



## CASE REPORT

### Uveodermatologic Syndrome in a Siberian Husky: Clinical and Histopathological Findings

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#### ABSTRACT

A 2-year-old, intact male Siberian Husky was presented with corneal opacity, eye lid swelling, depigmentation, alopecia and erythema predominantly on face. Bilateral uveitis preceded periocular and nasal planum depigmentation. Ancillary tests excluded other systemic diseases. Histopathology of the skin revealed lichenoid interface dermatitis with pigmentary incontinence. Diffuse pyogranulomatous inflammation of the globes was also noted. Based on the clinical signs and characteristic histopathological findings, the dog was diagnosed as uveodermatologic syndrome (UDS). Further treatment was not attempted in this case and the dog was euthanized. This case report describes typical clinical and histopathologic features of UDS in a Siberian Husky.

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#### INTRODUCTION

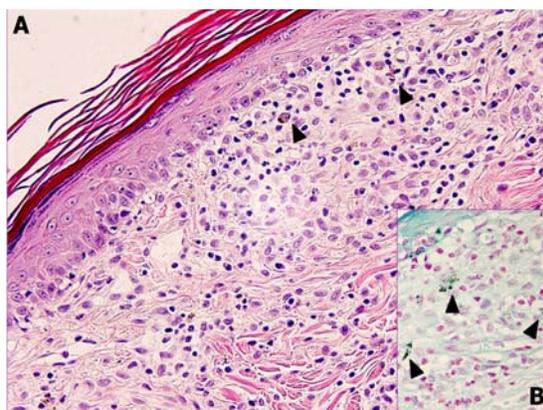
Vogt-Koyanagi-Harada syndrome (VKH) is a multi-systemic autoimmune disorders including ophthalmic (bilateral uveitis), neurologic (dysacusia and meningitis) and cutaneous signs (vitiligo, poliosis, and alopecia) in people (Gaudreau *et al.*, 2012). Similar to the human VKH syndrome, concurrent bilateral uveitis and depigmenting dermatitis was reported in Japanese Akita (Asakura *et al.*, 1977). Unlike with VKH syndrome, neurologic signs are rare in dogs and the term, uveodermatologic syndrome (UDS) has been used for this typical ocular and dermatologic disorder (Herrera and Duchene, 1998). The cause of UDS is still unclear, but immune-mediated reactions against melanocytes have been considered for the probable etiology, like human VKH syndrome (Yamaki *et al.*, 2000; Angles *et al.*, 2005). This report describes the clinical and histopathologic features of UDS in a Siberian Husky dog.

**History and clinical examination:** A 2-year-old, intact male Siberian Husky was presented with corneal opacity, eye lid swelling, depigmentation, alopecia and erythema of facial skin. Conjunctivitis and uveitis was diagnosed 1 year ago and periocular depigmentation was spread to nasal planum progressively over the recent 6 months. Antibiotics (30 mg/kg PO twice daily, Falexin®; Dong Wha Pharm Co., Ltd., Korea) was prescribed by the

referring veterinarian but the clinical signs got worsen. Physical examination showed erythema, erosin, depigmentation, crust and alopecia on the mucocutaneous junctions of the muzzle, eyelids, periocular skin and nasal planum (Fig. 1). Ophthalmic examination revealed blepharospasm, conjunctival hyperemia, diffuse corneal edema, mucopurulent discharge, third eyelid swelling and prolapsed of both eyes (Fig. 1C and D). Schirmer tear tests (Schirmer Tear Test; Schering-Plough Animal Health Co., NJ, USA), fluorescein tests was normal in both eyes and intraocular pressures (Tono-pen XL; Mentor, Norwell, MA, USA) was decreased for the right (8 mmHg) and left eye (6 mmHg). The menace response, dazzle response, direct and consensual pupillary light reflexes were absent. Two-dimensional B-mode ultrasonography in both eyes using a 7.5 MHz probe (Logiq400; GE healthcare, Milwaukee, WI, USA) was performed. The anterior chamber was shallow and opacification of lenses were marked in both eyes. Posterior globe wall was thickened and amorphous opacities were seen in the vitreous. Bilateral uveitis, cataract concurrent with depigmentated skin disorder was diagnosed. A complete blood count, serum chemistry profile and thyroid functions were normal. Multiple skin scrapings (superficial and deep) proved to be negative and cytology revealed secondary infection of few cocci. A presumptive diagnose of UDS was considered.



