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LUPUS IN THE DOG

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INTRODUCTION

There are four basic presentations of lupus erythematosus in the dog: Systemic lupus erythematosus (SLE), discoid lupus erythematosus (DLE), exfoliative cutaneous lupus erythematosus (ECLE), and vesicular cutaneous lupus erythematosus (VCLE). Interestingly, the latter two have a striking predilection for certain breeds. All forms affect the basement membrane zone (BMZ) of the skin, with antibody-antigen (Ab-Ag) complex deposition initiating an inflammatory response. Immunofluorescence will generally show a positive reaction (i.e., deposition of the AB-AG complexes) along the BMZ.

SYSTEMIC LUPUS ERYTHEMATOSUS as its name describes, often affects other organs in addition to the skin. German Shepherds dogs, Collies and Shetland Sheepdogs may have a genetic predisposition. The Ab-Ag complexes are deposited in the BMZ-equivalent areas of the kidney, joints, and sometimes the liver or lungs. Blood dyscrasias may result. Renal involvement implies a poorer prognosis. Clinical signs of the skin include depigmentation, alopecia, and scaling; these may be confined to the nasal planum and face or affect all peri-orificial areas, or occasionally be generalized. Diagnosis is by clinical signs and histopathology, which shows an interface dermatitis, typified by a mononuclear lichenoid (directly underneath the basement membrane zone) pattern, hydropic degeneration, thickening of the basement membrane zone, pigmented incontinence (pigment dropping out of the epidermis into the dermis where it is engulfed by macrophages) and Civatte bodies (dyskeratotic cells in the epidermis). SLE cases frequently will have a positive anti-nuclear antibody (ANA) test, as well as rarer antibodies to specific nuclear antigens such as the one termed Ro.

Treatment generally involves some form of short-acting oral glucocorticoid. Usually this is prednisone or prednisolone, started at a dosage of 1 mg/kg given twice daily. This dosage is reduced slowly over the course of six to eight weeks to an every 48 hour regimen, ideally at 0.5 mg/kg. Dogs that have severe polyuria/polydipsia may be switched to oral methylprednisolone at dosages similar to those of prednisone. The author and others feel that some dogs may not be able to metabolize prednisone into the active drug, prednisolone. Usually, another medication is needed to control all the clinical signs. Often this is azathioprine, at a dosage of 2.2 mg/kg, given
orally once daily for one month, then every 48 hours thereafter. Azathioprine is a purine analog which functions as an antimetabolite, and also has anti-inflammatory effects. Azathioprine has a lag phase of four to six weeks before it reaches its full potential as an immunosuppressant drug. It is not good at inducing remission but rather at maintaining remission. Therefore, it is given concurrently with glucocorticoids but eventually allows the veterinarian to lower the dose (i.e. it is a "steroid-sparing" drug). Another such drug is chlorambucil: this drug, an alkylating agent, is similar to cyclophosphamide but does not cause the hemorrhagic cystitis so often seen with the latter drug. Its cost in the USA limits its use to small dogs. Its dosage is 0.1-0.2 mg/kg/day until there is at least 75% improvement in clinical signs. At this point, every other day administration of chlorambucil is initiated. If the disease is quiescent after several weeks, the dosage of chlorambucil is further reduced in a gradual manner. Chlorambucil is usually not good at inducing remission, therefore a glucocorticoid must be given concurrently.

Cyclosporine has also been used in the treatment of canine SLE – the author eagerly awaits a case series with long term follow-up.

DISCOID LUPUS ERYTHEMATOSUS (DLE) is common in dogs². It is most common in the long nose breeds (the author has never seen it in a bulldog). This is also a disease of young to middle aged-dogs. Clinical signs are usually limited to the face and most commonly involve depigmentation and ulceration of the nasal planum, the lips, the periorbital area, membrana nictitans, and oral cavity. Silver to grey well-circumscribed scaling areas may be seen on the inner pinna. In general, discoid lupus is more likely to show depigmentation and less likely to be encrusted, compared to pemphigus foliaceus. A variant occurs (most commonly in the Australian herding breeds) whereby the nose is eroded through to the cartilage and deforms the nasal septa; there is some controversy as to whether this is truly a variant of DLE, or something else. Differential diagnoses of nasal planum depigmentation comprises a long list, but includes other auto-immune cutaneous diseases, pyoderma, cutaneous lymphoma, dermatomyositis, and occasionally, deep fungal infections.

