Diagnosis and Management of Pemphigus Complex Autoimmune Skin Diseases in Dogs - Case Report

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ABSTRACT

Autoimmune skin diseases have been recognized for decades in humans and dogs. Out of 357 canine cases of various skin affections presented to the Referral Veterinary Polyclinic, Indian Veterinary Research Institute, Izatnagar, 8 cases were suspected to be of autoimmune etiology. Those cases were having history of pruritus, alopecia, scaling, and erythema, ulceration at muco-cutaneous junction of face, footpad and ventral abdomen. Clinical examination revealed normal rectal temperature, heart rate and respiration rate in four dogs whereas fever, lameness and recumbency were noticed in other four dogs. No significant changes noticed in haematobiochemical values. Coagulase negative Staphylococcus spp. was isolated from skin swabs. Histopathologic examination of skin biopsy samples revealed monoclonal cell infiltration, epidermal spongiosis with discontinuity in epidermis which is suggestive of Pemphigus foliaceus. Therapeutic management was done with Prednisolone @ 2 mg/Kg BW, PO, BID for initial 10 days and then with maintenance dose @ 1 mg/Kg BW, PO, BID for another 15 days, Tab. Cefadroxil @ 22 mg/kg BW, PO, BID for 28 days to control secondary bacterial infection along with supportive therapy using antioxidant, Omega 3 and Omega 6 fatty acids supplementation and Ketoconazole plus Chlorhexidine shampoo for topical application. Marked improvement was noticed after two weeks of therapy and complete recovery was noticed after eight weeks.

INTRODUCTION

Canine autoimmune skin diseases are relatively uncommon, but clinically challenging dermatologic conditions. An accurate diagnosis is of crucial importance for correct therapy and management. The pemphigus complex encompasses a group of autoimmune blistering skin diseases with intraepidermal separation resulting from cell–cell detachment by acantholysis. They are classified based on the level of blistering in the epidermis, and both superficial (pemphigus foliaceus, IgA pemphigus) and deep (pemphigus vulgaris, pemphigus vegetans and paraneoplastic pemphigus) variants are recognized [1]. Pemphigus foliaceus is most common autoimmune skin disease in canine which starts with face and then extends to whole body [2]. Epidermal cells possess cell to cell or cell to matrix adhesions, when autoantibodies form against these adhesions then blistering skin disease takes place [3]. Autoantibodies targeting keratinocyte desmosomes may be included in pemphigus group of diseases. In pemphigus foliaceus, loss of adhesion leads to intrasinosal or subcorneal pustule or vesicle formation which is transient in nature and ultimately results in the formation of crusts [4]. Footpads often have hyperkeratosis and fissures with involvement of head, face and ears in 80% of cases [5]. German shepherd breed is having predisposition for mucous membrane pemphigoid [6]. The diagnosis of the condition is mainly by clinical, histopathologic and immunologic examination [7]. Treatment generally consists of immunosuppressive agents like prednisolone, azathioprine with careful tapering but remission is also possible in some cases [8]. In the present case study, diagnosis and successful therapeutic management of autoimmune skin disease in eight dogs has been described.

CASE PRESENTATION

Case details and clinical examination

Out of 357 canine cases of various skin affections presented in Referral Veterinary polyclinic, Indian Veterinary Research Institute, Izatnagar, 8 cases were suspected to be of autoimmune etiology. The breeds of the dogs affected were Spitz (2), Labrador retriever (2), German shepherd (2), Dalmatian (1) and Mongrel (1). Major clinical signs noticed were pruritus, alopecia, scaling, erythema, ulceration at muco-cutaneous junction of face, footpad and ventral abdomen (Figure 1). Clinical examination revealed normal rectal temperature, heart rate and respiration rate in four dogs whereas fever, lameness with footpad inflammation and recumbency were noticed in other four dogs. Skin swabs were
collected and sent to the laboratory for culture examination. Skin scrapings were taken for the examination of mite infestation. Skin biopsy samples were taken for histopathology. Blood samples were submitted for haemato-biochemical examination. Haematological analysis was carried out as per standard method [9]. Biochemical analysis was done with semi-auto analyzer.

**Diagnosis and treatment**

Skin scraping examination was found to be negative for mite infestation. Isolation and identification of the bacterial culture from the skin swabs revealed presence of coagulase negative *Staphylococcus* spp in some of the cases. There was no significant change noticed in haemato-biochemical parameters in diseased animals compared to healthy control (Table 1). Histopathologic examination of the skin biopsy samples revealed discontinuity in the epidermal layer of skin with heavy infiltration of mononuclear cells and presence of acantholytic keratinocytes arranged in string of pearls along with epidermal spongiosis and bacterial colonies (Figure 2). Based on the clinical signs and histopathological findings these cases were diagnosed as pemphigus complex autoimmune skin diseases. All the cases were treated with immunosuppressive dose of Prednisolone @ 2 mg/Kg BW, PO, BID for initial 10 days and then with maintenance dose @ 1 mg/Kg BW, PO, BID for another 15 days, Tab. Cefadroxil @ 22 mg/kg BW, PO, BID for 28 days to control secondary bacterial infection along with supportive therapy using antioxidant (Ascorbic acid @ 30 mg/kg BW, PO, OD), Omega 3 and Omega 6 fatty acids supplementation (Syr. Nutriccoat Advance™ @1 tsp/10kg BW, PO, BID) and Ketochlor™ (combination of Ketoconazole 1% w/w with Chlorhexidine 2.1 % w/w) shampoo for topical application. After two weeks of therapy, animals showed marked improvement in condition with reduction of inflammatory reaction, pruritus and the complete recovery was noticed after eight weeks (Figure 3).

