CASE REPORT

Uveodermatological syndrome (Vogt–Koyanagi–Harada-like syndrome) with generalized depigmentation in a Dachshund

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Abstract
A 3-year-old, female, black and tan Dachshund was referred with visual impairment, bilateral anterior and posterior uveitis, poliosis, and generalized dermal depigmentation. Complete blood counts and biochemical parameters, including T₃ and T₄, were normal. The skin biopsy showed lichenoid dermatoses with dermal infiltration of histiocytes and lymphocytes suggesting uveodermatological syndrome. Medical treatment was initiated with oral prednisone and azathioprine, and topical prednisolone and atropine. The clinical signs improved, vision was retained, and the skin began to repigment 2 months following the initiation of therapy.

Key Words: Vogt–Koyanagi–Harada, uveitis, depigmentation, dog, Dachshund

INTRODUCTION
The Vogt–Koyanagi–Harada (VKH) syndrome is a bilateral, diffuse, granulomatous uveitis associated with vitiligo (depigmentation of the skin), poliosis (hair whitening), alopecia, and signs of meningeal irritation with or without auditory disturbances which was first described in humans by Vogt (1906), Harada (1926), and Koyanagi (1929).¹

A similar disease called uveodermatological syndrome (UDS) has been recognized in dogs in the last 20 years. Asakura and coworkers published the first report of a panuveitis with dermal depigmentation in two young Akitas.² Since then, several cases were described in Canada,³ Japan,⁴ the United States,⁵–¹³ France,¹⁴ the UK,¹⁵ and Brazil.¹⁶ Most of the cases were reported in Akitas;²,⁴,⁸,¹⁰–¹²,¹⁵,¹⁶ however, the disease was also described in the Australian Sheepdog,⁷,¹⁴ the Golden Retriever,⁶,⁷ the Old English Sheepdog,⁶,⁷ the Samoyed,³ the Shetland Sheepdog,⁷,⁹ the Siberian Husky,⁷,¹⁴ the Irish Setter,⁷ the Saint Bernard,⁷ the Alaskan Malamute,¹³ and the Chow Chow.¹⁷

The cause of the syndrome remains unknown in both humans and dogs, but an immune-mediated reaction against melanocytes is implicated.¹,⁴–⁶,¹²,¹³,¹⁸ Histopathologic studies in humans and dogs have revealed severe inflammation, with loss of melanocytes in the uvea and skin.¹,⁶,⁷,¹¹,¹³

Clinical signs in dogs include bilateral panuveitis associated with retinal detachment and localized dermal depigmentation of the eyelids, lips, nose, and less commonly of the scrotum, vulva, foot pads and anus.²–¹⁷ Neurological signs were reported in one young Akita¹⁵ and generalized depigmentation was noted in a Shetland Sheepdog.⁹ Human and canine patients with this syndrome are treated generally with a high dose of systemic corticosteroids and, when necessary, immunosuppressive drugs. However, the long-term prognosis is not good for vision because severe complications, including synechia, cataracts and glaucoma, often lead to visual loss.

The purpose of this study is to present a case of UDS in a Dachshund with poliosis and complete dermal depigmentation. To the best of our knowledge, this is the first report of the disease in the Dachshund, and the second case in a dog associated with total generalized depigmentation and poliosis.

CASE REPORT
A 3-year-old female black and tan Dachshund had presented with a history of hyphema in the left eye 10 months previously, and a dermatological disease with alopecia and pruritus 7 months prior to the presentation, followed by progressive depigmentation of the head and the rest of the body. Tearing, conjunctival redness, visual impairment, and depigmentation of the hair over 90% of the head and body (Fig. 1) with a generalized pruritus, were noted at the initial referral visit. Ophthalmic examination revealed marked bilateral episcleral congestion, mild corneal oedema, miosis, intraocular pressure less than 10 mmHg (Schiotz), moderate aqueous flare, posterior synechiae, and anterior lens capsule opacities. Depigmentation of the iris on both eyes was also present (Figs 2 and 3). The fundi were not visible because of the opacities in the visual axis. Erythema, generalized vitiligo
and poliosis, and localized alopecia in the ventral zone of the neck were also present.

