IMPA – part two: clinical signs, diagnosis and treatment

Author : Karen L Perry

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ABSTRACT

The clinical signs associated with immune-mediated polyarthritis (IMPA) can be variable and this may make diagnosis challenging. However, the main obstacle to the diagnosis of IMPA is a failure to include the disease as a differential.

Arthrocentesis is the most valuable tool in both the diagnosis and monitoring of IMPA cases. While many other diagnostic tests can also be useful, the risk/benefit of these additional tests should be carefully considered, with them only being performed if the outcome is likely to alter case management or prognosis.

Treatment of IMPA generally starts with corticosteroid therapy, but combination therapy with cytotoxic drugs or immunomodulatory medications may also be necessary. The response to treatment and the potential side effects of medications must be monitored closely. Owners must be counselled appropriately following a diagnosis of IMPA as the prognosis must be considered guarded, with many cases requiring long-term or lifelong medication and the medications themselves can have severe side effects.

This article follows on from the first (VT45.39) that discussed the pathophysiology and classification of immune-mediated polyarthritis (IMPA).

In this part, the emphasis will be on the clinical signs associated with this condition, as well as the diagnostic tests recommended to facilitate classification where possible. Treatment can be complex and frustrating, but the options will be discussed in addition to the associated prognoses.

Signalment

Idiopathic IMPA is most commonly, but not exclusively, diagnosed in dogs younger than six years of either gender, with large breeds reportedly more commonly affected (Hopper, 1993; Bennett and May, 1995). However, other studies have reported contrasting results, with dogs weighing less than 10kg being more likely to be diagnosed (Stull et al, 2008) and, therefore, signalment cannot be used to exclude IMPA as a differential.

Some authors suggest a breed predilection in German shepherd dogs, Dobermann pinschers, collies, spaniels, retrievers, terriers and poodles. Polyarthritis associated with systemic lupus erythematosus (SLE) is reported more commonly in German shepherd dogs, collies, Shetland sheepdogs, beagles and poodles of any age, with females more commonly affected. Rheumatoid arthritis typically affects young to middle-aged members of toy and small breeds of either gender (Giger et al, 1985; Lees et al,1986; Pedersen et al, 1976; Pedersen et al, 1976b).

Clinical signs

The onset of clinical signs associated with IMPA can be either acute or chronic (Innes, 2012). The clinical severity can be highly variable, with presentations ranging from a complete inability to stand, with multiple and obvious joint effusions, at one end of the spectrum to low-grade, insidious onset stiffness or even lameness in a single limb at the opposite end (Innes, 2012).

IMPA should be considered as a differential diagnosis for any dog or cat with signs of multiple joint pain or swelling, generalised stiffness, shifting lameness, or pyrexia of unknown origin (PUO; Dunn and Dunn, 1998). In one study of diagnostic investigations in 101 dogs with PUO, IMPA accounted for 20% of all diagnoses (Dunn and Dunn, 1998). On the basis of these results, it was suggested that in investigating unexplained pyrexia, a diagnosis of IMPA should be excluded before other, less common diagnoses are considered.

Figure 1. A five-year old griffon Bruxellois suffering from erosive polyarthritis affecting both carpi, the metacarpo-phalangeal joints, the inter-phalangeal joints and to a less severe extent, both stifles and both elbows. Note the subluxation and instability of the carpi.

Reported clinical signs are variable and include reluctance to walk, spontaneous vocalisation, lameness, exercise intolerance, lymphadenopathy, spinal pain, fever and inability to stand (Jacques et al, 2002; Bennett, 1987b; Clements et al, 2004; Webb et al, 2002). Inactivity stiffness is common and this may persist for several minutes after rising in contrast to that noted in osteoarthritis, in which stiffness typically only lasts for a few seconds after rising (Innes, 2012).

Decreased range of motion, effusion, heat and pain upon manipulation of the joints may be appreciated (Clements et al, 2004). Bilaterally symmetrical joint involvement is common and the joints most often affected (in descending frequency) are the carpal, tarsal, stifle and elbow joints (Clements et al, 2004).

While multiple symmetric joint pain and swelling is typical, some cases are asymmetric. IMPA can present as only affecting a single joint, but this is unusual. However, even if only one joint appears clinically inflamed and swollen, the clinician is advised to obtain samples from other joints and use

the opportunity to distinguish between inflammation of a single joint and inflammation of multiple joints; in some cases this can help the clinician distinguish between IMPA and infective arthritis.

Although some cases present with only a few joints apparently affected, additional joints may succumb to disease as time progresses. With disease progression, secondary osteoarthritis changes may appear in affected joints with circumferential joint thickening and fibrosis (Innes, 2012).

Sometimes, systemic signs such as pyrexia, inappetence, anorexia and weight loss may be the only signs noted (Roush et al ,1989; Houlton and Jefferies, 1989; Little and Carmichael, 1990; Thilagar et al, 1990; Woodard et al, 1991; Dougherty et al, 1991; Thoren-Tolling and Ryden, 1991; De Haan and Andreasen, 1992; Spreng, 1993; Fournel et al, 1992; Hopper, 1993; Bennett and May, 1995; Dunn and Dunn, 1998).

In one study, articular pain was only noted on examination in 16 out of 40 dogs (Jacques et al, 2002), lameness was only noted in one-third of cases and systemic signs were the only clinical signs in 10% of dogs. This can make diagnosis challenging as the signs can be subtle and could be encountered in a number of other disease processes (Jacques et al, 2002).

The signs of secondary IMPA can also be completely masked by those of the primary disorder where one is present. Incomplete response to therapy for primary disorders commonly accompanied by IMPA should prompt evaluation of joints for inflammation. Clinical signs in cases of erosive arthritis are largely similar with the addition of deformity, subluxation and instability of joints in chronic cases (**Figure 1**).

