Case Report

Disseminated Discoid Lupus Erythematosus in a Dog

Masahiko Nagata^{1)*}, Kenji Rinpou²⁾, Hiroko Nanko³⁾

¹⁾*Animal Dermatology Center, ASC*

²⁾*Rinpou Animal Hospital*

³⁾*Department of Dermatology, Tokyo Koseinenkin Hospital*

Abstract: A 12-year-old male beagle dog presented with disseminated scaly alopecia, infiltrative erythema on the face and extremities, and mild lymphadenopathy. Histopathological findings showed hyperkeratosis with follicular plugging, hydropic degeneration of the basal cell layer, and inflammation of lymphocytes and plasma cells with mucinosis of the superficial dermis and perifollicular areas. Direct immunofluorescence study showed linear deposition of IgG at the dermal-epidermal junction. Complete blood counts revealed mild anemia and leukopenia, but antinuclear antibody was negative. The present case closely resembled those found in humans with disseminated discoid lupus erythematosus. The dog improved with avoidance of sunlight and systemic prednisolone therapy, but required continuous low-dose steroid administration.

Key words: alopecia, cutaneous LE, mucinosis

INTRODUCTION

Lupus erythematosus (LE) is a disease that affects multiple organ systems and has a broad range of clinical manifestations^{11, 17, 25, 26)}. It may take the form of an isolated cutaneous eruption or a fatal systemic illness^{11, 17, 25, 26)}. The term systemic LE (SLE) has been employed to designate individuals who have a systemic disease characterized by the association of immunological abnormalities with

pathological changes affecting a number of organ systems, in particular the skin, joints, and vasculature^{11, 17, 25, 26)}. The term discoid LE (DLE), on the other hand, has been employed to designate individuals who have a lupus disease process involving only the skin with no systemic manifestations²⁶⁾. Also, DLE is used as a morphologic term indicating an oval, disc-shaped, scarring, erythematous lesion characterized by adherent scale formation, follicular plugging, and telangiectasia in humans²⁶⁾. In humans, typical DLE is basically classified into localized and disseminated forms^{17, 25, 26)}, although the understanding of cutaneous LE has become more complex. In dogs, DLE has been reported only in its localized form in the literature^{4, 6, 7, 10, 15, 16, 18–20, 22, 23, 30)}. Here, we report the first case of a dog with disseminated DLE.

*Correspondence to:

M. Nagata (Animal Dermatology Center, ASC)
1-3-2 Jindaijihigashi Chofu, Tokyo 182-0012, Japan
TEL +81-424-80-9342 FAX +81-424-41-6095
E-mail: nagata@ra2.so-net.ne.jp

Fig. 1. Clinical feature of the dog. Scaly alopecia with mild erythema was observed on the whole body.

Fig. 2. Clinical feature of the dog. Note scaly erythema with hypotrichosis and follicular casts on the trunk.

CASE REPORT

A 12-year-old male beagle presented with a 1-month history of scaly alopecia, which occurred initially in the lumbosacral area. The dog was treated with systemic antibiotics at a veterinary clinic, but the lesions did not resolve, and became rapidly widespread. The dog had disseminated scaly alopecia with follicular casts and mild erythema on the whole body including both dorsal and ventral aspects (Figs. 1 and 2), severe infiltrative erythema on the extremities (Fig. 3) and around the nose and cheek, hyperkeratosis on the margin of the pads, and mild lymphadenopathy. The dog's general condition was otherwise good, and there was no history of recent infection or drug administration prior to onset of this dermatosis.

Fig. 3. Clinical feature of the dog. Note alopecia with severe infiltrative erythema on the extremities and hyperkeratosis on margin of the pads.

Skin biopsies from scaly alopecia and infiltrative erythema were obtained. Histopathological findings of the scaly alopecia showed severe hyperkeratosis with follicular plugging, hydropic degeneration with lymphocyte inflammatory infiltrate of the basal cell layer, and moderate inflammation of lymphocytes and plasma cells with edema at the superficial dermis and perifollicular areas (Figs. 4 and 5). Histopathological findings of the infiltrative erythema showed severe inflammation of lymphocytes and plasma cells at the superficial dermis and perifollicular areas. In the specimens of the scaly alopecia, Toluidine blue staining demonstrated mucin deposition at the superficial dermis and perifollicular area (Fig. 6), and PAS staining demonstrated an irregularly thickened basement membrane. Direct immunofluorescence study of the skin lesions revealed linear deposition of IgG at the dermal-epidermal junction (Fig. 7). Complete blood counts showed mild anemia and leukopenia (especially neutropenia and lymphopenia), but serum biochemical analysis and urinalysis revealed no abnormalities. An antinuclear antibody test and a Coombs' test were negative.