A presumptive diagnose of UDS was made, and blood and skin samples were taken. The initial treatment consisted of topical 1% prednisolone (Prednefrin Forte: Allergan, Buenos Aires, Argentina) six times daily, topical 1% atropine (Isoptoatropina 1%: Alcon, Buenos Aires, Argentina) three times daily, and oral prednisone (Meticorten 5 mg: Schering Plough, Buenos Aires, Argentina) at 1 mg kg$^{-1}$ day$^{-1}$.

Laboratory studies revealed normal complete blood counts and biochemical parameters including normal T$_3$ and T$_4$. Marked improvement of the ocular signs, including vision, was seen 1 week later with decreased episcleral congestion, corneal edema, and flare. Intraocular pressure increased to 15 mmHg (Schiortz) but miosis remained the same. The fundi could now be partially examined using indirect and direct ophthalmoscopy, revealing marked depigmentation of...
the nontapetal fundus with some choroid and sclera visible, and mottled tapetal fundus.

The skin biopsy showed a lichenoid dermatoses with orthokeratotic hyperkeratosis and a dermal cellular infiltrate composed of histiocytes, lymphocytes, melanophages, and neutrophils, suggesting UDS (Fig. 4). When the result of the biopsy became known, prednisone was increased to 2 mg kg\(^{-1}\) day\(^{-1}\), and azathioprine (Imuran 50 mg: Glaxo Wellcome, Buenos Aires, Argentina) was added at 2 mg kg\(^{-1}\) 3 weeks later. The therapeutic schedule is summarized in Table 1. Complete blood counts were performed weekly while the azathioprine was administrated at 2 mg kg\(^{-1}\) and the only change was a decrease to 5500/mm\(^3\) in the count of leucocytes with 5% of lymphocytes. No other clinical changes were observed.

After 2 months of immunosuppressive treatment, the iris and skin began to repigment (Figs 5, 6 and 7) and no new signs of dermatitis or pruritus were seen. No recurrence of the uveitis was noted and the vision remained useful after a follow up of 7 months on azathioprine.

**DISCUSSION**

VKH syndrome occurs worldwide with a predilection for more darkly pigmented races.\(^1,19\)–\(^22\) VKH represents 6.8–9.2% of all uveitis referrals in Japan,\(^1\) 2.5% in Brazil,\(^19\) 15% in Argentina,\(^22\) and 1–4% in the United States.\(^1\)

Women seem to be affected more frequently than men (2.5:1).\(^1,19\)–\(^22\)

Since a similar disease without the central nervous system signs was first described in dogs by Asakura *et al.* in 1977,\(^2\) it has been occasionally reported by different authors.\(^3\)–\(^16\) The Akita seems to be predisposed to the syndrome because most of the cases affect this breed. Of the 72 cases described in the literature, 58 (80.5%) affected Akitas,\(^2,4,8\)–\(^12,14\)–\(^16\) The case described in the present study is the first described in a Dachshund. There is no marked sex predisposition for UDS even though a trend towards males has been described.\(^7,16\) Related to age, a range from 6 months to 6 years has been reported. Morgan reported a mean of 2.8 years and Barros and coworkers diagnosed the disease in 13 of 21 Akitas (61.9%) at an age between 13 and 30 months.\(^16,17\)

The etiology of the disease remains unclear and the pathogenesis is poorly understood in both humans and dogs. It is thought to be an autoimmune disease against melanocytes but virus infection could also play a role as a cause of the syndrome.\(^1,21\) The autoimmune mechanism could be influenced by genetic or hereditary factors.\(^1,4,15\) A T-cell-mediated immune process against choroidal melanocytes in humans has been demonstrated to be involved in the autoimmune inflammatory process,\(^1,18\) and specific circulating antimelanin and antiretinal autoantibodies occur in both human and canine patients.\(^1,11,12\) Melanocytes in the corneal limbus are also attacked by lymphocytes in the same way as

