Veterinary Autoimmunity

Autoimmune Diseases in Domestic Animals

LAUREL J. GERSHWIN

Department of Pathology, Microbiology, and Immunology, School of Veterinary Medicine, University of California, Davis, California, USA

ABSTRACT: The first spontaneous animal model of autoimmunity was the New Zealand black mouse, discovered in 1959. Interestingly, although several models of induced autoimmunity were demonstrated in a variety of rodents, the recognition of autoimmune disease in dogs came somewhat later. Dog breeding and selection of traits within certain dog breeds have become an important enterprise with intensive husbandry and selection criteria being applied to each breed standard. This has resulted in breeding for specific phenotypic characteristics. This selection has inadvertently led to the propagation of a number of autoimmune diseases in dogs. For example, systemic lupus erythematosus (SLE), autoimmune hemolytic anemia and thrombocytopenia, autoimmune myasthenia gravis, and diabetes mellitus are now fairly common. In the final analysis, the appearance of autoimmunity in dogs reflects their breeding selection and illustrates the importance of genetics in the development of autoimmune disease.

KEYWORDS: autoimmune disease; canine; feline; equine; systemic lupus erythematosus; immune-mediated disease; antinuclear antibody; case reports

INTRODUCTION

The concept of "one medicine" has become a popular idea in recent years, due to the realization that many diseases that occur in human patients are also recognized in nonhuman species, specifically domestic animals. While this concept is sufficiently broad to include infectious diseases, allergic/atopic disease, and developmental diseases, autoimmunity is high on the list of pathogenic etiology that is similar between humans and domestic animals. This article reviews some of the more common autoimmune diseases in animals, which have been illustrated with case histories.

Address for correspondence: Laurel J. Gershwin, D.V.M. Ph.D., Department of Pathology, Microbiology, and Immunology, School of Veterinary Medicine, University of California, Davis, One Shields Ave., Davis, CA 95616. Voice: 530-752-6643; fax: 530-752-3349.
ljgershwin@ucdavis.edu

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The overlapping factors of environment and genetics are important in autoimmune disease in both human and animal patients. While we are often unsure of the causal factors we do find higher incidence of certain autoimmune diseases in some breeds of dogs. For example, just as there is a correlation between HLA type and diabetes mellitus in humans we see an increased incidence of this disease in certain canine families, particularly those with the DLA haplotype DRB1009, DQA1001, and DQB1008.[1] For example, autoimmune thyroiditis occurs with increased frequency in Great Danes, Golden Retrievers, Cocker Spaniels, Old English Sheepdogs, and Beagles (to name a few).[2,3] Some of these breeds are susceptible to multiple autoimmune diseases, such as the Old English Sheep Dog and autoimmune hemolytic anemia. In addition, the predominance of systemic lupus erythematosus (SLE) in human females is also observed in female canine patients. SLE is also commonly seen more frequently in certain breeds.[2,4] While less common in cats than in dogs, autoimmune diseases occur in this species as well.[5] The occurrence of autoimmune myasthenia gravis in dogs is further evidence that autoimmunity in animals can affect a single system as well as multiple systems as seen in SLE. The hallmark observation of antiacetylcholine receptor antibodies has been well validated in spontaneously occurring canine myasthenia gravis.[6] A diagnosis of autoimmune thrombocytopenia in dogs is supported by the finding of a positive immunofluorescence test for antimegakaryocyte antibodies as seen in Case 3.[7]

CASE REPORTS

SLE

The criteria for diagnosis of this disease in human patients include a positive antinuclear antibody (ANA) test and involvement of two or more body systems. Diagnosis of SLE in canine patients follows the same rule.[2,8] Most commonly canine SLE patients present either with hemolytic anemia, skin disease, or shifting leg lameness. The following cases demonstrate this disease in the canine patient.

Case 1: Example of a Canine SLE Case

Signalment: A 9-year-old male Bernese Mountain Dog is presented to the veterinarian for weakness, joint pain, and fever.

After physical examination the following findings were noted: The patient was lethargic, unable to rise, febrile (T = 105.2°F), and panting heavily with stridor. Bilateral carpal pain was noted.