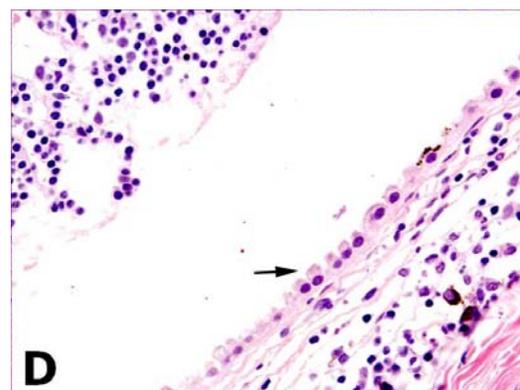
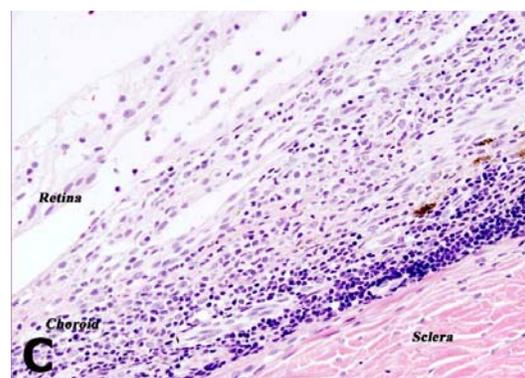
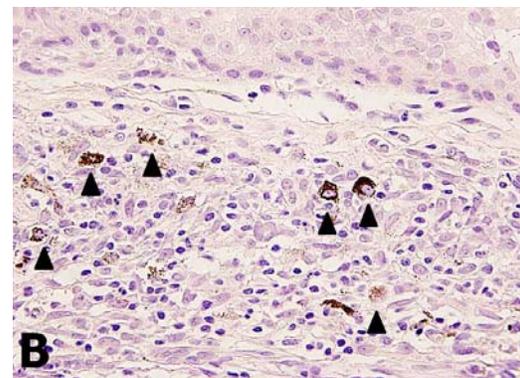
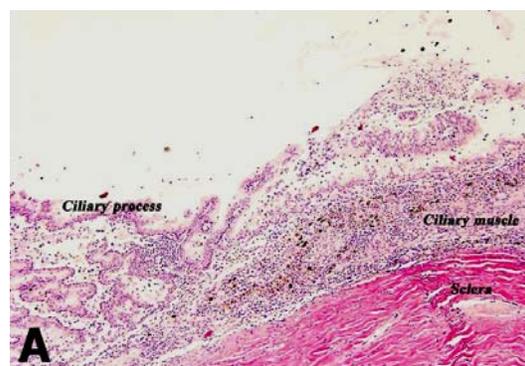
**Fig. 1:** Appearance of the ocular and dermatologic lesions in a 2-year-old Siberian Husky. MR images demonstrating an IAC in a dog. (A, B) Depigmentation, ulceration, and alopecia of the nasal planum and periocular area were noted. (C, D) Close-up of the dog showed diffuse corneal edema, mucopurulent discharge, prolapsed and swollen third eyelid of both eyes (C: right eye, D: left eye).



**Fig. 2:** Photomicrographs of histopathologic examination of the nasal planum. (A) Lichenoid interface dermatitis with histiocytes and lymphocytes was present. Melanocytes were absent from the basal cells and scattered melanin granules in the dermal macrophages (pigmentary incontinence) were noted (H&E stain, X 100). (B) Coarse and fine melanin granules in the macrophages were stained blue-green (arrowheads) (Schmorl's stain, X 400).

**Differentials and diagnosis:** Vitiligo, cutaneous lymphoma, discoid lupus erythematosus, pemphigus foliaceus and pemphigus erythematosus should be differentiated for the dermatologic lesions and infectious causes for the bilateral uveitis should be excluded. Further diagnostic procedures were included PCR for the systemic viral and parasites infections, and skin biopsy. However, the owner declined to further diagnosis or therapy due to the economic burden and the dog was euthanized. Skin specimens from the nasal planum and globes were obtained for histologic examination.

