscle membrane (acquired) or from genetical, structural or functional abnormalities of ACh receptors (congenital). In acquired form auto antibodies usually, IgG are generated against ACh receptors which blocks neuromuscular transmission either by directly interfering with the action of ACh on receptors or activation of compliment mediated lysis of post-synaptic membrane (Drachman, 1994, Dewey *et al*., 1997). Congenital form which occurs due to an inherited deficiency of these Ach receptors is common in Jack Russell Terriers, Springer Spaniels, and Fox Terriers (Couturier *et al*., 2009). Myasthenia gravis involves spectrum of clinical signs and disease has been classified in to three types, viz., focal, chronic generalized and acute fulminant generalized myasthenia (Dewey *et al*., 1997). Focal form is characterized by variable degree of facial, pharyngeal, laryngeal and esophageal dysfunction. Chronic generalized form, and acute fulminant generalized forms distinguished primarily by the rate with which clinical

signs develop. Dogs have generalized muscular weakness which worsens with exercise, non-ambulatory tetraparesis, and severe dyspnea. Megaesophagus is common in all forms of disease which is responsible for chronic regurgitation and aspiration pneumonia (Shelton *et al*., 1990, Webb *et al*., 1997). Diagnosis is based on history and clinical signs. Confirmatory diagnosis requires demonstration of serum antibodies that reacts with alpha bungarotoxin extracted ACh receptors in muscles by immunoprecipitation or radioimmunoassay. Test is highly sensitive and specific for autoimmune myasthenia gravis (Shelton, 2002). Also there is increase in strength of muscle after administration of short acting anti-cholinesterase like edrophonium chloride (Tensilon). Antibodies have also been detected to muscle protein 'titin' and Ca2+ channel receptor 'raynodine (RyR)' (Tizard, 2009). Canine nicotinic ACh receptor alpha subunit gene has been cloned successfully and ELISA has been developed to diagnose dogs with antibodies to these receptors (Yoshioka *et al*., 1999).

The disease can be managed on long term anticholinesterase therapy in order to prolong the interaction of ACh with receptors. Pyridostigmine bromide at 1-3 mg/kg q 8-12 hr or Neostigmine at 0.04 mg/kg IM q 6hr can be given to myasthenic dogs. But these treatments have minimal effect on esophageal motility. Shelton and Lindstrom (2001) treated 53 dogs diagnosed positive for autoimmune canine myasthenia gravis with anticholiesterase therapy only and reported clinical and immunological remission in 47 dogs within an average period of 6.4 month. Corticosteroid therapy started with lower dose and gradually increased dose has been reported to manage disease in some cases (Maddison *et al*., 1984).

b) Masticatory muscle myositis (MMM)

It is an immune mediated inflammatory disorder selectively affecting the muscles of mastication in canines. The common muscles involved are masseter, temporalis and pterygoid muscles. It's basis as immune mediated disease has been confirmed by detection of auto antibodies against 2M myosin muscle fibers which is unique isoform of myosin primarily present in masseter muscles of dogs (Shelton *et al*., 1987), as well as infiltration of mononuclear cells and clinical response to immunosuppressive therapy (Van Vleet and Valen-

tine, 2005, Taylor, 2000). Syndrome of masticatory muscle myositis is common in large breed dogs like German shepherd, Cavalier King Charles Spaniels with bilaterally symmetrical involvement of muscle. Both acute and chronic forms of MMM have been described in dogs (Lewis, 1994). Acute form is characterized by swelling of masticatory muscles with myalgia, reluctance to open mouth, difficulty in eating and drooling of saliva (Clooten *et al*., 2003). Swelling of muscles may results in exophthalamos, terminating in keratitis and conjunctivitis (Brogdon *et al*., 1991). Mostly MMM occurs as chronic condition which leads to severe progressive muscle atrophy and affected dogs are unable to open mouth fully. Masticatory muscle myositis is progressive disease and affected dogs may develop aspiration pneumonia or complications of corticosteroid therapy leading to death.

Masticatory muscle myositis is diagnosed on the basis of clinicopathological abnormalities like myalgia, difficulty in opening the jaw, increased serum creatine kinase (CK), leukocytosis with neutrophilia and occasionally lymphocytes or eosinophils. But these findings being non-specific, confirmatory diagnosis is based on demonstration of antibodies against type 2M muscle fibers in muscle biopsy as well as histopathological findings like inflammatory or degenerative lesions (necrosis and phagocytosis of 2M fibers with infiltration of lymphocytes and plasma cells) affecting the M2 myofibrils (Van Vleet and Valentine, 2005).

Corticosteroids are commonly used to treat the MMM in dogs with prednisolone at 1-2 mg/kg BW orally twice a day with gradual reduction in the dose rate up on clinical remission. Cytotoxic drugs like azathioprine might be required in dogs unresponsive to prednisolone therapy. To avoid the side effects like muscle weakness by corticosteroid therapy, doses of prednisolone should be gradually increased for effective therapy (Shelton, 2002). The disease is having good prognosis if treated properly, but relapses may occur (Taylor, 2000, Lewis, 1994).

c) Polymyositis

It is a generalized autoimmune myositis that occurs most commonly in adult dogs of large breeds like German Shepherds (Tizard, 2009) and is presented with variable signs like progressive muscle weakness not associated with exercise, changes in laryngeal muscle function leading to change in the voice, and shifting leg lameness. Megaesophagus may lead to dysphagia and, if severe, can result in regurgitation and aspiration pneumonia (Presthus and Lindboe, 1988). Animals may be febrile and develop leukocytosis and eosinophilia. The disease may be acute or gradual in onset with primary sign relating to involvement of masticatory muscles, so both MMM and polymyositis needs to be considered for confirmatory diagnosis (Van Vleet and Valentine, 2005). The syndrome of polymyositis may be accompanied by the variety of diseases like SLE (Krum *et al*., 1977). Pathological changes include degenerative changes in muscle fibers, necrosis, vacuolation and affected muscles may be infiltrated by lymphocytes and plasma cells. Serum biochemistry shows an increase in serum levels of muscle enzymes like Creatinine Kinase (CK), Aspartate Aminotransferase (AST) and Aldolase (Gorman and Werner, 1986a, Presthus and Lindboe, 1988). Immunophenotyping revealed that the lymphocytes that invade affected muscles are mainly of cytotoxic (CD8+) type (Neumann and Bilzer, 2006). Corticosteroid therapy is effective in most cases (prednisolone at 0.5-1 mg/kg PO q24hr), but care should be taken to rule out infectious causes like toxoplasmosis, fungal and bacterial infections before initiation of therapy.

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