

UVEODERMATOLOGICAL SYNDROME IN A COCKER-POODLE MIXED-BREED DOG (*Síndrome uveodermatológica em um cão mestiço*)

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ABSTRACT – The uveodermatological syndrome, an auto-immune disorder having ophthalmic and dermal signs, has been described frequently in Akita dogs, rarely in other purebred dogs but none description of this syndrome in mixed breed dogs has been reported. In this paper, we describe the syndrome in a Cocker-Poodle mixed breed dog.

Key words: dermal depigmentation, uveitis, uveodermatological syndrome (UDS), Vogt-Koyanagi-Harada Syndrome (VKHS).

RESUMO – A síndrome uveodermatológica, um distúrbio auto-imune que apresenta sinais oculares e cutâneos, tem sido descrita freqüentemente em cães da raça Akita, raramente, em outras raças e não há relato em cães mestiços. Neste artigo, descreve-se a síndrome em um cão mestiço Cocker com Poodle.

Palavras chave: despigmentação cutânea, uveíte, síndrome uveodermatológica (SUD), síndrome Vogt-Koyanagi-Harada (SVKH).

Introduction

The Vogt-Koyanagi-Harada (VKH) syndrome is a well known disease in human beings. It was first described by Vogt in 1906, by Koyanagi in 1929 and by Harada in 1926. The cause of this syndrome in human beings has been a mystery, but since 1969 there has been substantial evidence that it is an immune-mediated disease in which melanocytes are the target cells (MORGAN, 1989).

In man, the VKH syndrome has four recognized phases: (1) prodromal, characterized by neurologic and auditory manifestations; (2) acute uveitis, characterized by diffuse choroiditis, which may manifest as exudative retinal detachments and papillitis, with or without clinical signs of intraocular inflammation; (3) chronic, characterized by the variable development of depigmentation of the fundus (sunset glow fundus) and limbus (Sugiura sign), as well as poliosis, vitiligo and alopecia; and (4) chronic-recurrent, which may interrupt the chronic phase with iridocyclitis, which can be recurrent, chronic or both (READ *et al.*, 2001a).

The first report of dogs having a similar

disorder to the VKH syndrome of human beings was made in Japan in 1977 in Akita dogs (ASAKURA *et al.*, 1977). The Akita has been notably the most affected dog breed (ASAKURA *et al.*, 1977; HASEGAWA, 1985; ROMATOWSKI, 1985; BEDFORD, 1986; COTTRELL; BARNETT, 1987; FURLONG *et al.*, 1989; LINDLEY *et al.*, 1990; BARROS *et al.*, 1991; MURPHY *et al.*, 1991). There have been reports of the occurrence of this disease in other breeds as Samoyed, Irish Setter (BUSSANICH *et al.*, 1982), Golden Retriever, Old English Sheepdog, Saint Bernard, Shetland Sheepdog (KERN *et al.*, 1985), Australian Shepherd (FABRIÈS, 1984; KERN *et al.*, 1985), Siberian Husky (FABRIÈS, 1984; KERN *et al.*, 1985; TACHIKAWA *et al.*, 1990; VERCELLI; TARAGLIO, 1990; GUAGUERE-LUCAS *et al.*, 1995; DENEROLLE *et al.*, 2000), Chow Chow (MORGAN, 1989; WARMOES, 1999), Dachshund (HERRERA and DUCHENE, 1998) and Fox Terrier (SLINCKX; FONTAINE, 1999).