Biopsy results from the nasal planum showed lichenoid interface dermatitis (Fig. 2A). The infiltrated inflammatory cells were composed of histiocytes, lymphocytes and melanophages. Epidermal melanocytes were absent and pigmentary incontinence (scattered melanin granules in macrophages) was confirmed using



**Fig. 3:** Histopathology of the enucleated globes from a 2-year-old Siberian Husky. (A) Diffuse lymphocytic and histiocytic inflammation of iris and ciliary body (anterior uveitis) were noted (H&E stain, X 40). (B) Pigmentary incontinence (arrowheads) and inflammatory cells were marked in the iris (H&E stain, X400). (C) Pyogranulomatous inflammation of the retina and choroid were also noted (H&E stain, X100). (D) Retinal degeneration and detachment with hypertrophic retinal pigment epithelium cells (arrow) were revealed (H&E stain, X 400).

Schmorl's stain (Fig. 2B). Histopathological examination of the enucleated globes revealed diffuse pyogranulomatous inflammation of the iris, ciliary body (anterior uveitis) and retina and choroid (posterior uveitis) (Fig. 3). Lymphocytic and histiocytic inflammation with several macrophages containing melanin granules in the cytoplasm were present (Fig. 3C). Bilateral retinal degeneration and detachment were also shown (Fig. 3D). These findings were consistent with the diagnosis of UDS. Based on the history, ophthalmic examination results, and the skin lesions with histological findings, the dog was diagnosed as UDS.

## DISCUSSION

Cause of the VKH syndrome in human is not fully understood. Th1 autoimmune reaction against proteins in melanocytes is considered possible causes and human leukocyte antigen class II alleles have been documented as risk genes (Yamaki *et al.*, 2000; Gaudreau *et al.*, 2012). Similar immune mechanism is possible for the UDS in dogs. One report described dog leukocyte antigen system DQA\*00201 is highly associated with UDS (Angles *et al.*, 2005). Other experiment revealed immunization of Akita dogs with tyrosinase-related protein1 developed UDS, which was suggesting a genetic component to the disease (Yamaki *et al.*, 2000; 2005). Thus, UDS is the most commonly affected northern breeds, Akitas, Siberian husky, Alaskan malamutes and Samoyed (Angles *et al.*, 2005; Pye, 2009). Other reported breeds included Irish setter, Golden retriever, Old English sheepdog, Saint Bernard, Shetland sheepdog, Chow Chow, Dashshund, Fox terrier, Basset hound, Brazilian fila, Jack Russell terrier and rat terrier (Herrera and Duchene, 1998; Baiker *et al.*, 2011; Blackwood *et al.*, 2011). There is no sex predilection and reported ages are variable (6 months to 13 years) (Pye, 2009). Characteristic features of UDS are bilateral uveitis followed by cutaneous depigmentation. Usually ocular signs are observed prior to the dermatologic signs (Herrera and Duchene, 1998). Long term prognosis of UDS is guarded and lifelong therapy using systemic immunosuppressive medication is usually needed (Blackwood *et al.*, 2011). Due to secondary glaucoma, cataract, and visual loss is common in uncontrolled cases, early diagnosis and aggressive treatment is essential (Baiker *et al.*, 2011).

In this case, young Siberian Husky had a bilateral uveitis followed by cutaneous depigmentation prominently affecting head. The dog was predisposed breed for UDS and clinical signs were consistent with UDS. There are no definite diagnostic tests for UDS (Read *et al.*, 2001). Characteristic clinical features, exclusion of other possible disease, and supportive histopathologic results (lichenoid interface dermatitis with histiocytes and mononuclear cells, pigmentary incontinence, diffuses pyogranuloma-

tous inflammation of the globes, and retinal detachment) were critical for diagnosis of UDS in this dog.

Both topical and systemic steroids are treatment of choice and other immunosuppressive drugs, such as azathioprine, cyclosporine, tetracycline and niacinamide, or cyclophosphamide can be used as steroid-sparing drugs (Pye, 2009). Triamcinolone and dexamethasone are used in refractory cases (Blackwood *et al.*, 2011). Treatment should be initiated earlier to increase the chance to recover, but prognosis for vision in the most cases is often guarded (Herrera and Duchene, 1998; Baiker *et al.*, 2011). Early diagnosis and aggressive treatment was not properly implemented, and the dog was blinded at the time of presentation.

**Conclusion:** This case report demonstrated the characteristic clinical and histopathologic features of UDS in a Siberian Husky dog. Bilateral uveitis in certain breeds should be considered for UDS, because early and aggressive treatment is important for the prognosis of this disease.

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