**DISCUSSION**

Autoimmune skin diseases have been described in human and dogs for decades. Now there is a need to arrange the animal autoimmune skin diseases into those in which lesions are due to autoantibody action or by direct attack of cytotoxic T-cells [10]. Pemphigus foliaceus is the most common form of the pemphigus complex in dogs and possibly the most common of all immune mediated skin diseases [11]. In the present case study, skin lesions like erythema, ulceration at muco-cutaneous junction of face, footpad and ventral abdomen region were noticed in affected dogs. All forms of pemphigus are characterized by the presence of autoantibodies directed against keratinocyte desmosomal proteins which results loss of adhesions between keratinocytes [12]. In pemphigus foliaceus, this loss of adhesion leads to intraspinosal or subcorneal pustule or vesicle formation ultimately leading to the formation of crusts. Pemphigus foliaceus can be localized or generalized, and lesions have usually been noted first on the face, particularly the dorsal aspect of the nose.

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**Figure 1** Animals having various affections of autoimmune disorder.
[13]. Skin lesions like alopecia, scaling, crusting, and epidermal collarettes have been commonly reported in pemphigus foliaceus [10].

Definitive diagnosis of pemphigus foliaceus was made by histopathological findings of skin biopsy samples in association with classical clinical signs, supportive cytology and response to therapy. Histopathological findings revealed infiltration of mononuclear cells and presence of acantholytic cells along with epidermal spongiosis and bacterial colonies. Histology and biopsy of skin specimen plays valuable role in differential diagnosis of group of disease causing erosion and ulcers and is main preliminary diagnostic technique for autoimmune skin disorder. Presence of acantholytic cells, eosinophilic or neutrophilic infiltration with bacterial colonies has also been documented previously [13]. Presence of pustules or vesicles with marked acantholysis of keratinocytes is one of the most important histological features of pemphigus foliaceus [14]. Neutrophilic or eosinophilic infiltration is typically present in large numbers within pustules [14]. Desmocollin-1 is a calcium dependent cadherin and its highest expression has been reported in the pustular lesions of superficial epidermal layers caused by pemphigus foliaceus [15]. Autoantibodies targeting desmocollin 1 have been detected in the serum of human patients with pemphigus foliaceus and anti-desmocollin 1 auto reactivity appears to be mostly restricted to atypical pemphigus foliaceus variants in which a strong neutrophilic inflammation accompanies blister formation [16]. Insecticide contact triggered

Figure 2 Microphotograph showing discontinuity in the epidermal layer of skin with heavy infiltration of mononuclear cells with bacterial colonies and epidermal spongiosis (H & E, 100X).

Figure 3 Post-treatment recovery and improvement in skin condition.
Table 1: Haemato-biochemical profile of autoimmune skin disease affected animals.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Diseased animals</th>
<th>Healthy control</th>
</tr>
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<tbody>
<tr>
<td>Haemoglobin (g/dl)</td>
<td>12.41±0.10</td>
<td>13.50±1.26</td>
</tr>
<tr>
<td>PCV (%)</td>
<td>35.26±1.50</td>
<td>37.24±0.18</td>
</tr>
<tr>
<td>TEC (x10³ cells/µl)</td>
<td>6.32±0.35</td>
<td>6.58±0.76</td>
</tr>
<tr>
<td>TLC (x10³ cells/µl)</td>
<td>9.27±0.06</td>
<td>7.36±0.42</td>
</tr>
<tr>
<td>Neutrophils (%)</td>
<td>70.23±1.21</td>
<td>68.67±1.62</td>
</tr>
<tr>
<td>Lymphocytes (%)</td>
<td>26.84±1.72</td>
<td>29.25±1.17</td>
</tr>
<tr>
<td>Monocytes (%)</td>
<td>2.62±0.26</td>
<td>2.14±0.34</td>
</tr>
<tr>
<td>Eosinophils (%)</td>
<td>0.80±0.20</td>
<td>1.02±0.05</td>
</tr>
<tr>
<td>Basophils (%)</td>
<td>0.17±0.16</td>
<td>0.18±0.09</td>
</tr>
<tr>
<td>Total protein (g/dl)</td>
<td>6.16±0.23</td>
<td>5.92±0.95</td>
</tr>
<tr>
<td>Albumin (g/dl)</td>
<td>2.73±0.08</td>
<td>2.62±0.81</td>
</tr>
<tr>
<td>Globulin (g/dl)</td>
<td>3.33±0.41</td>
<td>3.21±0.75</td>
</tr>
<tr>
<td>A/G ratio</td>
<td>0.91±0.03</td>
<td>0.87±0.18</td>
</tr>
<tr>
<td>ALP (IU/L)</td>
<td>62.56±3.82</td>
<td>45.64±1.13</td>
</tr>
<tr>
<td>SGPT (IU/L)</td>
<td>37.24±2.18</td>
<td>34.58±2.72</td>
</tr>
<tr>
<td>SGOT (IU/L)</td>
<td>26.43±2.05</td>
<td>28.36±1.76</td>
</tr>
<tr>
<td>Blood urea nitrogen (mg/dl)</td>
<td>12.32±1.06</td>
<td>11.24±0.03</td>
</tr>
<tr>
<td>Creatinine (mg/dl)</td>
<td>1.04±0.08</td>
<td>0.98±0.03</td>
</tr>
</tbody>
</table>

Various side-effects in the form of haemorrhagic cystitis after daily administration [19]. Beneficial effects of omega-3 fatty acids have also been described for autoimmune disorders in companion animals [20]. Based on clinical signs, histopathological examination and response to immunosuppressive therapy the conditions were diagnosed as pemphigus complex autoimmune skin diseases.

CONCLUSION

In the present case study, successful therapeutic management of autoimmune skin diseases with immunosuppressive dose of prednisolone along with supportive therapy in dogs has been described.

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REFERENCES


