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Clinical Features in 9 Dogs with Immune-Mediated Polyarthritis

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Abstract : Nine dogs with history of lameness and anorexia were presented. On physical examination, all dogs had gait abnormality and six dogs had high body temperature. Their clinical signs were mostly episodic, and only non-specific symptoms were occasionally observed. Arthrocentesis was performed in all dogs, and immune-mediated polyarthritis (IMPA) was diagnosed. Definitive rheumatoid arthritis (RA) and systemic lupus erythematous (SLE) were diagnosed in one dogs, one each. Prednisolone (PDS) was chosen as the first-line therapy for all dogs, except for the one with RA. Most cases responded to PDS but some cases including those of SLE and RA were refractory to PDS. IMPA can be challenging to diagnose due to its vague symptom and is commonly implicated in 'fever of unknown origin'. Therefore, clinicians should consider IMPA as a differential diagnosis when the patient has fever with systemic, non-specific signs, such as anorexia and depression, but does not respond to antibiotics.

Key words **:** immune mediated polyarthritis, fever, arthrocentesis, lameness.

Introduction

Polyarthritis is defined as neutrophilic inflammation of two or more joints (10). Noninfectious inflammatory polyarthritis includes immune-mediated polyarthritis (IMPA), which diagnosed as increased TNCC and neutrophil concentration without infectious sign. It is further categorized into erosive and non-erosive arthritis based on the presence or absence of radiographically evident joint destruction, respectively (7,8,9).

Idiopathic IMPA is a non-erosive polyarthritis where there are no identifiable causes or underlying diseases and currently the most common cause (50%-60%) of IMPA in dogs (7,10). Non-erosive IMPA can occur as a feature of systemic lupus erythematous (SLE), which is an autoimmune polysystemic disorder (7,10). The erosive type is relatively very rare and represents only about 1% of all canine polyarthritis cases (4,7). Rheumatoid arthritis (RA) is the most common form of erosive IMPA in dogs (4). The diagnostic criteria for RA and SLE for humans were modified and implemented in small animals (2,4).

IMPA can cause non-specific systemic signs as well as lameness, stiffness, and/or swelling in joints. IMPA is most commonly diagnosis of 'fever of unknown origin', accounting for 20%. In addition to fever, it can cause weight loss, lethargy, and reluctance to move (2,11).

Three types of drugs can be used to treat IMPA in dogs: non-steroidal anti-inflammatory drugs (NSAIDs), glucocorticoids, and non-steroidal immunosuppressive agents (4). The drug type, dosage, and combination can be selected according to disease severity, and response to initial drug. Here we describe the clinical manifestation, diagnosis, and management of nine dogs diagnosed as IMPA.

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Case

Medical records of nine dogs diagnosed as IMPA between 2014 and 2017 at the Veterinary Teaching Hospital of Chungnam National University were reviewed. The age of dogs at admission ranged from 3 to 14 years (median age, 8.5 years); middle-aged dogs (4-8 years) were dominantly present in our study (55%). Seven dogs were female (two spayed, five intact) and two dogs were neutered male. The nine dogs comprised six breeds, with Maltese (n = 4) and other dogs included one each of the following breeds: Toy Poodle, Pomeranian, Yorkshire Terrier, Lhasa Apso, and mixed breed.

Clinical signs on presentation included gait abnormality (n = 9), high body temperature (n = 6), lethargy (n = 5), anorexia (n = 4), and urinary and defecation disorder (n = 1). Gait abnormalities were implicated in reluctance to walk or move (n = 4), eggshell walk (n = 2), and lameness (n = 3).

Physical examination was performed for all dogs at the initial presentation. The median rectal temperature was 39.2°C. Six of the dogs were febrile (temperature > 39.4°C) at presentation or had a history of being febrile as reported by the local/referring veterinarian; three of these dogs had temperature > 40°C. Joint swelling and pain was noted in three dogs during the initial physical examination. Other physical examination abnormalities included mildly elevated respiratory rate (n = 1) and back pain (n = 3). Gait abnormality and high body temperature were identified as occurring intermittently in three dogs (Table 1).

Radiographs of affected joints were taken for all dogs. The radiographic evidence of abnormalities was noted in five dogs and revealed joint effusion (n = 2), degenerative change (n = 2), soft tissue swelling (n = 1), and erosive lesions (n = 1). At the initial presentation, erosive lesions were not identified in any dog. One dog had persistent gait abnormality, and radiography which was taken several months after the initial pre-

Table 1. Incidence rates of clinical signs of dogs diagnosed as IMPA

	Number (percentage)	
	Permanent	Intermittent
Gait abnormality	6 (66%)	3 (33%)
High body temperature	3 (33%)	3 (33%)
Lethargy	5 (55%)	
Anorexia	4 (44%)	
Urinary and defecation disorder	1 (11%)	

sentation showed erosive lesions in six joints.

Arthrocentesis was performed in all dogs. Synovial fluid samples from 51 joints were analyzed by smear examination. Of these, 48 samples contained > 5 cells per field at 400 × magnification (normal, two cells) and elevated nondegenerative neutrophil concentrations of 20-98% (reference range, < 10%). No infectious agent was identified on synovial smear.