Based on these clinical and histopathologic findings with direct immunofluorescence test, the present dermatosis was compatible with LE. The skin lesions were apparently different from those in typical canine DLE, and no diagnostic criteria for definitive SLE were met. These findings suggest that the present case closely resembled those found in humans with disseminated DLE.

Fig. 4. Histopathology of the scaly alopecia. Note moderate inflammation of lymphocytes and plasma cells at the superficial dermis and perifollicular areas, and hyperkeratosis with follicular plugging. H&E.

Fig. 5. High magnification of Fig. 4. Note hydropic degeneration with lymphocyte inflammatory infiltrate at the basal cell layer and severe hyperkeratosis overlying the epidermis. H&E.

Fig. 6. Histopathology of the scaly alopecia. Note mucin deposition at the superficial dermis and perifollicular areas. Toluidine blue staining.

Fig. 7. Direct immunofluorescence test of the scaly alopecia. Note linear deposition of IgG at the dermal-epidermal junction.

The dog's condition was improved with oral prednisolone (Predonine, Shionogi & Co., Ltd, Osaka, Japan) 1 mg/kg BID, dl- α -tocopheryl nicotinate (Juvela N, Eisai Co., Ltd., Tokyo, Japan) 200 mg SID, and avoidance of sunlight, but administration of prednisolone 1 mg/kg EOD was required continuously. Griseofulvin (Grisovin-FP, Sankyo, Tokyo, Japan) 30 mg/kg BID was then administered as an immunomodulating drug^{13,27}. Then the prednisolone dose was reduced to 0.1 mg/kg EOD, even though it was difficult to discontinue the steroid therapy. The dog had been managed without severe skin lesions for approximately 1 year, except for episodic flares with sunlight exposure. Unfortunately, further follow-up was impossible.

DISCUSSION

The term "disseminated DLE" was introduced by O'Leary in 1934¹⁴. The term disseminated was employed in part to refer to the widespread distribution of LE skin lesions^{14,26}. It was also ambiguously employed to refer to the transition from a disease limited to the skin to a systemic illness¹⁴. In dogs, previous reports of DLE were limited to the localized form. Skin lesions were distributed on the nose in 81.0% of 42 cases, the bridge of the nose in 50.0% of 6 cases, the pinnae in 14.3% of 42 cases, the oral membrane in 13.6% of 22 cases, the lip in 7.1% of 42 cases, the periorbital areas 7.1% in 42 cases, and the pads in 6.3% of 32 cases reported

Table 1. Classification of LE in humans (Tsuchida *et al.*)

CLE (Cutaneous LE): disease limited to the skin.
ILE (Intermediate LE)
I: Basically CLE with mild generalized signs and laboratory abnormalities.
II: Basically SLE, but diagnostic criteria are not met, with apparent generalized signs (i.e., arthralgia, fever) and laboratory abnormalities (i.e., positive ANA, leukopenia).
SLE (Systemic LE)
I: Lack of signs below.
II: Apparent renal and central neurological disorders, thrombocytopenia, hemolytic anemia, and/or serositis exist.

in the literature^{4, 6, 7, 10, 15, 16, 18–20, 22, 23, 30}. Those of the genitalia and the body were rarely reported^{4, 6, 7, 10, 15, 16, 18–20, 22, 23, 30}. To our knowledge, this is a first report of a dog with disseminated DLE in the literature.

It is apparent that the most important differential diagnosis is SLE. Canine DLE-associated skin lesions were erythema in 83.9% of 31 cases, scaling 81.7, 25, 26% in 32 cases, depigmentation in 80.6% of 31 cases, erosion or ulcer with or without vesiculobullous lesions in 78.1% of 32 cases, and alopecia in 66.7% of 6 cases reported in the literature^{4, 6, 7, 10, 15, 16, 18–20, 22, 23, 30}. These lesions are also observed in dogs with SLE, but they are more generalized and pleomorphic^{1, 3, 5–7, 20, 21}. In humans, cutaneous lesions of SLE and DLE may be clinically and histologically indistinguishable. Thus, the term cutaneous LE (CLE) is employed as an umbrella term to refer to all skin lesions that have been specifically associated with LE^{24, 25}. In most human textbooks, LE-specific skin lesions are classified as acute CLE; localized and generalized, subacute CLE; annular and papulosquamous, and chronic CLE; classical DLE (localized and generalized), hypertrophic LE, lupus panniculitis, mucosal LE, lupus tumidus, chilblain lupus, and DLE-lichen planus overlap^{11, 17, 24–26}. From this classification, the present case closely resembled those found in humans with generalized DLE.