In a series of 30 cases of rheumatoid arthritis (Bennett, 1987) just under a third of cases had signs of systemic illness in addition to lameness including pyrexia, lethargy and inappetence/anorexia. Six animals had clinical evidence of respiratory disease and one had a severe tonsillitis/pharyngitis. Three dogs had subcutaneous swellings (one over the acromion process and two over the olecranon). Most dogs had bilaterally symmetric polyarthritis, but two had clinical disease limited to a single joint.

Signs of joint disease included pain on manipulation – particularly at the extremes of joint motion – synovial effusion and soft tissue thickening around the joint. For two-thirds of cases the lameness was of gradual onset, but in one-third it was acute. Two-thirds of the dogs showed signs of inactivity stiffness. The most commonly affected joints (in decreasing order) were the stifle, carpus, hip, elbow and tarsus. Seven dogs also showed involvement of the digital joints. Subluxation and instability of various joints occurred in a minority of cases in this series. Peripheral lymphadenopathy was present in eight cases (Bennett, 1987).

Diagnostic tests

The main obstacle to the diagnosis of IMPA is a failure to include the disease as a differential. Arthrocentesis should be performed as part of the diagnostic investigation in any dog with a fever of unknown origin even in the absence of orthopaedic clinical signs (Rondeau et al, 2005).

Arthrocentesis is the most important diagnostic tool. The diagnosis of IMPA requires evidence of articular inflammation in several joints. This depends on cytology from a minimum of three synovial fluid samples from three different joints. It is recommended to sample at least four joints and to continue sampling until a minimum of three acceptable samples are obtained.

It is easier to get sufficient volumes from effused joints or from larger joints such as the shoulder, stifle, elbow and hip (**Figure 2**). However, IMPA often preferentially targets smaller joints, particularly the carpus and tarsus (Innes, 2012). Aseptic technique, sedation and proper restraint are advised. Synovial fluid analysis should include an assessment of the gross appearance of the fluid from each joint, noting volume, viscosity, colour and transparency.

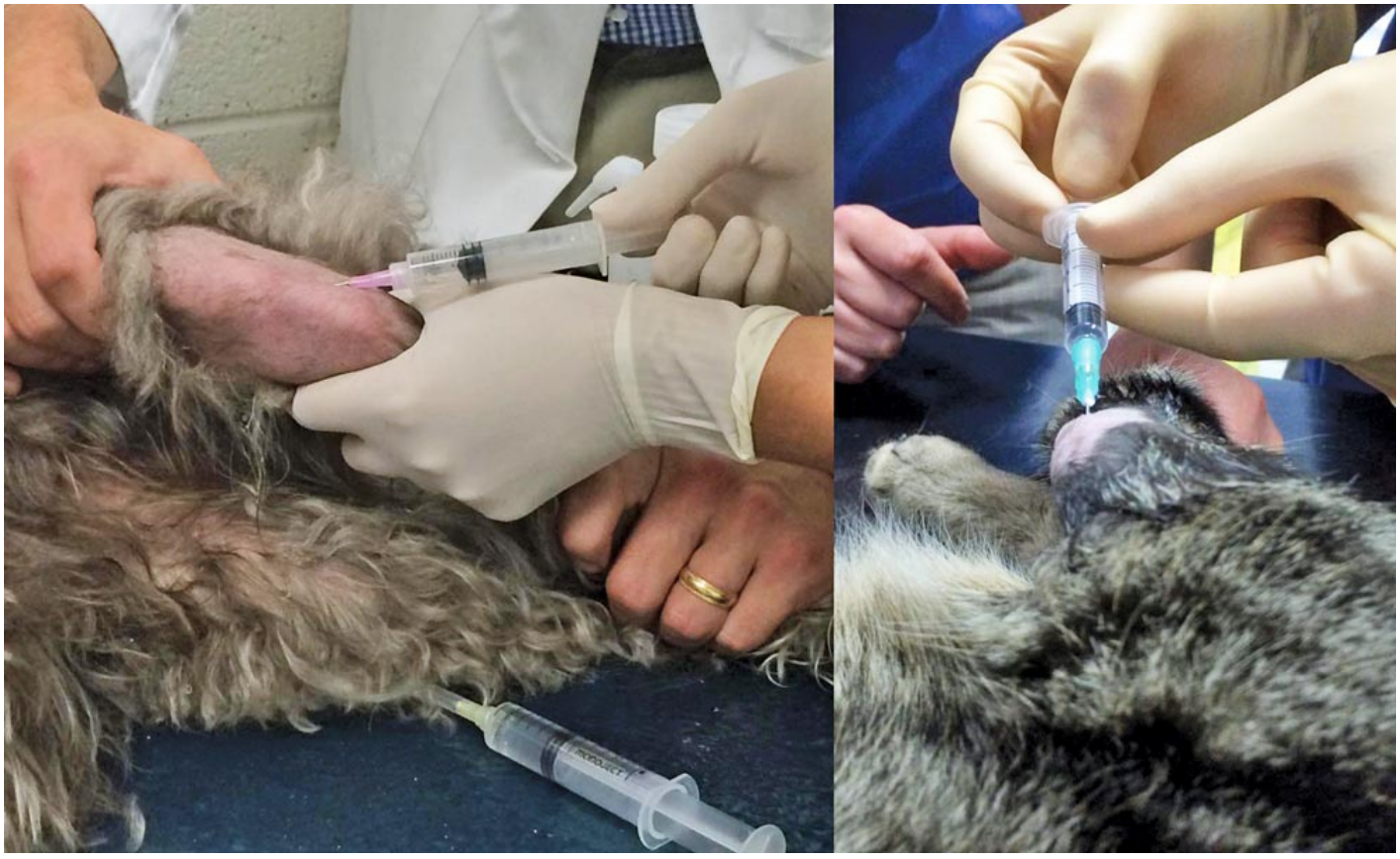

Figure 2. Arthrocentesis being performed from the stifle joints of a Labradoodle (left) and a domestic shorthaired cat (right). Note differing syringe and needle sizes may be selected based on both patient size and personal preference.

Cytologic evaluation should include total and differential cell counts, as well as careful assessment

of cell morphology; a subjective assessment of a freshly stained smear can guide the clinician but should not be relied on to distinguish between IMPA and infective arthritis (Gibson et al, 1999).