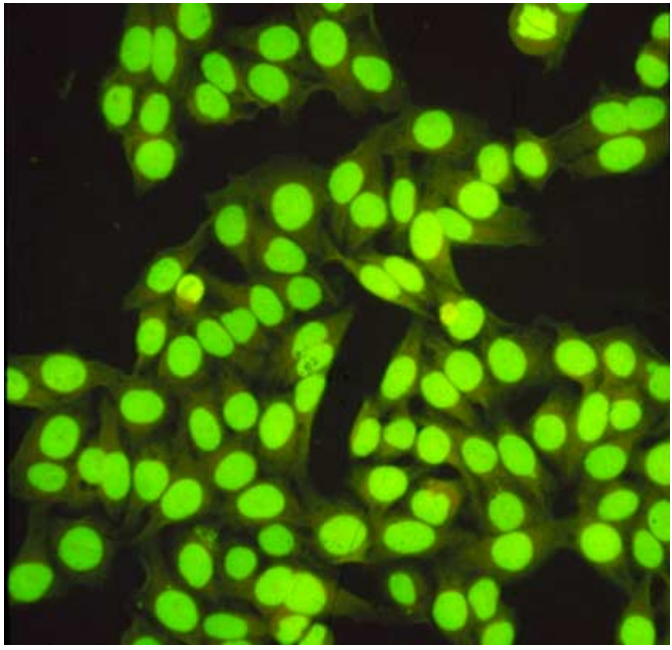

FIGURE 1. Positive indirect immunofluorescence test on dog serum demonstrating the presence of antinuclear antibodies (ANA) with a homogeneous pattern.

Laboratory data: The CBC showed a hematocrit of 39.5%, WBC of 26,600/μL, with a differential consisting of: segmented neutrophils 98%, lymphocytes 1%, and eosinophils 1%. Chemistry panel revealed: Alk-P = 903 (N = 10–150), ALT = 121 (N = 5–60), AST = 72 (N = 5–55), CK = 214 (N = 10–200), GGT = 15 (N = 0–10), lipase = 1344 (N = 100–500), albumin = 2.3 (N = 2.6–4.3, TCO_2 = 15 (N = 17–24), and T4 = 0.7 μg/dL. Urinalysis: S.G. = 1.051 g/dL, 3+ protein, pH = 8.5, and a protein:creatinine ratio of 31.26. A right carpal joint tap showed marked neutrophilic inflammation. Titers for tick-borne diseases were performed as these often cause transient positive ANA titers. These were negative for Borreliosis and Rocky Mountain Spotted Fever. An antinuclear antibody titer was positive at 1:320 with a homogeneous pattern (FIG. 1). The diagnosis of SLE was made.

Case 2: Second Example of a Canine SLE Case

Signalment: An 8-year-old spayed female poodle cross presented with erosive lesions on nasal planum and footpads.

After physical examination the following physical findings were noted: The dog was bright and alert, but walked with difficulty due to erosive

lesions on the footpads. On the nasal planum there were erosive lesions (FIG. 2A, B).

Laboratory data: The ANA was positive at 1:128. A biopsy of affected skin was stained with immunofluorescence for the deposition of IgG and complement. It was positive for both, at dermal–epidermal junction ("lupus band") (FIG. 3).

Cases 1 and 2 illustrate two presentations of canine SLE. The first case showed polyarthritis, with inflammatory, nonseptic joints. It also showed a 3+ protein in the urine, which was very likely caused by glomerular damage from immune complex deposition. Case 2 had a dermatologic presentation with lesions on the face and the footpads. The immunofluorescence staining confirmed the immune nature of these lesions. The ANA in both cases was positive. The diagnosis of SLE was made.

FIGURE 2. (**A**) Dog with erosive lesions on nasal planum. (**B**) Same dog showing erosive lesions on footpads.

FIGURE 2. Continued.

Immune-mediated Thrombocytopenia

Case 3: Example of an Autoimmune Thrombocytopenia Case

Signalment: A 2-year-old female Vizsla presented with thrombocytopenia, hematemesis, and melena/diarrhea.

Pertinent history and physical exam findings: This dog was presented to the veterinarian after the owner had noted the presence of lumps on her back that were purplish and increasing in size. When the dog refused to eat, the owner examined her mouth and found the presence of petechiations on the oral mucosa. At this time the owner also noted similar lesions on the skin of the abdomen.

Pertinent physical exam findings: Upon presentation to the veterinarian the dog appeared generally alert and responsive. The body temperature was normal