Antinuclear antibody (ANA) titers were measured in eight dogs, and of those, one was positive with a titer of 1:800. An ANA-negative dog having three major signs as well as lupus erythematosus cells on blood smear was diagnosed as definitive SLE. Rheumatoid factor (RF) measurements were taken for five dogs. The results were positive in one dog; however, according to the RA criteria, this patient was identified as suggestive RA and another patient that erosive lesion was shown in radiography was diagnosed as definitive RA.

Prednisolone (PDS) was chosen as the first-line therapy for all dogs, except for the one with RA. PDS was highly effective in most cases (n = 5) of IMPA. In these cases, PDS dosage was tapered depending on the response to treatment.

The dog with definitive RA was successfully managed with a continuous administration of leflunomide and piroxicam. A combination of cyclosporine and PDS was first administered in the dog with definitive SLE and was started in dog with suggestive RA in whom the initial treatment with only PDS failed. The dog with suggestive RA responded to this medication and was treated with tapering PDS. The symptoms of SLE were initially well-controlled with the combination of two medicines for the first 4 months. However the clinical signs such as lameness and joint pain started to develop and be deteriorated. Despite the addition of leflunomide, the dog did not respond to medications. The dog survived for nearly 1 year after diagnosis and died two months after worsening of the clinical condition (Table 2).

Discussion

Over a three-year period, IMPA was diagnosed in nine dogs and was classified into subtypes. Clinical and radiographic findings of dogs with IMPA were analyzed to elevate diagnostic possibility.

In a study of 40 dogs with polyarthritis, only one third of them had true lameness (3). In our cases, obvious lameness was identified in only three dogs. Although all cases were related to gait abnormalities, most cases showed vague clinical signs, such as reluctance to stand and reduced movement. These vague symptoms often may be misunderstood as lethargy.

IMPA can show intermittent clinical signs, particularly in terms of gait abnormality and high body temperature. Therefore, clinicians and owners may judge that symptoms of IMPA get improved, or may confirm only non-specific clinical signs without lameness or fever.

Radiographic changes of the degenerative joint disease were noted in two dogs. No radiographic change was identified in most IMPA cases (n = 4) except for RA. Erosive arthritis is characterized by radiographically evident joint destruction (10). However, radiographic images of two dogs including suggestive and definitive RA did not show erosive lesions at the initial presentation. Dog with definitive RA revisited the hospital because of recurrent lameness six months after the initial presentation, and erosive lesions were identified in the radiographic image at this point. As reported previously, it takes about six months for erosive lesions to be evident on radiographic changes (5). Acquiring only one radiographic image to identify the type of IMPA is not sufficient to diagnose erosive IMPA. Therefore, it is necessary to check another radiography for erosive changes when patients have relapsing symptoms or are suspected as having erosive IMPA.

It is sometimes difficult to diagnose IMPA due to its intermittent symptoms and vague clinical manifestations. Five of the dogs that were diagnosed as IMPA had a history of being administered antibiotics or/and NSAIDs. Clinicians should consider IMPA as a differential diagnosis when a patient with vague gait abnormality has a fever that does not respond to antibiotics. On reviewing the frequency polyarthritis in dogs since 2014, only two dogs with said conditions were reported between 2014 and 2015 but seven between 2016 and 2017, indicating a rise in the occurrence in last two years. It is believed that understanding the clinical features better can elevate diagnostic possibility and avoid misdiagnosis.

Three types of drugs are used for the management of

Table 2. Treatment and prognosis of 4 patients that were refractory to or relapsed after initial medications

Type (tested number)		Initial drug	Relapse/refractory case	Follow-up	Duration of treatment
Idiopathic		PDS	Increase dose of PDS	The dose of PDS was tapered after remission	4 months
SLE	Definitive (1/8)	PDS + cyclosporine	Add leflunomide	Survived for 1 year	12 months
RA	Suggestive (1/5)	PDS	Add cyclosporine	Switched to meloxicam after remission	20 months
	Definitive (1/5)	Leflunomide + piroxicam	Increase dose of leflunomide	Maintain medication	13 months

IMPA and they have different indications. NSAIDs can be used to control pain and inflammation in patients with mild IMPA (5). NSAIDs were prescribed for two dogs; one had mild clinical signs after tapering PDS and another one had already been administered immunosuppressants. Glucocorticoids are the cornerstone of therapy and can be considered initially in patients with IMPA (4,10). In cases that patients have relapse or are refractory to PDS, other immunosuppressants can be tried, including cyclosporine, mycophenolate, and leflunomide. Most PDS-administered patients (n = 5) responded well but some (n = 3) were refractory, of which one had SLE.

Most patients with definitive RA or SLE were refractory to initial treatment. Because RF/ANA tilter or their criteria were not applied in all patients, there is lack of evidence that these types were associated with worse prognostic factor in our study. However, dogs with RA may have poorer prognosis than nonerosive IMPA and need life-long therapy, because disease process of RA is progressive and irreversible (4,5). As SLE is the result of widespread immune complex deposition with multiple organ involvement, patients have various prognoses depending on the organ affected and the extent of damage to the organ (1,6). Therefore, it is necessary for clinician to identify relation between IMPA type and prognosis. It may be helpful to determine optimal treatment and prognosis.

It is challenging for clinicians to diagnose and manage IMPA due to its characteristics, such as inconsistent epidemiology and non-specific and intermittent clinical signs. However, understanding the clinical features of IMPA and considering IMPA as a differential diagnosis in cases of ‘fever of unknown origin’ or vague lameness would help reach an accurate diagnosis.

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