Suppurative inflammation in synovial fluid has been defined as nucleated cell counts more than 3,000/µL or more than two cells/hpf (when automated cell counts are not performed) and neutrophils comprising more than 12% of nucleated cells within the fluid (Jacques et al, 2002; Clements et al, 2004). Other tests such as mucin clot tests and total protein content of the synovial fluid may be valuable but are not necessary to reliably diagnose polyarthritis (Parry, 1999). If any suspicion of infective arthritis arises, the clinician should also submit synovial fluid in a blood culture bottle for culture and sensitivity testing (Innes, 2012): however, blood and urine cultures may be more rewarding.

In some cases, it may not be possible to obtain sufficient synovial fluid for cytology. This may be the case in small dogs and cats, particularly if the disease is low grade with minimal effusion and if the smaller distal limb joints are primarily affected. It may also be more difficult to obtain fluid in chronic cases with synovial proliferation and thickened joint capsules. Synovial biopsy may be used in such instances and this may help to confirm the presence of infiltration of the synovium with B-lymphocytes and T-lymphocytes, macrophages and neutrophils (Innes, 2012).

Once the presence of polyarthritis has been confirmed, specific measures are taken to classify the type of polyarthritis. Further information on this was provided in the first article. Classification provides a definitive diagnosis that improves the accuracy of the prognosis and allows preparation of an appropriate therapeutic plan. The process is primarily targeted at trying to identify an initiating cause.

A thorough review of physical abnormalities and clinical history can assist in differentiating primary from secondary IMPA. A careful and thorough clinical examination, including an ophthalmologic examination, is mandatory (Innes, 2012). Review of the physical examination findings and clinical pathology results should identify criteria of SLE if present: cytopenia (haemolytic anaemia or thrombocytopenia), dermatological lesions, protein-losing nephropathy (urine protein-to-creatinine ratio), myositis, myocarditis or pericarditis, pleuritis and glossitis (Pedersen et al, 2000; Scott et al, 1983).

Because immunosuppression is the goal of therapy for idiopathic IMPA, previous evaluation for infectious disorders is important. A full blood count, urinalysis and serum biochemistry are recommended, along with titres for tick-borne diseases if appropriate. Imaging of the thorax, abdomen and heart is recommended. Endocarditis is one possible initiating factor for IMPA and careful auscultation of the heart is essential, but echocardiography is recommended for its increased sensitivity in detection of valvular lesions (Davidson, 2003; Peddle and Sleeper, 2007; Innes, 2012).

Haematology

Haematologic tests may typically reveal anaemia (autoimmune or anaemia of chronic disease), leukocytosis or leukopenia, neutrophilia with a left shift and thrombocytopenia (Bennett, 1987; Bennett, 1987b). Thrombocytopenia and leukopenia are especially seen in cases of SLE (Bennett, 1987c). Serum biochemistry tests may show urea, creatinine, alkaline phosphatase, alanine transferase and aspartate transferase concentrations to be elevated (Bennett, 1987b; Bennett, 1987c). Raised serum creatine kinase and aldolase concentrations may be seen in cases complicated by myositis (Bennett and Kelly, 1987). Protein-losing nephropathy or enteropathy may occasionally be encountered owing to immune complex deposition; this may lead to decreased serum albumin concentrations (Innes, 2012). Globulins may be increased as the result of auto-antibody production. Urinalysis may demonstrate proteinuria that may be detected as a result of glomerulonephropathy (Innes, 2012).

Radiography

Radiography can permit differentiation between non-erosive and erosive forms of IMPA (Davidson, 2003). Radiographic features of IMPA often show bilateral symmetry and the distal limb joints tend to be affected to a greater degree (Innes, 2012). Radiographs of affected joints in non-erosive IMPA typically show only synovial effusion and soft tissue swelling with or without mild periarticular osteophytes (Davidson, 2003; Innes, 2012). With chronicity, erosive polyarthritis is characterised by severe osteoarthrosis, subchondral sclerosis, bone loss, subluxation or luxation of joints and, in some cases, periarticular bone proliferation and mineralisation of periarticular soft tissues such as tendons and ligaments (enthesopathy; Davidson, 2003; Innes, 2012; **Figure 3**).