In dogs, the disease lacks the systemic component, and is called uveodermatological syndrome (UDS). The ocular signs are usually the first abnormality noticed, which include bilateral anterior and posterior uveitis to severe

panuveitis. Retinal detachment, optic neuritis, or changes in choroidal pigments may also be present. The dermatological signs include depigmentation of the eyelids, lips, nose and, less commonly of the scrotum, vulva, footpads, and anus. Neurological signs are rare, described only twice, in one Akita (COTTRELL and BARNETT, 1987) and in one Siberian Husky (DENEROLLE *et al.*, 2000), but the suggestion of the neurological disease was made based only in behavioral changes, additional neurological evaluation was not performed. Corticosteroids have been usually the treatment of choice for human beings and dogs. Other

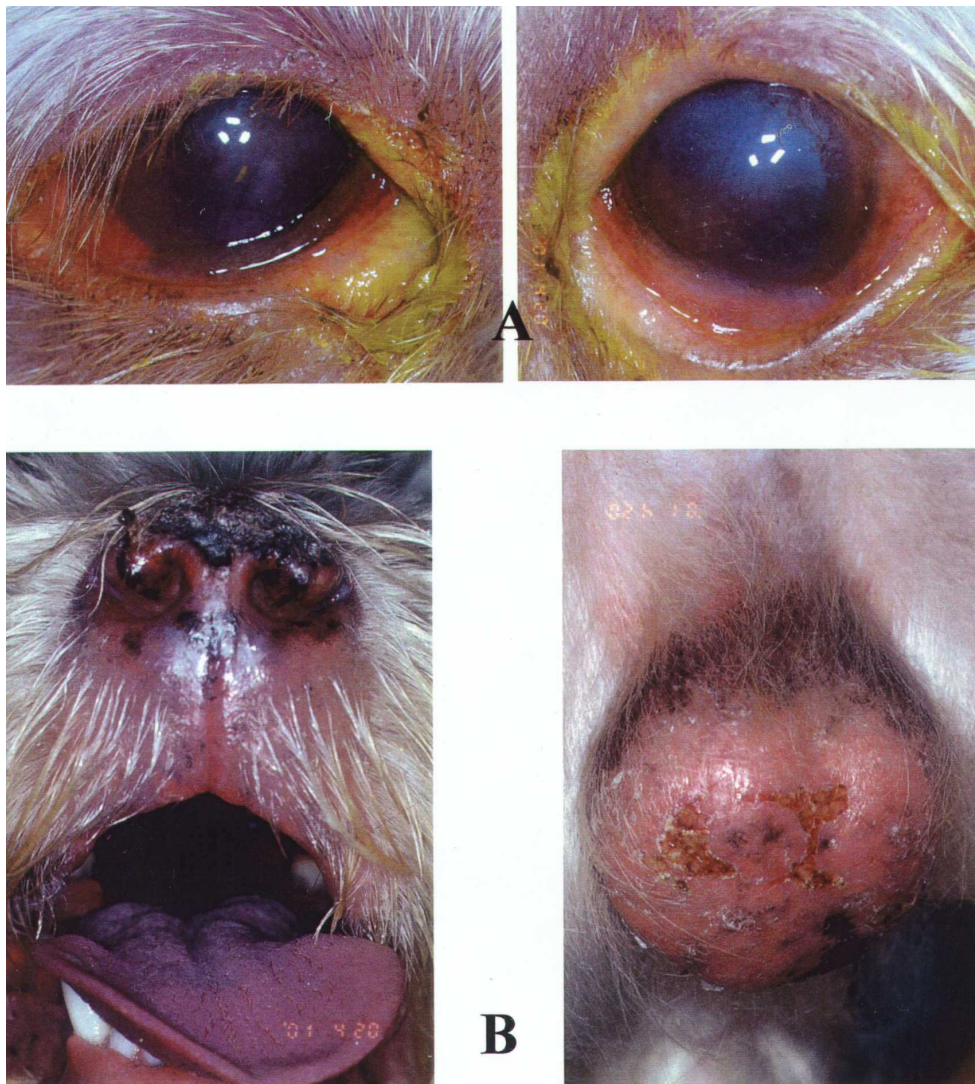
immunosuppressive drugs can be associated when necessary.

This syndrome is not a life threatening disease, however the prognosis for vision is poor, because severe complications often lead to visual loss.

Case Report

A 2 $\frac{1}{2}$ -year-old male mixed breed dog (English Cocker Spaniel x Poodle) was referred with a history of eye redness in the last 5 months. The owner reported visual impairment and the use of several systemic and topical medications with no success.

