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Type I immune-mediated polyarthritis with azathioprine therapy in a Shih-tzu dog

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Abstract : A 2-month-old female Shih-tzu dog was referred because of lameness, exercise intolerance, depression, elbow and stifle joint swelling. Physical examination, complete blood counts, serum-chemistry, radiography, synovial fluid analysis, antinuclear antibody test, and rheumatoid factor measurement were initiated. On radiography, soft tissue swelling of elbow and stifle joints without erosiveness were founded. The results of synovial fluid analysis revealed severe neutrophilic pleocytosis (nondegenerative), decreased viscosity, increased turbidity, positive on mucin-clot test, and negative on bacterial culture. The results of rheumatoid factor measurement and antinuclear antibody test were negative and below 1 : 40, respectively. Based on all tests, we diagnosed this case as juvenile onset type I immune-mediated polyarthritis. Azathioprine (1 mg/kg body weight, per os q 24 h, for 4 weeks) was then administered and clinical signs improved gradually. Four weeks after azathioprine administration, clinical signs were disappeared. This report describes the clinical findings, imaging characteristics, synovial fluid findings, and other laboratory results of type I immune-mediated polyarthritis and successful management with azathioprine therapy.

Key Words : azathioprine, dog, type I immune-mediated polyarthritis (IMPA)

Introduction

Canine idiopathic immune-mediated polyarthritis (IMPA) is differentiated into 4 subgroups; those with polyarthritis alone (type I), those associated with an infective disease process elsewhere in the body (type II), those in association with gastro-intestinal disease (type III) and those in association with malignant neoplastic disease (type IV) [2, 4, 6]. Idiopathic, noninfectious and nonerosive arthritis was first reported in 1976 [13], and idiopathic immune-mediated polyarthritis is now recognized as the most common type of immune-mediated arthritis condition in dogs [2, 6].

Case Report

A 2-month-old female Shih-tzu dog was referred because of lameness, exercise intolerance, lethargy and elbow and stifle joints swelling with pain. Abnormal gait was first noticed 1 week before presentation. Clinical signs such as depression, exercise intolerance and anorexia were developed and worsened progressively. Physical examination revealed all stifle and elbow joints swelling and painful reaction on those joints. Body temperature was within normal range.

The patient was not vaccinated, thus we checked canine distemper virus (CDV) antigen in serum through reverse-transcriptase polymerase chain reaction (RT-PCR) to rule out canine distemper virus infection and then result was negative.

The results of complete blood count (CBC) profiles, serum chemistry profiles and urinalysis were normal. Radiographic findings of elbow and stifle joints revealed soft tissue swelling and nonerosiveness (Fig. 1). Thorax,

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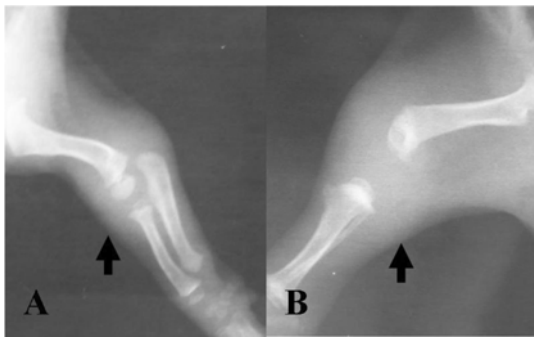

Fig. 1. Radiographic findings of the left elbow (A) and right stifle joints (B). Radiographs of clinically affected joints revealed soft tissue swelling without erosiveness (arrow).

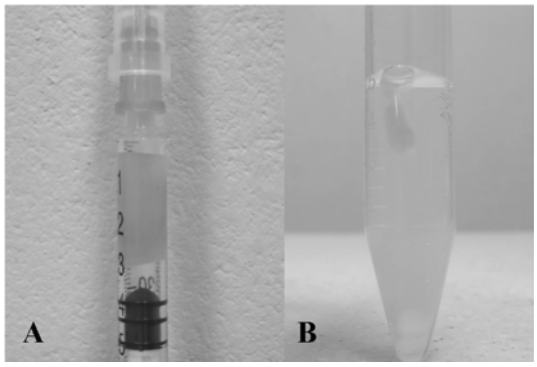

Fig. 2. Synovial fluid of this case. A: Light-pink colored synovial fluid was collected. Viscosity was decreased. B: The result of mucin-clot test was positive.