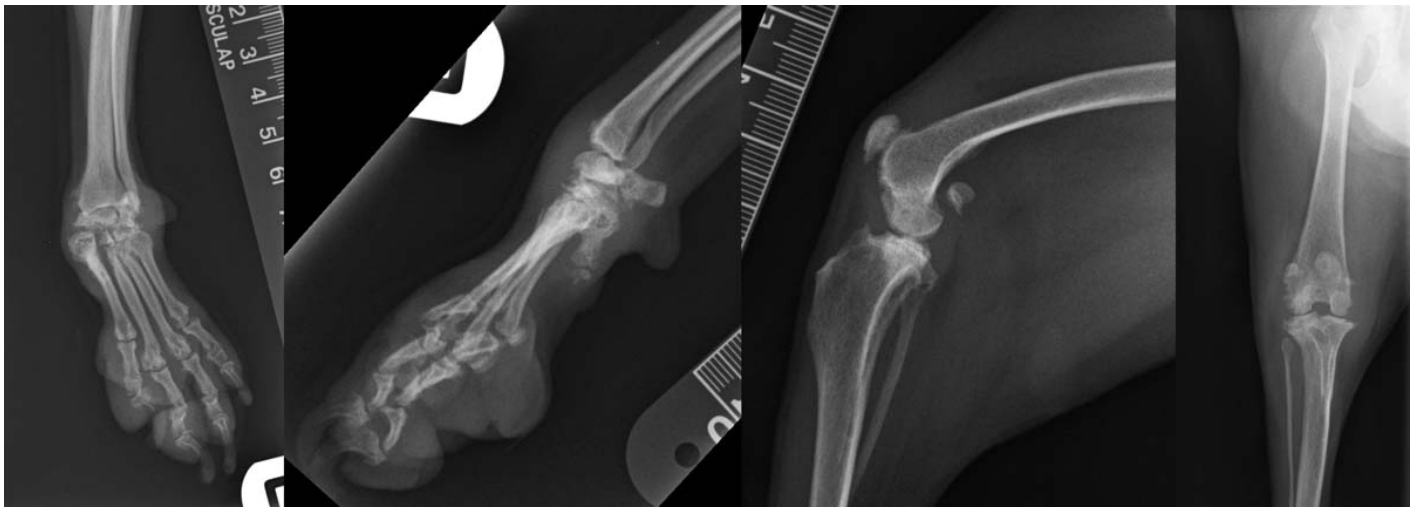

Figure 3. Dorsopalmar and mediolateral views of the left carpus and digits and caudocranial and mediolateral views of the left stifle of the Griffon Bruxellois in **Figure 1.** Note the severe osteoarthrosis, subchondral sclerosis, bone loss and subluxation of the carpus in addition to the marked soft tissue swelling.

However, the clinician should be aware erosions take some time to appear following the onset of

disease. In addition, in some cases, erosions are initially seen in only a small number of joints, even though inflammation is present in many joints. Some specific forms of erosive IMPA can also result in marked periosteal proliferative bone formation (Innes, 2012).

Serology

Autoantibodies are well-established phenomena in human and canine IMPA. Rheumatoid factors (RF) are anti-immunoglobulin (Ig) antibodies of IgM and IgA classes against the fragment crystallisable (Fc) portion of IgG (Bell et al, 1993; Carter et al, 1989). RF and IgG can form immune complexes that contribute to the disease process.

However, the appearance of RFs in serum is not specific for canine rheumatoid arthritis; they can be a feature of other chronic inflammatory conditions. As such, assays for RF are useful only in helping to categorise a case of IMPA. These tests should not be used as diagnostic tests for canine IMPA or canine rheumatoid arthritis.

About 80% of human rheumatoid arthritis patients are positive for RF and the remainder are said to be “seronegative”, so the appearance of RF is not essential for a diagnosis of rheumatoid arthritis in humans (Innes, 2012). Similarly, with the Rose-Waaler test, RF is present on serological testing in 25% to 75% of dogs with erosive rheumatoid arthritis (Lewis, 1994; Pedersen et al, 2000).

Anti-nuclear antibodies (ANA) are autoantibodies directed at epitopes within the cell nucleus. In humans, a high ANA titre is indicative of, but not specific for, SLE, with 80% to 90% of SLE patients having raised ANA titres. Raised ANA titres are also noted in a variety of chronic inflammatory conditions. The authors of a study suggested measurement of ANA was not a useful diagnostic test in dogs with no major clinical or clinicopathologic abnormalities suggestive of SLE.

In contrast, there was a good chance results of the ANA would be positive and the dog would be found to have SLE if at least two major signs were present. Findings suggest it would be reasonable to limit use of the ANA assay to those dogs that have at least one major sign compatible with a diagnosis of SLE (Smee et al, 2007).

Synovial biopsy

Synovial biopsy can be used, as detailed previously, when representative synovial fluid samples cannot be obtained. It can also support the diagnosis of rheumatoid arthritis if histopathological changes typical of the disease process are found, such as periarticular fibrosis, synovial hyperplasia, villous hypertrophy and formation of pannus (Lewis, 1994; Pedersen et al, 2000).

Additional tests

Some cases of IMPA are complicated by extra-articular disease and there may be an indication for

additional investigations, such as electromyography and muscle biopsy, when polymyositis is suspected (Bennett and Kelly, 1987) or cerebrospinal fluid analysis when aseptic meningitis is suspected because of concurrent spinal pain (Webb et al, 2002).

However, the clinician should carefully consider the risk/benefit of additional tests, particularly if they carry some risk for the patient. If the outcome of the test will not change the management of the case then the value of the test becomes debatable (Innes, 2012).

Treatment

IMPA requires both treatment of the underlying immunologic trigger, if identified, and treatment of joint inflammation. Failure to achieve this goal may result in persistence or recurrence of clinical signs of IMPA (Colopy et al, 2010).

IMPA associated with significant concurrent systemic disease warrants treatment of the primary disorder first and synovitis second. Antimicrobial, antiparasitic, antineoplastic and nutritional therapies are prioritised. Analgesic and anti-inflammatory therapy can accompany treatment of the primary disorder if dictated by the level of discomfort associated with arthritis (Davidson, 2003).

While this is the ideal scenario it should be recognised in many instances no underlying cause is identified. This does not necessarily mean an underlying cause does not exist, but immunosuppression is normally the management option of choice in these instances.

Numerous regimes have been proposed and involve treatment with a single drug or combination treatment with corticosteroids, cytotoxic drugs or newer immunomodulating drugs (Colopy et al, 2010). Efficacy of individual drugs or dosages is difficult to assess as combination treatment is common and controlled prospective trials are unavailable. Regardless of treatment regimen, efficacy is best assessed by both clinical signs and cytologic evaluation of synovial fluid samples (Colopy et al, 2010).

Corticosteroids are the most widely used treatment for IMPA in dogs, with the most common medication used being immunosuppressive doses (2mg/kg to 4mg/kg) of prednisolone (Innes, 2012). Although initial response rate has been reported to be as high as 81% (Clements et al, 2004), adverse effects are common. Adverse effects range from polyuria, polydipsia and polyphagia to more serious complications such as diabetes mellitus, urinary tract infections, pyoderma and breakdown of collagen in tendons and ligaments (Colopy et al, 2010).

As a result, alternative or combination treatment is often sought, either to avoid complications associated with treatment with corticosteroids or for treatment of unresponsive disease (Bennett, 1995). Refractory cases, cases showing marked corticosteroid-
related side effects and those with erosive disease or multisystem disease may require more aggressive drug therapy (Abercromby et al, 2007). In these cases, an immunosuppressive drug

(most commonly cyclophosphamide or azathioprine) is often used in combination with prednisolone.