Diagnosis is based on biopsy which reveals an interface dermatitis, similar to SLE. An ANA test is negative. Dogs with DLE may have antibodies to the Ro antigen.¹

The author’s first choice to treat DLE has utilized the combination of tetracycline and niacinamide (called nicotinamide in Europe). The dosage is 500 mg of each drug given orally three times daily. If the dog is less than 10 kg, this dosage is reduced to 250 mg of each drug given orally three times daily. A lag phase exists before full effect, usually four to eight weeks. However, these drugs will induce as well as maintain remission. Once control of the disease is achieved the drugs may be reduced in some dogs to twice a day or even once a day therapy. Some dogs may need topical corticosteroids, such as 0.1% betamethasone bid to sid, or low doses (0.25 mg/kg every other day) of prednisolone for maximum control. The overall success rate in discoid lupus with this combination of niacinamide and tetracycline is 65-70%.³ Side effects of niacinamide and tetracycline are uncommon but vomiting, diarrhea, anorexia and lethargy have been noted, usually due to the niacinamide. Very rare cases in dogs have been seen with hepatotoxicity or neurologic signs (hindlimb weakness/inability to rise). It should be emphasized that in many dogs, restriction to sun exposure is helpful. Doxycycline (5mh/kg bid) may be used in place of tetracycline.
A topical treatment for DLE that the author has been impressed with in a small number of cases is tacrolimus 0.1% ointment [Protopic: Fujisawa], applied initially twice daily, then reduced to daily or every other day frequency depending upon response. In a number of cases this may be the only treatment necessary. This is a semi-expensive product in the USA (30 gm tube = $70-120). It seems to be very well tolerated in the dog, with few if any adverse effects.

A recent article describes successful treatment of a dog with a generalized variant of DLE with oral hydroxychloroquine (HCQ), an anti-malarial drug often used in the treatment of DLE in humans. The treatment protocol was 5 mg/kg once daily along with 0.1% tacrolimus ointment the first two weeks and restriction of sun exposure. Two flares were treated with tacrolimus and topical glucocorticoids, but essentially the dog was well maintained on the HCQ for a follow-up period of a year. Because of concerns in humans, a retinal examination should be done prior to, and every 6 months, of treatment. In the USA, the drug is of low cost.

**EXFOLIATIVE CUTANEOUS LUPUS ERYTHEMATOSUS** (ECLE) (aka lupoid dermatosis of German short-haired pointers) is a hereditary disease which usually occurs within the first year of life. Thus far it has only been described in German short-haired pointers, many of which are related; initial inspection of pedigrees is suggestive of an autosomal recessive mode of inheritance. Affected dogs present with localized to generalized scale (sometimes with follicular casting) and alopecia. The disease may be progressive or may wax and wane. Pruritus is minimal. Rare dogs may have blood dyscrasias or joint disease. Histology shows hyperkeratosis, basal cell degeneration and apoptotic epidermal cells. Often sebaceous adenitis and/or a lack of sebaceous glands are noted. Treatment has not usually been successful – cyclosporine, HCQ, and adalimumab have been used without notable success. The author is aware of one dog that initially responded to niacinamide and tetracycline, and another to prednisolone and azathioprine.

**VESICULAR CUTANEOUS LUPUS ERYTHEMATOSUS** (VCLE) (aka ulcerative dermatosis of collies and Shetland sheepdogs). This is an ulcerative dermatitis seen primarily in the Shetland sheepdog and rough collie dog, and their crosses. An adult onset disease, seen more often in the summer months (UV light exacerbation/triggering?), lesions are annular, polycyclic and serpiginous ulcerations distributed over sparsely haired areas of the body. Axilla and inguinal areas especially are affected. Histology shows a lymphocyte-rich interface dermatitis and folliculitis, with vesication at the dermal-epidermal junction. Treatment varies, as does its success: some dogs do well on the niacinamide/tetracycline regimen noted above, some to cyclosporine, and some to the prednisolone/azathioprine regimen as with SLE. Unfortunately, some dogs do not respond at all to treatment. One report describes successful treatment using cyclosporine.

**References**