The clinical and biologic signs of canine LE, especially SLE, are highly diverse and constitute a major diagnostic challenge, despite the availability of diagnostic criteria such as those of Halliwell and Gorman and the 1982 revised American Rheumatism Association's criteria (with minor modifications)^{2, 7, 28}. The antinuclear antibody (ANA) test is

most reliable, but not gold standard. It has been reported that about 10% of human patients with SLE are ANA negative²⁵. These patients might have unique anticytoplasmic antibodies, which are not detected when conventional ANA test substrates are employed^{17, 25}. Thus, negative immunoserology does not exclude the diagnosis of SLE. It is also believed that some human patients with DLE occasionally have the higher ANA levels that are characteristically found in patients with overt SLE²⁵. These phenomena have been discussed in depth in human, and several novel concepts and classifications have been proposed to date^{8, 9, 12, 24, 31}. In these reports, Tsuchida *et al.* analyzed the association between the type of LE-specific skin lesion and the severity of extracutaneous manifestations of LE according to a two-dimensional coordinate axis system, and proposed a unique classification (Table 1)^{29, 31}. Patients with acute lupus skin lesions could usually be classified as suffering from SLE, whereas monomorphic patients with localized discoid lesions rarely exhibited extracutaneous manifestations in the classification³¹. Further assessments using these criteria showed that LE could be classified into three groups, CLE (CLE and ILE I), a mild type (ILE II and SLE I) and a serious type (SLE II) of SLE, according to the responsiveness to treatment and the clinical course^{9, 12}. The dog under study here could be reclassified as ILE II, a mild type of SLE, using the classification.

In this case, griseofulvin appeared to be effective in controlling symptoms. Griseofulvin is a fungistatic antibiotic that also has immunomodulating properties^{13, 27}. It has been reported that griseofulvin decreases IFN- γ -induced HLA-DR molecules on human epidermal keratinocytes²⁷. In addition, it has been reported that griseofulvin has a potency

to down-regulate reactive proliferation of the Langerhans cell, which play an important role as immunocompetent cell in the skin¹³. Thus, it is postulated that griseofulvin could induce “down-regulatory” signals within LE lesions.

In current investigations of canine LE, the immunoserologic aspects have always drawn attention. However, the pattern of skin lesions expressed by an individual LE patient could provide insight as to the position on the spectrum where the illness might best be placed. Thus, it is apparent that clinical features, especially skin lesions, should be investigated further as a key to accurate understanding and management of this disorder.

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犬の播種状円板状エリテマトーデスの1例

永田雅彦^{1)*}, 林宝謙治²⁾, 南光弘子³⁾

¹⁾ASC どうぶつ皮膚病センター, ²⁾林宝動物病院, ³⁾東京厚生年金病院

要約: 12歳齢, 雄のビーグルに, 体表リンパ節腫大を伴う顔と四肢を中心とする落屑性脱毛と浸潤性紅斑が認められた。皮膚病理組織では角栓を伴う角化亢進, 基底層の液状変性, 真皮浅層および付属器周囲のムチン沈着を伴う単核球浸潤が認められた。直接蛍光抗体法で真皮表皮境界に線状のIgG沈着を認めた。血液検査で軽度の貧血と白血球減少がみられたが, 抗核抗体は陰性であった。以上より, 人に生じる播種状円板状エリテマトーデスに合致したエリテマトーデスと診断した。光線回避, プレドニゾロン経口投与による改善を認めたが, 低用量プレドニゾロンによる維持療法が必要であった。

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* 連絡先: 永田雅彦 (ASC どうぶつ皮膚病センター)
〒180-0012 東京都調布市深大寺東町1-3-2
TEL 0424-80-9342 FAX 0424-41-6095
E-mail: nagata@ra2.so-net.ne.jp