**Table 1** Therapeutic schedule used after histopathologic diagnosis

<table>
<thead>
<tr>
<th>Week</th>
<th>Oral prednisone</th>
<th>Oral azathioprine</th>
<th>Topical prednisolone</th>
<th>Topical atropine</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2 mg kg(^{-1}) day(^{-1})</td>
<td>–</td>
<td>6 times daily</td>
<td>3 times daily</td>
</tr>
<tr>
<td>2</td>
<td>2 mg kg(^{-1}) day(^{-1})</td>
<td>–</td>
<td>6 times daily</td>
<td>3 times daily</td>
</tr>
<tr>
<td>3</td>
<td>1 mg kg(^{-1}) day(^{-1})</td>
<td>–</td>
<td>6 times daily</td>
<td>3 times daily</td>
</tr>
<tr>
<td>4</td>
<td>0.5 mg kg(^{-1}) every 2nd day</td>
<td>2 mg kg(^{-1}) every 2nd day</td>
<td>4 times daily</td>
<td>3 times daily</td>
</tr>
<tr>
<td>5</td>
<td>0.5 mg kg(^{-1}) every 2nd day</td>
<td>2 mg kg(^{-1}) every 2nd day</td>
<td>4 times daily</td>
<td>–</td>
</tr>
<tr>
<td>6 to last visit</td>
<td>–</td>
<td>1 mg kg(^{-1}) every 2nd day</td>
<td>–</td>
<td>–</td>
</tr>
</tbody>
</table>

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in the uvea in humans, and the vitiligo in the skin also results from the same immunological mechanism.21

UDS-associated uveitis in dogs may be complicated by retinal detachment, cataract formation, and glaucoma. The depigmentation of the skin is usually localized and follows the inflammation of the uvea. In just one case nonspecific neurological signs were reported, and in another unusual case depigmentation of the skin became generalized.9,15 In this case bilateral uveitis was present associated with generalized vitiligo and poliosis involving approximately 90% of the body.

Laboratory analysis revealed no significant abnormalities in all canine cases reported.3,4,7–9,11,12 In our case, complete blood counts and biochemical parameters, including T3 and T4, were also performed with normal results. Thyroid evaluation was indicated as thyroiditis may be associated with VKH syndrome in humans.23

Histopathological findings are similar in humans and dogs. The uveal inflammation consists of diffuse granulomatous or nongranulomatous infiltrates of lymphocytes, macrophages and plasma cells along the iris, ciliary body and choroid, causing a marked increase in their thickness, and is usually associated with retinal detachments.1,2,7,8,11 Dalen-Fuch’s nodules consisting of macrophages, epithelioid cells, lymphocytes and altered retinal pigment epithelium have been described in humans1 and dogs.8 In another report the inflammatory cells appeared to surround and sequester uveal melanocytes and free melanin granules, especially in zones where depigmentation was evident.11 Biopsy of the vitiliginous skin in previous reports has demonstrated decreased or absent melanin along the basal skin layer associated with lichenoid inflammatory infiltrates composed of histiocytic cells, neutrophils, and plasma cells.1,5,6,7,13 In the case presented here, the result of the biopsy was consistent with those previous reports, showing an inflammatory infiltrate composed of histiocytes, melanophages, lymphocytes, and neutrophils.

The purpose of the therapy is to suppress the immune-mediated inflammation with early and aggressive use of systemic corticosteroids at immunosuppressive doses. The uveitis must also be aggressively treated with topical corticosteroids and mydriatics. The most commonly used oral corticosteroid in both humans and dogs is prednisone at 1–2 mg kg⁻¹ day⁻¹.1,17 In some cases oral prednisone must be combined with other immunosuppressive agents, such as cyclophosphamide (per os or intravenously at 1–2 mg kg⁻¹ day⁻¹), or azathioprine (1–2 mg kg⁻¹ day⁻¹).1,19 Cyclosporine (7–10 mg kg⁻¹ day⁻¹) has also been described in humans as immunosuppressive treatment of VKH.1,24,25 Therapy should be long term in order to retain good or average visual outcomes and to maintain clinical remission of the disease. In one study in humans the mean duration of systemic corticosteroid therapy was 5.6 months,1 and in another study combined prednisone and cyclophosphamide was used for a period ranging from 4 weeks to 6 years.19

The case herein described underwent a combined initial immunosuppressive therapy with prednisone and azathioprine which was gradually tapered. In addition, topical prednisolone and atropine were applied. The maintenance therapy consisted of oral azathioprine on alternate days long term. A rapid improvement of clinical signs in the eyes and skin was observed after starting the therapy and repigmentation started after 2 months of treatment.

Poor visual outcome has been reported in dogs because of the uveal inflammation, retinal detachment, and several ocular complications which often lead to visual loss. Visual prognosis depends on an early diagnosis and aggressive and prolonged immunosuppressive therapy. In this case vision has been maintained with the long-term therapy.

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