Combination therapy may result in remission in one to four weeks and the drugs are then usually continued for an additional one to three months before gradual withdrawal and reversion to low to moderate doses of prednisolone to maintain remission.

In some cases, side effects of therapy can be significant, requiring dose reduction or substitution of a different drug. Other drugs sometimes used for IMPA management in dogs and cats include ciclosporin and leflunomide (Innes, 2012).

Leflunomide is a newer immunomodulatory agent showing promise in the treatment of refractory immunological disease in dogs and cats; the dosage is 4mg/kg every 24 hours with adjustment on the basis of trough plasma levels of 20µg/mL. Leflunomide can be considered for IMPA unresponsive to conventional therapy (Pedersen et al, 2000). The efficacy and safety of leflunomide was studied in 14 dogs with IMPA (Colopy et al, 2010). The mean initial dose was 3mg/kg PO once daily and treatment duration for the starting dosage ranged from one to six weeks. Of 14 dogs treated, eight had complete resolution of clinical signs of IMPA initially, five had a partial response to treatment and one had minimal response to treatment. Adverse effects from treatment with leflunomide were not observed during the treatment period.

Information on the treatment of dogs with SLE is limited. Recommended protocols have included treatment with prednisolone only (Fournel et al, 1992), prednisolone with levamisole (Fournel et al, 1992) and prednisolone with cyclophosphamide (Bennett, 1987c). Cyclophosphamide should never be used for longer than four months because of the danger of haemorrhagic cystitis or bladder malignancy; if cytotoxic drugs are necessary for longer, azathioprine should be used in place of cyclophosphamide (Bennett, 1987c).

Therapy recommendations for erosive IMPA dictate combination corticosteroid and cytotoxic drug administration. Immunosuppressive doses of prednisolone are combined with either cyclophosphamide (50mg/m^2) or azathioprine (50mg/m^2). In general, cyclophosphamide is given for four consecutive days of each week. Azathioprine is given daily for two to three weeks, then on alternating days.

Cats are much more susceptible to azathioprine toxicity and its use cannot be recommended in this species.

Both cyclophosphamide and azathioprine require close monitoring for myelosuppression. Chlorambucil can be substituted for cyclophosphamide once remission has been attained if necessary in the dog (2mg/m^2 to 6mg/m^2 every 48 hours) or for azathioprine altogether in the cat (2mg every four days); Lewis, 1994; Pedersen et al, 2000).

Mycophenolate mofetil (20mg/kg/day to 40mg/kg/day) and levamisole (5mg/kg PO q48 hours) have also been used in combination with prednisolone in refractory cases or to treat relapses (Ohno et al, 2006; Clements et al, 2004). Combination treatment using 7mg of methotrexate and 70mg leflunomide given weekly orally has been used in cats with rheumatoid arthritis (Hanna, 2005). Seven of 12 cats showed marked improvement, usually within four weeks, and serious toxicity was not noted.

In human medicine, a therapeutic revolution has taken place in the treatment of rheumatoid arthritis and other IMPAs. TNF-? antagonists including infliximab, etanercept and adalimumab, have transformed the treatment of human rheumatoid arthritis and spondyloarthropathies (Wong et al, 2008) and have shown clear benefit in a series of randomised, controlled trials (Lin et al, 2008). Unfortunately, the high cost of these agents has precluded their use in other species. It seems unlikely such protein-based agents will be cost-effective enough to be developed for veterinary patients (Innes, 2012). Another specialised management method that has been reported in canine SLE patients is a plasmapheresis/immunoadsorption technique where immune complexes are removed from the circulation (Matus et al, 1985); although good results have been reported, this is a highly specialised therapeutic regime and is not widely available.

Surgical management is occasionally used in dogs and cats with IMPA, but case selection is paramount. Arthrodesis, excision arthroplasty and total joint replacement may all be considered as potential salvage procedures. However, such procedures should only be considered if justified by the potential functional benefits. For example, surgery may be justified if the disease is clinically localised to the joints to be operated, but not if there is major involvement of other major joints in the operative limbs.

In the author’s experience, carpal and tarsal arthrodesis have been the most frequently performed surgical procedures for IMPA patients (**Figure 4**). This reflects not only the preferential localisation of IMPA to these joints in many patients, but also the generally acceptable functional outcome following arthrodesis of these joints (Innes, 2012).