abdomen and other joints showed no remarkable findings on radiography. Arthrocentesis was performed on left elbow joint and right stifle joint. Turbidity, protein concentration (4 g/dl; reference range; < 2.5 g/dl) and white blood cell counts (5.0×10^9 cells/L; reference range: $< 3.0 \times 10^9$ cells/L) were increased. Viscosity was decreased and mucin-clot test was positive on synovial fluid analysis (Fig. 2). Non-degenerated neutrophils were predominated on cytologic examination (non-degenerative neutrophilic pleocytosis) (Fig. 3). In addition, bacterial and fungal cultures were performed on the synovial fluid, and the results were all negative.

Rheumatoid factor (RF) measurement and antinuclear antibody (ANA) test were performed to rule out rheumatoid arthritis and systemic lupus erythematosus. Results of these tests were negative and below 1 : 40, respectively (AnTech Diagnostics, USA).

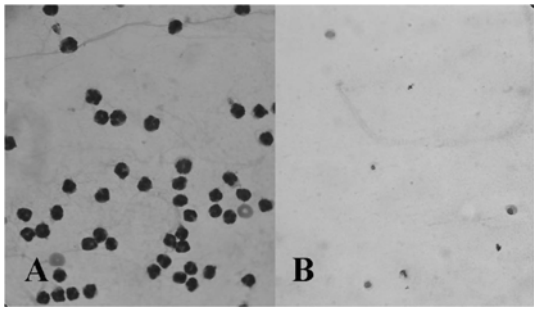

Fig. 3. Synovial fluid cytology of this case. A: Non-degenerative neutrophils were predominated before immune suppressive therapy. B: Neutrophils were disappeared after azathioprine therapy. Few monocytoid cells were shown.

Based on all tests, we diagnosed this case as juvenile onset type I immune-mediated polyarthritis.

Azathioprine (1 mg/kg body weight, per os q 24 h) therapy was initiated and clinical signs were improved gradually. Four weeks after azathioprine administration, clinical signs were disappeared. Until recently (> 1 year after diagnosis), clinical signs were not relapsed.

Discussion

Juvenile onset IMPA was not common in young dogs. Juvenile onset polyarthritis has been reported in the Akita [4]. However, dogs of Chinese Shar Pei and Akita breeds were the breed-associated immune-mediated polyarthritis [4, 6]. Generally, non-erosive immune-mediated polyarthritis have been reported in young to middle aged dogs [2, 4, 6, 9, 13]. In a recent report [6], mean ± SD age at referral was 4.9 ± 2.5 years in type I IMPA, however this case was referred at 2 months old.

Gastro-intestinal signs including vomiting, diarrhea, anorexia were observed in type III IMPA patients. Systemic or gastro-intestinal diseases were ruled out based on normal CBC profiles, serum-chemistry profiles, urinalysis, and radiography in this case. Therefore, we suspected that anorexia in this case would be induced by pain.

Several characteristics of this case were similar to previous reports about type I IMPA [2, 4, 6]. However, some characteristics were different from the previous reports.

Stiffness was the most common clinical sign in type I IMPA patients and affected dogs showed pyrexia, lymphadenopathy, depression, exercise intolerance and

lameness [6]. Most of them had clinical signs of joint involvement (swelling, pain, or heat) in all limbs [2, 6]. Carpal joints were most commonly affected, followed by hock joints, stifle joints, and elbow joints. The clinical signs in the present case were lameness, exercise intolerance, and lethargy. Moreover, affected joints were both elbow and stifle joints and indicated swelling with pain. Other joints showed normal appearances. The absence of erosive changes, presence of soft tissue swelling and joint effusion on radiography were general indications in type I IMPA [6]. The radiographic finding of this case was soft tissue swelling of affected joints.

Various results of blood profiles and urinalysis were reported [2, 4, 6], and these tests showed normal findings in the present case. Results of RF measurements and ANA test in most immune-mediated polyarthritis cases were negative or insignificant levels [1, 2, 5, 6]. The present case showed similar results for both RF and ANA (negative and a low titer, respectively).

Synovial fluid analysis is important diagnostic tool in IMPA cases. The synovial fluid from affected joints was generally increased in quantity, watery and turbid in appearance. The mucin clot test showed generally poor result, however positive result was occasionally revealed. The white blood cell count was usually high, and most of the white blood cells were polymorphonuclear cells [2-4, 6, 8, 9, 11-13]. The synovial fluid analysis in our case indicated similar results to previous reports.