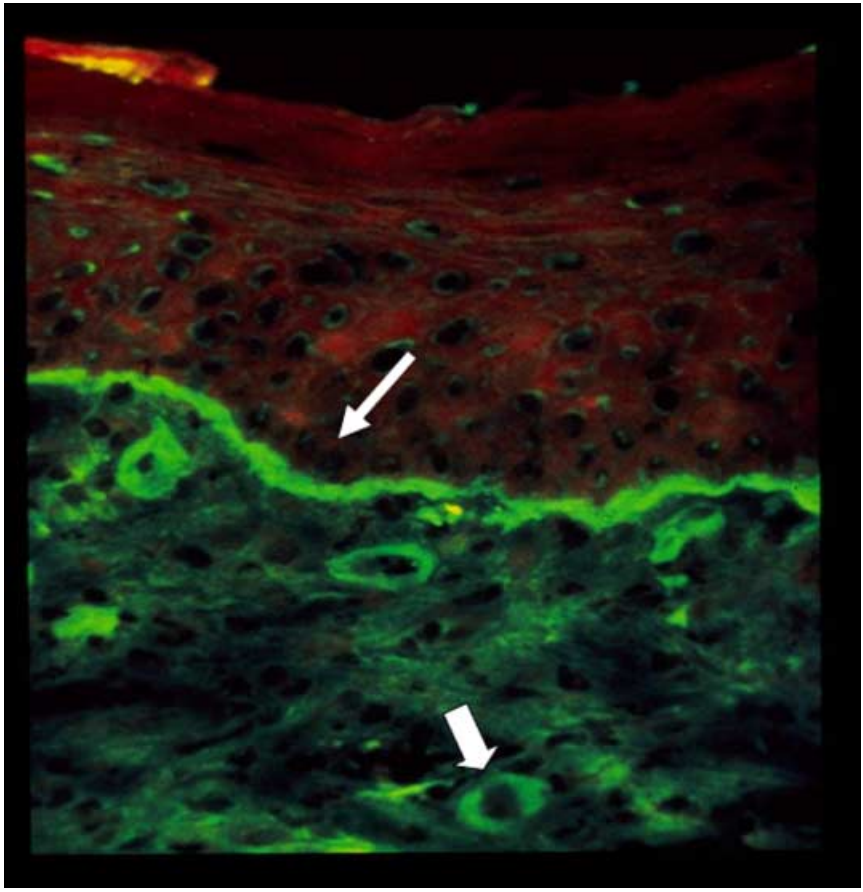

FIGURE 3. Immunofluorescence showing deposition of IgG at dermal–epidermal junction (*thin arrow*); and mononuclear cell with cytoplasmic IgG in dermis (*thick arrow*) in a skin biopsy from erosive lesions shown in FIGURE 2.

at 101.6°F. The heart and respiratory rates were normal at HR = 60 and RR = 28, and mucus membranes showed a healthy pink color with a capillary refill time normal at 1 s. Upon examination of the skin and hair coat it was noted that there were petechiations on the ventral abdomen, inside of the pinnae, and around the anus. Ecchymosis was noted on the medial aspect of the right stifle with central clearing. Subcutaneous masses were present on the dorsum and on right stifle (3–4 mm). Additional petechiae were noted on the gums and in the back of the throat. No oral or tonsillar masses were seen.

Laboratory data: An initial CBC revealed a severe thrombocytopenia <5000 (164,000–510,000) and elevated fibrinogen 332 (90–255), HCT 52.8 (37–55), and WBC 7200 (5700–16,300). An ophthalmology exam showed the

presence of iridal hemorrhage, which is highly suggestive of a systemic coagulopathy. There was no blood in the urine. A bone marrow aspirate was performed and it showed the presence of marked megakaryocytic hyperplasia, mild erythroid hypoplasia, mild-to-moderate plasma cell hyperplasia. Immunofluorescent staining for the presence of antimegakaryocyte antibody showed that as expected there were plasma cells showing 3+ to 4+ fluorescence. More importantly there were megakaryocytes showing fluorescence ranging in intensity from 1+ to 3+. This test was interpreted as being positive for antimegakaryocyte antibody. The diagnosis of autoimmune thrombocytopenia was made. In dogs, AITP can occur as a disease alone, with autoimmune hemolytic anemia, and as a component of SLE.

Case 4: Example of a Canine Rheumatoid Arthritis Case

Signalment: A 5-year-old spayed female Shetland sheepdog presented with chronic lameness in left foreleg.

Pertinent physical exam findings: On presentation to the veterinarian this dog showed a severe hyperextension of the flexor tendon and laxity of the carpus joint. There were indications that other joints were also affected. The dog was obese.

Radiology and joint survey: Examination revealed that the left and right shoulders and elbows did not show any abnormalities. In contrast, the left carpus showed the presence of soft tissue swelling and subluxation with the collapse of the radiocarpal and intercarpal joints. There was a periosteal response involving the proximal to mid diaphyseal portion of the second metacarpal bone. There was a small amount of soft tissue swelling present in the right carpus. Neither tarsus showed evidence of lesions.

Other tests: Joint fluid culture and sensitivity showed no growth. An ANA test was negative, and a rheumatoid factor latex agglutination test was weakly positive. This case was diagnosed as rheumatoid arthritis.

DISCUSSION

The cases presented demonstrate only a small segment of the autoimmune disease seen in domestic animals. More definitive diagnosis of these cases with determination of antigen specificity is progressing. Subgroups of canine antinuclear antibodies have recently been described and correlated with clinical findings.[9] The presence of positive ANA in bacterial or protozoan diseases has been documented.[10] Antigen specificity has also been examined for erythrocyte autoantibodies in dogs with autoimmune hemolytic anemia.[11] The relevance of the ANA test for diagnosis of autoimmune disease in dogs and other animals has often been questioned due to the presence of these antibodies in animals infected with several bacterial, protozoan, and tick-borne

pathogens.[10] The availability of other more specific assays will assist in more accurate diagnosis.

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