FIGURA 1 – A) CORNEAL OPACITY AND NEW VESSELS OF THE CORNEA OF RIGHT AND LEFT EYES. B) DERMAL DEPIGMENTATION OF THE NASAL PLANUM AND SCROTUM WITH EROSIONS AND CRUSTS.



The first ophthalmic examination revealed mild enlargement of the eyes, moderate mucous discharge, moderate to severe conjunctival hyperemia; opacity and vessels at the corneal surface. In the anterior chamber, there was an intense flare and rubeosis iridis. The pupillary light reflexes in both eyes were absent. The lens were cataractous, hence the ocular fundi could not be evaluated (FIGURA 1A). The IOP was 10 mmHg (TONOPEN) in both eyes. The dog had depigmentation of the lips, nasal planum, and scrotum (FIGURA 1B). Complete blood count has been performed. The treatment was prednisone 1mg/kg once a day; dexamethasone + neomycin + polymyxin four times a day; 1% atropine ophthalmic solution - twice a day for three days, and, once a day afterwards after one week, at the first examination, hyphema developed in the anterior chamber. The laboratory analysis (complete blood count, biochemistry) was normal, so a presumptive diagnosis of UDS was made. Skin samples were taken for histological examination. One month later, the eyes were smaller, there was no conjunctival hyperemia, and the hyphema had disappeared, thereafter the medication was tapered and then discontinued. One month after the medication has been discontinued, the owner claimed that the dog eyes became red again, and at the ophthalmic examination, it has been observed that the ophthalmic signs had gotten worse. The medication (oral prednisone and topical dexamethasone + neomycin + polymyxin) was introduced again. Meanwhile, the result of the histological analysis had shown features compatible with the UDS.

Discussion

The VKH syndrome (VKHS) in human beings is considered a chronic, bilateral, granulomatous ocular and multisystemic inflammatory condition of unknown cause (READ *et al.*, 2001a). It affects primarily Asians, Latinos, Native Americans or Asian Indians. Women appear to be affected more commonly than men. VKH disease may occur at all ages, including childhood (READ *et al.*, 2000). Experimental data continue to support an autoimmune etiology for VKH disease, directed most probably against an melanocyte antigenic component,

possibly tyrosinase or tyrosinase-related protein (YAMAKI *et al.*, 2000), an identified 75kDa protein obtained from cultured human melanous cells (G-361) (KONDO *et al.*, 1994) and the S-100 protein (GLODDEK *et al.*, 1999). There are some evidence about the involvement of the Epstein-Barr virus in the pathogenesis of the VKHS (MINODA *et al.*, 1999). In some cases, it is thought that the trigger is a cutaneous injury (RATHIMAN *et al.*, 1999). There is likely a genetic predisposition, since specific HLA types have been associated with the disease (READ *et al.*, 2001a).

There are no specific diagnostic tests for the VKH disease. The diagnosis is therefore based on a combination of suggestive clinical and ancillary test findings when other uveitic conditions have been excluded (READ *et al.*, 2001b).

The features of the VKH syndrome may be shared by multiple other entities, such as sarcoidosis, sympathetic ophthalmia, syphilitic uveitis, tuberculosis uveitis, Lyme disease, posterior scleritis, intraocular lymphoma, central serous choroidopathy and uveal effusion syndrome (READ *et al.*, 2001a). The most affected breed has been the Akita, although other breeds can be affected.

There is no sexual predisposition (HASEGAWA, 1985; MORGAN, 1989; BARROS *et al.*, 1991) and the age of onset is 7-72 months (BARROS *et al.*, 1991).

As in human beings, the cause of the UDS in dogs remains unknown. Routine parameters are normal, and immune-function tests are usually nondiagnostic (MORGAN, 1989). Hereditary condition is suggested (HASEGAWA, 1985; COTTRELL; BARNETT, 1987)

Histologically, canine ocular lesions closely resemble those of humans. The uveal tract is diffusely infiltrated with lymphocytes, plasma cells, epithelioid cells and pigment-laden cells (BUSSANICH *et al.*, 1982; KERN *et al.*, 1985; MORGAN, 1989; LINDLEY *et al.*, 1990). In the inflamed areas, electron microscopy has demonstrated numerous macrophages containing ingested melanosomes (BUSSANICH *et al.*, 1982).

