Immune Mediated Polyarthropathy
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INTRODUCTION
The term polyarthropathy describes disease in multiple affected joints of the dog or cat patient. Immune mediated polyarthropathy (IMPA) is just one category of disease and implies an inflammatory process that occurs secondary to a significant immune system response. This can occur without a finite trigger, but can also be associated with infectious, neoplastic, other primary inflammatory, and intestinal disease. When present, identifying the underlying trigger is vital to implementing the best multimodal approach to therapeutic recovery.

PHYSIOLOGY
A type 3 (immune complex mediated) hypersensitivity reaction is believed to be the cause of non-erosive IMPA. In this process, immune complexes (antigen:antibody) from non-joint diseases OR primary joint disease accumulate in the joint space. Complement activation leads to cytokine release, inflammation, & influx of neutrophils, leading to tissue damage. In erosive disease (1% of immune mediated disease with more guarded prognosis), antibodies against Type II collagen as well as a Type IV hypersensitivity reaction are involved in tissue destruction and ongoing inflammation.

‘Idiopathic’ polyarthritis is the most commonly described immune-mediated polyarthropathy. Four subtypes exist: I – no underlying disease; II – reactive to infection or distant inflammatory disease; III – enteropathic associated; and IV: neoplastic. Immune-mediated disease of the joints can also occur with the following conditions (not further discussed at this time): vaccine induced polyarthritis, drug-induced polyarthritis, polyarthritis/polymyositis syndrome, steroid responsive meningitis-arteritis, juvenile onset polyarthritis of Akitas, familial Chinese Shar Pei Fever, and systemic lupus erythematous-like disease.

PATIENT HISTORY & CLINICAL SIGNS
Young to middle-aged, medium to large breed dogs are overrepresented for idiopathic polyarthritis. However, any size dog, breed, or age should be considered. Feline patients also should be considered, although incidence is less common. Breeds over represented in some studies include Labrador Retrievers, German Shepherds, and Cocker Spaniels.

Clinical signs reported can be of chronic OR acute duration. Joint swelling is not always perceived. Weight loss, lethargy, malaise, stiff or altered gait (‘walking on egg shells’), reluctance to rise, and inappetence are not uncommon. Physical exam may yield fever, bilateral limb joint pain and/or swelling, lameness, and/or those associated findings with the primary disease. Joints including the TMJ and vertebral facets can also be involved. There exist patients that do not show apparent joint pain or swelling, however fever is often present in these patients. This disease should be considered when more common sources of fever have been ruled out.
DIAGNOSIS
A minimum database to evaluate for primary and/or concurrent disease should include: CBC, serum chemistry, urinalysis, infectious disease serology (i.e. Lyme, Anaplasma, Ehrlichia, RMSF, Bartonella, FELV, FIV, & what is endemic to the region), and urine culture. Mild hypoalbuminemia, non-regenerative anemia, and leukocytosis are frequent findings but not pathognomonic for this disease process. In the presence of a heart murmur, echocardiogram to evaluate for endocarditis is also warranted.

Imaging studies to include thoracic x-rays and abdominal ultrasound are recommended to look for inciting pathology. Radiographs of painful or swollen joints should be pursued to assess for other causes of joint disease, and if idiopathic polyarthritis is suspected, presence or absence of erosive lesions. Subchondral bone destruction is consistent with erosive disease.

Definitive diagnosis is achieved with arthrocentesis. Carpi, stifles, and hocks are most common to be affected but any joint is possible. Synovial fluid should be evaluated via bacterial (aerobic, anaerobic) culture, fluid analysis, and cytology (via fluid analysis +/- slide cytology). Joint culture to include Mycoplasma should also be considered, especially in refractory cases. Positive cultures are consistent with a septic process and medical management will change accordingly. In septic processes, as well as degenerative joint disease, hemarthrosis, neoplastic arthropathy, and trauma, it is more typical for one joint to be affected, but this is not always the case. Idiopathic polyarthritis is confirmed with a greater than normal cell count (often >5000 cells/uL) of non-degenerative neutrophils, or less commonly mononuclear cells, in multiple joints. Sedation +/- propofol is typically used to perform arthrocentesis although general anesthesia may be needed in extremely painful cases. The site must be steriley prepped before acquisition of samples. Visually, diseased joint fluid will have decreased viscosity and a turbid, opaque nature. Less commonly employed lab tests for this disease process include Rheumatoid Factor, which is typically assessed when erosive lesions are present and no primary disease is found. Positive ANA titers can be seen with SLE-like disease, but can also be elevated in infectious, neoplastic, and other inflammatory disorders and are not routinely performed in the author’s cases.

TREATMENT OPTIONS
Management should include therapy of the primary disease (if identified), inflammation, and pain. For Type II-IV disease, treatment of the primary disease, along with pain management often results in resolution of the joint disease. However, steroids are occasionally necessary and this is especially true with most tick-associated polyarthropathies. The use of NSAIDS is typically withheld pending culture and cytology results, in case steroid therapy is deemed warranted. In Type I disease, prednisone or prednisolone is the most often used medication – starting dosages of 1-2 mg/kg per day have been show to be effective. This author typically starts at the lower end of the dosing range. If tapering steroids result in relapse of clinical signs, additional immune modulation is recommended for disease control and eventual longterm use (to allow the cessation of steroid therapy). Once remission is achieved, steroid taper typically occurs at 25% of the initial dose every 2 weeks, pending patient clinical status. Faster tapers have been employed in pets suffering from excessive steroid side effects. Additional immune modulatory therapy including azathioprine, leflunomide, mycophenolate, and cyclosporine has all been successful in the author’s clinical practice. With immune suppressant therapy,
monitoring for secondary infection is important.

Doxycycline (5 mg/kg PO BID) alone has been successful in some patients who present with acute disease and test positive for a tick-borne illness such as Lyme or Anaplasma. If a septic process is suspected, a more broad spectrum antibiotic should be considered based on sensitivity results.

Additional therapy can include omega-3 fatty acid supplements as well as joint supplements such as glucosamine chondroitin sulfate. Arthrodesis and intra-articular injections are often not needed, but have been implemented in cases of collapsed joints and refractory disease.

Response is typically noted within the first week of treatment. Monitoring should include resolution of labwork changes, palpable joint effusion improvement, and owner report of resolution of clinical signs. Repeat arthrocentesis can be performed to prove resolution of inflammation, however this is rarely elected. Canine C-reactive protein, an acute phase protein produced by the liver, has shown some promise for monitoring.

PROGNOSIS
Erosive polyarthropathies typically require multi-modal longterm therapy. Permanent joint damage is common and remission rates are poor. Type II-IV non-erosive polyarthropathy has a fair to good prognosis, as long as the underlying disease is resolved/goes into remission. Type I also has a good rate of remission, although relapses are possible.

SELECTED REFERENCES