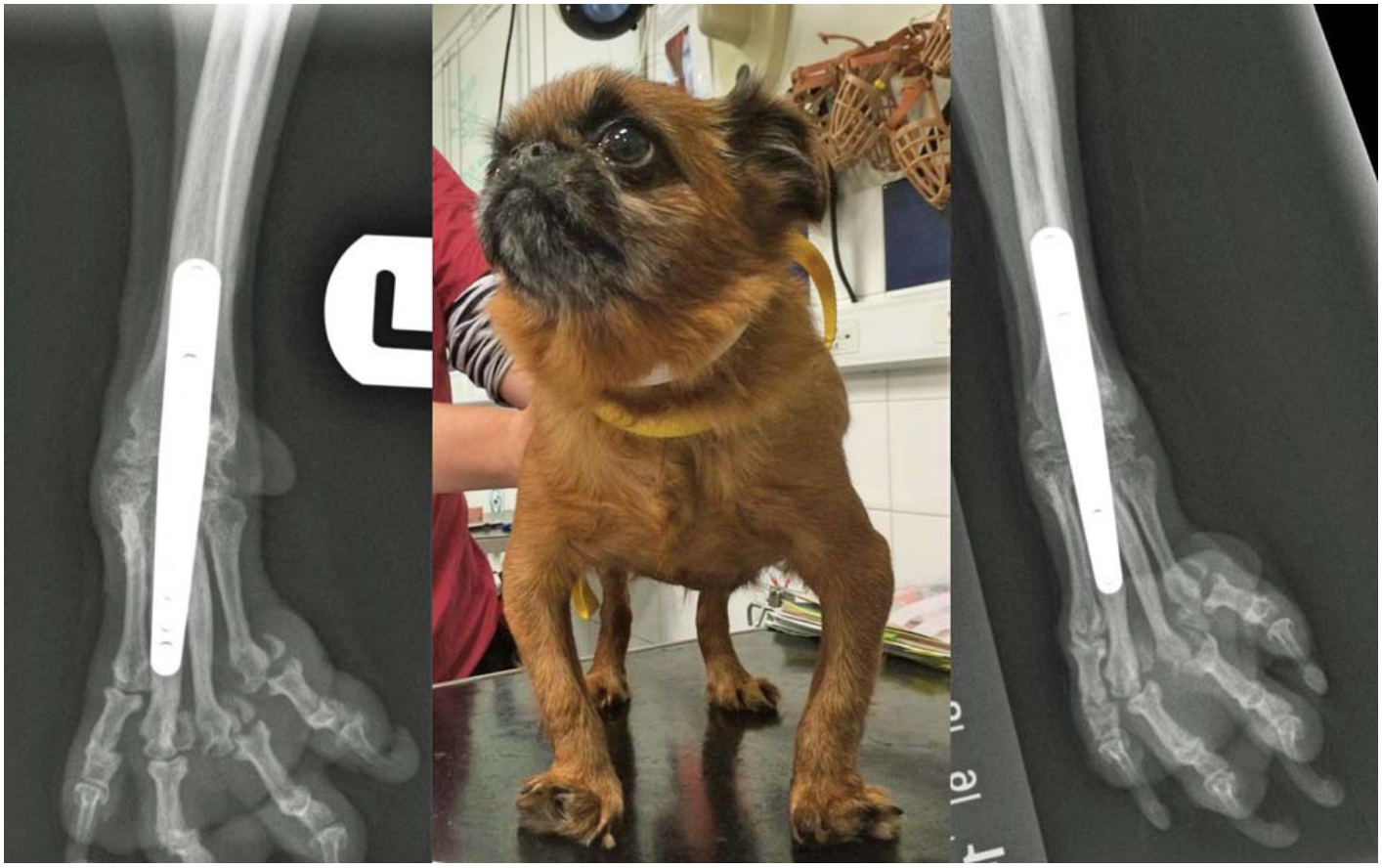

Figure 4. Dorsopalmar views of both left (left) and right (right) carpi and photograph following bilateral pancarpal arthrodesis in the same griffon Bruxellois seen in **Figures 1** and **3.** This was performed following control of the erosive polyarthritis using combination medical therapy to ameliorate the disability due to the severe bilateral carpal laxity, which was irreversible.

Synovectomy has been used as a procedure to reduce pain and possibly slow the progression of disease in people, but it has not been widely reported in the veterinary literature. The increase in arthroscopic surgery in small animals might make arthroscopic synovectomy worth considering in selected patients (Innes, 2012).

Monitoring

The success of drug therapy in achieving remission and the risks of adverse events should not be judged based on clinical findings alone. Regular assessment of clinicopathologic parameters, including haematology, serum biochemistry, synovial fluid analysis and urinalysis is necessary to monitor drug therapy in IMPA cases (Innes, 2012). Regular re-examination of dogs with suspected SLE is also necessary to check for additional system involvement (Bennett, 1987c).

Treatment often begins with immunosuppressive levels of corticosteroids alone. Two weeks after

initiation of therapy, arthrocentesis and synovial fluid cytology should be repeated. Effective control of IMPA is reflected by normalisation of synovial cell counts and predominance of mononuclear cells in addition to clinical improvement.

Corticosteroid doses are gradually tapered with continued improvement of clinical signs and normalisation of synovial fluid. Repeated arthrocentesis is important for assessing response to therapy and maintenance of remission. Combination therapy may be necessary as previously discussed if the initial response to corticosteroids is incomplete or if tapering doses result in relapse (Davidson, 2003).

Concerns have been raised repeated arthrocentesis might contribute to an inflammatory response that could subsequently interfere with cytologic interpretation of synovial fluid (Berg et al, 2009). However, a study investigating the effect of repeated arthrocentesis on cytologic analysis of synovial fluid in dogs found serial arthrocentesis did not appear to induce detectable neutrophilic joint inflammation, at least in healthy dogs (Berg et al, 2009). Serial arthrocentesis at three-week intervals was rarely associated with mild mononuclear joint inflammation, but not neutrophilic inflammation, and was not considered likely to impact on decisions regarding the therapeutic plan in IMPA cases (Berg et al, 2009).

Some evidence suggests C-reactive protein may also be used to assess treatment efficacy (Kjelgaard-Hansen et al, 2006). C-reactive protein is one of the important acute phase proteins and its serum concentration increases rapidly in response to inflammation or tissue destruction (Ceron et al, 2005). This could have a positive effect on management of IMPA cases in enabling early detection of undesirable inflammatory activity unbiased by treatment (Kjelgaard-Hansen et al, 2006). A retrospective study looking at the use of
C-reactive protein in monitoring of canine polyarthritis found it can be used as both a diagnostic aid for IMPA and also as an index for therapeutic response in IMPA cases (Ohno et al, 2006). Interestingly, the initial response of C-reactive protein to corticosteroid treatment also seemed to be useful as a prognostic factor with respect to disease course and likelihood of being able to discontinue immunosuppressive drugs (Ohno et al, 2006).

Prognosis

Limited information is available on the success rates of treatment for canine and feline IMPA and the prognosis appears to vary.

The largest case series reported to date for canine idiopathic type-one IMPA included 39 dogs (Clements et al, 2004). In this cohort, chemotherapeutic immunosuppression resulted in complete cure in 56% of dogs. While 81% responded initially to treatment with prednisolone, 31% of these dogs subsequently relapsed or required continuous anti-inflammatory treatment or were euthanised because of persistent disease (Clements et al, 2004). Continuous medication was required in seven of 39 dogs, relapses were treated successfully in five of 39 dogs and six of 39 dogs died or

were euthanised as a result of disease. Thus, most dogs with type-one IMPA responded to initial immunosuppressive treatment, but approximately one-third of dogs relapsed, required further treatment or both.