Depigmentation of the hair and skin usually follows the onset of ocular signs. Dermal depigmentation often involves the eyelids, nasal planum, lips, scrotum, and footpads (MORGAN,

1989). Few cases have involved generalized vitiligo (CAMPBELL *et al.*, 1986; HERRERA and DUCHENE, 1998).

Dermatohistopathologic findings include an interface dermatitis composed of large histiocytic cells, small mononuclear cells, and plasma cells. Other manifestations are irregular epidermal hyperplasia with hyperkeratosis and pigmentary incontinence with decreased numbers of epidermal melanocytes (BOLDY *et al.*, 1989). There is one report about the association of anti-retinal antibodies with UDS (MURPHY *et al.*, 1991).

The general guidelines in the therapy involve 1 to 2 mg/kg per day of oral prednisone (MORGAN, 1989). By analogy with human experience in VKH disease, systemic corticosteroids should be continued at relatively high doses for at least two or three months, and perhaps for as long as six months (ROMATOWSKI, 1985). Unfortunately, the prognosis for vision is often poor.

The macroscopic and microscopic lesions in the case presented in this paper were consistent with the uveodermatological syndrome described in dogs.

The veterinary practitioner should maintain a suspicion for this uveodermatological syndrome not only in the Akita dog, but in any dog displaying signals that remind those of this particular disease.

References

- ASAKURA, S.; TAKAHASHI, K.; ONISHI, T. Vogt-Koyanagi-Harada syndrome (uveitis diffusa acuta) in the dog. **Japanese Journal of Veterinary Medicine**, v. 673, p. 445-455, 1977.
- BARROS, P.S.M.; SAFATLE, A.M.V.; MALERBA, T.A.; YRIO, K.; ALVARENGA, J.; LARSSON, M. H. M. A. Uveitis and dermal depigmentation (Vogt-Koyanagi-Harada-like syndrome) in Akita dogs I. Clinical aspects. **Brazilian Journal of Veterinary Research and Animal Science**, São Paulo, v. 28, n. 1, p. 75-79, 1991
- BEDFORD, P.G.C. Uveodermatological syndrome in the Japanese Akita. **Veterinary Record**, London, v.18, n.5, p.134, 1986.
- BOLDY, K.L.; FURLONG, R.C.; HOLLAND, G.N. Uveodermatologic syndrome in the dog: clinical characteristics and treatment of a disorder similar to human Vogt-Koyanagi-Harada syndrome. **Veterinary Focus**, v. 3, n. 1, p. 112-114, 1989.
- BUSSANICH, M.N.; ROOTMAN, F.R.C.S.; DOLMAN, C.L. Granulomatous pan uveitis and dermal depigmentation in dogs. **Journal of the American Animal Hospital Association**, Lakewood, v. 18, p. 131-138, 1982.
- CAMPBELL, K.L.; MCLAUGHLIN, A.S.; REYNOLDS, H.A. Generalized leukoderma and poliosis following uveitis in the dog. **Journal of the American Animal Hospital Association**, Lakewood, v. 22, n. 1, p. 121-124, 1986.
- COTTRELL, B.D.; BARNETT, K.C. Harada's disease in the Japanese Akita. **Journal of Small Animal Practice**, London, v. 28, p. 517-521, 1987.
- DENEROLLE, P.; TESSIER, M.; MOLON-NOBLOT, S. [Nerve lesions in a Siberian Husky suffering from a uveodermatological syndrome]. **Pratique Medicale and Chirurgicale de l'Animal de Compagnie**, Paris, v. 35, n. 4, p. 273-278, 2000.
- FABRIÈS, L. Syndrome "VKH" chez le chien. Au sujet de deux cas cliniques. **Pratique Medicale and Chirurgicale de l'Animal de Compagnie**, v. 19, p. 393-397, 1984.
- FURLONG, R.C.; BOLDY, K.L.; HOLLAND, G.N.; STEINMETZ, R.L.; FOOS, R.Y. Uveodermatologic syndrome in dogs: a model of Vogt-Koyanagi-Harada syndrome. **Investigative Ophthalmology & Visual Science**, Bethesda, v. 30, n. 4, p. 86, 1989.
- GLODDEK, B.; LASSMANN, S.; GLODDEK, J.; ARNOLD, W. Role of S-100 beta as potential autoantigen in an autoimmune disease of the inner ear. **Journal of Neuroimmunology**, Amsterdam, v. 101, p. 39-46, 1999.
- GUAGUERE-LUCAS, J.; GUAGUERE, E.; LAFORGE, H.; MIALOT, M. Pseudo Vogt-Koyanagi-Harada syndrome in a Siberian Husky. **Pratique Medicale and Chirurgicale de l'Animal de Compagnie**, Paris, v. 27, n. 1, p. 41-47, 1995.
- HASEGAWA, A. Mucocutaneous ocular syndrome in Akita dogs. **Animal's Eye Research**, Ibaraki-ken, v. 4, p. 17-21, 1985.
- HERRERA, H.D.; DUCHENE, A.G. Uveodermatological syndrome (Vogt-Koyanagi-Harada-like syndrome) with generalized depigmentation in a Dachshund. **Veterinary Ophthalmology**, Oxford, v. 1, n. 1, p. 47-51, 1998.