Vaccination as a trigger for immune-mediated disease in dogs has been suggested [6, 7, 10]. One report [10] described that polyarthritis developed shortly after vaccination in 4 dogs. These dogs showed a sudden onset of lameness with several painful and swollen joints 3-15 days after vaccination. Our patient was not vaccinated, therefore vaccination was not a cause for IMPA in this case.

Most cases with type I IMPA responed to initial immunosuppressive therapy, however more than 28% of cases relapsed and required further treatment [2, 6, 14]. Final outcome results of previous reports [2, 6] were as following; slightly higher rates of recovery (44 to 56%), requirement for continuous medication (11 to 18%), and slightly lower rates of relapsed treated successfully (13 to 21%), and euthanasia or death (15 to 24%).

In other words, the ultimate goal of treatment is resolution of disease without recurrence. Numerous immune suppressive drugs have been used in IMPA. In one study [2], no single treatment regimen was completely successful. Most IMPA dogs responded to immunosuppression with prednisolone (81%), although 31% of these dogs subsequently had relapsed or required continuous anti-inflammatory treatment or were euthanized because of persistent disease [2, 6]. We choose sole therapy with azathioprine and the result was successful. Moreover, clinical signs have not relapsed for 1 year.

Conclusion

In conclusion, this report describes the clinical findings, imaging characteristics, synovial fluid findings, and other laboratory results of type I IMPA and successful management with azathioprine therapy.

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References

1. **Bennett D.** Immune-based erosive inflammatory joint disease of the dog: canine rheumatoid arthritis. 1. Clinical, radiological and raboratory investigations. J Small Anim Pract 1987, **28**, 779-797.
2. **Bennett D.** Immune-based non-erosive inflammatory joint disease of the dog. 3. Canine idiopathic polyarthritis. J Small Anim Pract 1987, **28**, 909-928.
3. **Brannan SR, Jerrard DA.** Synovial fluid analysis. J Emerg Med 2006, **30**, 331-339.
4. **Callum WH, Paul AM.** Immune-mediated Arthritis. In: Birchard SJ, Sherding RG (eds.). Saunders Manual of Small Animal Practice. 3rd ed. pp. 1227-1232, Saunders, Philadelphia, 2006.
5. **Choi E, Shin I, Youn H, Lee C.** Development of canine systemic lupus erythematosus model. J Vet Med A Physiol Pathol Clin Med 2004, **51**, 375-383.
6. **Clements DN, Gear RN, Tattersall J, Carmichael S, Bennett D.** Type I immune-mediated polyarthritis in dogs: 39 cases (1997-2002). J Am Vet Med Assoc 2004, **224**, 1323-1327.
7. **Duval D, Giger U.** Vaccine-associated immune-mediated hemolytic anemia in the dog. J Vet Intern

Med 1996, **10**, 290-295.

8. **Gibson NR, Carmichael S, Li A, Reid SW, Normand EH, Owen MR, Bennett D.** Value of direct smears of synovial fluid in the diagnosis of canine joint disease. Vet Rec 1999, **144**, 463-465.
9. **Jacques D, Cauzinille L, Bouvy B, Dupre G.** A retrospective study of 40 dogs with polyarthritis. Vet Surg 2002, **31**, 428-434.
10. **Kohn B, Garner M, Lübke S, Schmidt MFG, Bennett D, Brunnberg L.** Polyarthritis following vaccination in four dogs. Vet Comp Orthop Traumatol 2003, **16**, 6-10.
11. **MacWilliams PS, Friedrichs KR.** Laboratory evaluation and interpretation of synovial fluid. Vet Clin North Am Small Anim Pract 2003, **33**, 153-178.
12. **Pascual E, Jovani V.** Synovial fluid analysis. Best Pract Res Clin Rheumatol 2005, **19**, 371-386.
13. **Pedersen NC, Weisner K, Castles JJ, Ling GV, Weiser G.** Noninfectious canine arthritis: the inflammatory, nonerosive arthritides. J Am Vet Med Assoc 1976, **169**, 304-310.
14. **Renberg WC.** Pathophysiology and management of arthritis. Vet Clin North Am Small Anim Pract 2005, **35**, 1073-1091.