In the author's experience, once relapse occurs, control of disease the second time around can be more challenging to achieve and combination therapy may be more likely to be required.

The prognosis for cases of polyarthritis/polymyositis syndrome is considered to be worse than for non-erosive polyarthritis due to the presence of concomitant muscle involvement (Bennett and Kelly, 1987). Treatment in the six cases reported in one study was with prednisolone and cyclophosphamide for two months. Two cases had a poor response to treatment and were euthanised, two cases improved initially, but relapsed after completing treatment requiring further courses of prednisolone to control the condition, and two cases responded well, apparently making a complete recovery with no relapses noted during a 12-month follow-up (Bennett and Kelly, 1987).

The prognosis for cases of canine SLE must be guarded. The prognosis following treatment with corticosteroids in isolation is particularly so, with potentially a better prognosis for achieving remission with combination therapy (Fournel et al, 1992). Many cases will require constant medication or undergo relapse once treatment has finished (Bennett, 1987c)

Feline IMPA (types one to four) seems to follow a similar pattern, but has a somewhat more guarded prognosis. In one series, five of 13 cats made a complete recovery, but the remaining animals were euthanised within a short time frame (Bennett and Nash, 1988); these included four cats with paraneoplastic IMPA (type four).

Canine erosive polyarthritis has a guarded prognosis. Management is challenging, but may be more successful if cases are diagnosed and treated earlier (Davidson, 2003).

Aggressive combination immunosuppressive therapy is indicated to slow progression; to postpone joint subluxation, luxation, ankylosis and collapse and to minimise periarticular osteophyte production. These changes are irreversible. Caution must be used to ensure therapy does not result in serious complications, such as refractory sterile haemorrhagic cystitis, viral relapse, myelosuppression or opportunistic bacterial sepsis.

Therapy can be expected to continue at high dosages for three to six months and at maintenance levels for months to years (Davidson, 2003). In a series of 30 cases, none made a complete recovery, despite immunosuppressive treatment with corticosteroids with or without gold injections (Bennett, 1987). Lameness or stiffness persisted in all cases. Semierosive polyarthritis of greyhounds has a poor prognosis (Davidson, 2003).

Very little information exists on feline erosive progressive polyarthritis, but it is considered to have a guarded prognosis. However, more recent combination treatment protocols are showing promise

here (Hanna, 2005).

References

- Abercromby R, Innes J and May C (2007). Arthritis. In Houlton JCJ, Innes JF, Langley-Hobbs S (eds), *BSAVA Manual of Canine and Feline Musculoskeletal Disorders*, BSAVA, Cheltenham.
- Bell SC, Carter SD, May C et al (1993). IgA and IgM rheumatoid factors in canine rheumatoid arthritis, *J Small Anim Pract* **34**(6): 259-264.
- Bennett D (1995). Treatment of immune-based inflammatory arthropathies of the dog and cat. In Bonagura JD (ed), *Kirk's Current Veterinary Therapy XII*, W B Saunders, Philadelphia, PA: 1,188-1,196.
- Bennett D (1987). Immune-based erosive inflammatory joint disease of the dog – canine rheumatoid arthritis. 1. Clinical, radiological and laboratory investigations, *J Small Anim Pract* **28**(9): 779-797.
- Bennett D (1987b). Immune-based nonerosive inflammatory joint disease of the dog. 3. Canine idiopathic polyarthritis, *J Small Anim Pract* **28**(10): 909-928.
- Bennett D (1987c). Immune-based nonerosive inflammatory joint disease of the dog. 1. Canine systemic lupus erythematosus, *J Small Anim Pract* **28**(10): 871-889.
- Bennett D and Kelly DF (1987). Immune-based nonerosive inflammatory joint disease of the dog. 2. Polyarthritis polymyositis syndrome, *J Small Anim Pract* **28**(10): 891-908.
- Bennett D and May C (1995). Joint diseases of dogs and cats. In Ettinger S J and Feldman E C (eds), *Textbook of Veterinary Internal Medicine* (4th edn), Saunders, Philadelphia, PA: 2,032-2,077.
- Bennett D and Nash AS (1988). Feline immune-based polyarthritis – a study of 31 cases, *J Small Anim Pract* **29**(8): 501-523.
- Berg RIM, Sykes JE, Kass PH and Vernau W (2009). Effect of repeated arthrocentesis on cytologic analysis of synovial fluid in dogs, *J Vet Intern Med* **23**: 814-817.
- Carter SD, Bell SC, Bari ASM et al (1989). Immune-complexes and rheumatoid factors in canine arthritides, *Ann Rheum Dis* **48**: 986-991.
- Ceron JJ, Eckersall PD and Martynez-Subiela S (2005). Acute phase proteins in dogs and cats: current knowledge and future perspectives, *Vet Clin Pathol* **34**(2): 85-99.
- Clements DN, Gear RNA, Tattersall J et al (2004). Type I immune-mediated polyarthritis in dogs: 39 cases (1997–2002), *J Am Vet Med Assoc* **224**(8): 1,323-1,327.
- Colopy SA, Baker TA and Muir P (2010). Efficacy of leflunomide for treatment of immune-mediated polyarthritis in dogs: 14 cases (2006-2008), *J Am Vet Med Assoc* **236**(3): 312-318.
- Davidson AP (2003). Immune-mediated polyarthritis. In Slatter DH (ed), *Textbook of Small Animal Surgery* (3rd edn), WB Saunders, Philadelphia, PA: 2,246-2,250.
- De Haan JJ and Andreasen CB (1992). Calcium crystal-associated arthropathy (pseudogout) in a dog, *J Am Vet Med Assoc* **200**(7): 943-946.
- Dougherty SA, Center SA, Shaw EE et al (1991). Juvenile-onset polyarthritis syndrome in

akitas, *J Am Vet Med Assoc* **198**(5): 849.
- Dunn KJ and Dunn JK (1998). Diagnostic investigations in 101 dogs with pyrexia of unknown origin, *J Small Anim Pract* **39**(12): 574.
- Fournel C, Chabanne L, Caux C et al (1992). Canine systemic lupus-erythematosus: a study of 75 cases, *Lupus* **1**(3): 133-139.
- Gibson NR, Carmichael S, Li A et al (1999). Value of direct smears of synovial fluid in the diagnosis of canine joint disease, *Vet Rec* **144**(17): 463-465.
- Giger U et al (1985). Sulfadiazine-induced allergy in six Doberman pinschers, *J Am Vet Med Assoc* **186**(5): 479-484.
- Hanna FY (2005). Disease modifying treatment for feline rheumatoid arthritis, *Vet Comp Orthop Traumatol* **18**(2): 94-99.
- Hopper PE (1993). Immune-mediated joint diseases. In Slatter DH (ed), *Textbook of Small Animal Surgery* (2nd edn), Saunders, Philadelphia, PA: 1,928-1,937.
- Houlton JEF and Jefferies AR (1989). Infective polyarthritis and multiple discospondylitis in a dog due to *Erysipelothrix rhusiopathiae*, *J Small Anim Pract* **30**(1): 35-38.
- Innes JF (2012). Arthritis. In Tobias KM and Johnston SA (eds), *Veterinary Surgery: Small Animal*, Saunders Elsevier, Missouri, MO: 1,096-1,106.
- Jacques D, Cauzinille L, Bouvy B and Dupre G (2002). A retrospective study of 40 dogs with polyarthritis, *Vet Surg* **31**(5): 428-434.
- Kjelgaard-Hansen M, Jensen A L, Houser GA, Jessen L R and Kristensen A T (2006). Use of serum-C reactive protein as an early marker of inflammatory activity in canine type II immune-mediated polyarthritis: case report, *Acta Veterinaria Scandinavica* **48**: 9.
- Lees GE et al (1986). Polyarthritis associated with sulfadiazine administration in a Labrador retriever dog, *Southwest Vet* **37**: 14.
- Lewis RM (1994). Rheumatoid arthritis, *Vet Clin North Am: Small Anim Pract* **24**(4): 697-701.
- Lin J, Ziring D, Desai S et al (2008). TNF alpha blockade in human diseases: an overview of efficacy and safety, *Clin Immunol* **126**(1): 13-30.
- Little CJL and Carmichael S (1990). Trimethoprim-sulphonamide hypersensitivity in dogs, *Vet Rec* **127**(18): 459-460.
- Matus RE, Gordon BR, Leifer LE, Saal S and Hurvitz A (1985). Plasmaphoresis in five dogs with systemic immune-mediated disease, *J Am Vet Med Assoc* **187**(6): 595-599.
- Ohno K, Yokoyama Y, Nakashima K, Setoguchi A, Fujino Y and Tsujimoto H (2006). C-reactive protein concentration in canine idiopathic polyarthritis, *J Vet Med Sci* **68**(12): 1,275-1,279.
- Parry BW (1999). Synovial fluid. In Cowell RL, Tyler RD and Meinkoth JH (eds) (1999). *Diagnostic Cytology and Hematology of the Dog and Cat* (2nd edn), Mosby, St Louis, MO: 104-119.
- Peddle G and Sleeper MM (2007). Canine bacterial endocarditis: a review, *J Am Anim Hosp Assoc* **43**(5): 258-263.
- Pedersen NC et al (2000). Joint diseases of dogs and cats. In Ettinger SJ, Feldman EC (eds), *Textbook of Veterinary Internal Medicine* (5th edn), WB Saunders, Philadelphia:

1,862.
- Pedersen NC et al (1976). Non-infectious canine arthritis: rheumatoid arthritis, *J Am Vet Med Assoc* **169**(3): 295-303.
- Pedersen NC et al (1976b). Non-infectious canine arthritis: the inflammatory non-erosive arthritides, *J Am Vet Med Assoc* **169**(3): 304-310.
- Rondeau MP, Walton RM, Bissett S, Drobatz KJ and Washabau RJ (2005). Suppurative, nonseptic polyarthropathy in dogs, *J Vet Intern Med* **19**(5): 654-662.
- Roush JK, Manley PA and Dueland R T (1989). Rheumatoid arthritis subsequent to Borrelia burgdorferi infection in two dogs, *J Am Vet Med Assoc* **195**(7): 951-953.
- Scott DW et al (1983). Canine lupus erythematosus: 1: systemic lupus erythematosus, *J Am Anim Hosp Assoc* **19**: 461-179.
- Smee NM, Harkin KR and Wilkerson MJ (2007). Measurement of serum antinuclear antibody titer in dogs with and without systemic lupus erythematosus: 120 cases (1997-2005), *J Am Vet Med Assoc* **230**(8): 1,180-1,183.
- Spreng D (1993). Leishmanial polyarthritis in two dogs, *J Small Anim Pract* **34**(11): 559-563.
- Stull JW, Evason M, Carr AP and Waldner C (2008). Canine immune-mediated polyarthritis: clinical and laboratory findings in 83 cases in western Canada (1991-2001), *Can Vet J* **49**(12): 1,195-1,203.
- Thilagar S, Basheer AM and Dhanapalan P (1990). An unusual case of ehrlichiosis associated with polyarthritis in a dog – a case report, *Indian Vet J* **67**(3): 267-268.
- Thoren-Tolling K and Ryden L (1991). Serum autoantibodies and clinical/pathological features in German shepherd dogs with a lupus like syndrome, *Acta Vet Scand* **32**(1): 15-26.
- Webb AA, Taylor SM and Muir GD (2002). Steroid-responsive meningitis-arteritis in dogs with noninfectious, nonerosive, idiopathic, immune-mediated polyarthritis, *J Vet Intern Med* **16**(3): 269-273.
- Woodard JC, Riser WH, Bloomberg MS et al (1991). Erosive polyarthritis in two greyhounds, *J Am Vet Med Assoc* **198**(5): 873-876.
- Wong M, Ziring D, Korin Y et al (2008). TNF-alpha blockade in human diseases: mechanisms and future directions, *Clin Immunol* **126**(2): 121.