- KERN, T.J.; WALTON, D.K.; RIIS, R.C.; MANNING, T.O.; LARATTA, L.J.; KZIEZYC, J. Uveitis associated with poliosis and vitiligo in six dogs. **Journal of the American Animal Hospital Association**, Lakewood, v. 187, p. 408-414, 1985.
- KONDO, I.; YAMAKI, K.; SAKURAGI, S. [Analysis of the candidate antigen for Harada's disease.]. **Nippon Ganka Gakkai Zasshi**, Tokyo, v. 98, p. 596-603, 1994.
- LINDLEY, D.M.; BOOSINGER, T.R.; COX, N.R. Ocular histopathology of Vogt-Koyanagi-Harada-like syndrome in an Akita dog. **Veterinary Pathology**, Washington DC, v. 27, n. 4, p. 294-6, 1990.
- MINODA, H.; SAKAI, J.; SUGIURA, M.; SAKAI, J.; SUGIURA, M.; IMAI, S.; OSATO, T.; USUI, M. [High inducibility of Epstein-Barr virus replication in B lymphocytes in Vogt-Koyanagi-Harada disease.]. **Nippon Ganka Gakkai Zasshi**, Tokyo, v. 103, n. 4, p. 288-296, 1999.
- MORGAN, R.V. Vogt-Koyanagi-Harada syndrome in humans and dogs. **Compendium on Continuing Education for the Practicing Veterinarian**, Princeton Junction, v. 11, n. 10, p. 1211-1214, 1989.
- MURPHY, C.J.; BELLHORN, R.W.; THIRKILL, C. Anti-retinal antibodies associated with Vogt-Koyanagi-Harada-like syndrome in a dog. **Journal of the American Animal Hospital Association**, Lakewood, v. 27, n. 4, p. 399-402, 1991.
- RATHIMAN, S.R.; NAMPERUMALSAMY, P.; NOZIK, R.A.; CUNNINGHAM Jr, E.T. Vogt-Koyanagi-Harada syndrome after cutaneous injury. **Ophthalmology**, Hagerstown, v. 106, p. 635-638, 1999.
- READ, R.W.; HOLLAND, G.N.; RAO, N.A.; TABBARA, K.F.; OHNO, S.; ARELLANES-GARCIA, L.; PIVETTI-PEZZI, P.; TESSLER, H.H.; USUI, M. Revised diagnostic criteria for Vogt-Koyanagi-Harada disease: report of an International Committee on Nomenclature. **American Journal of Ophthalmology**, New York, v. 131, n. 5, p. 647-652, 2001a.
- READ, R.W.; RAO, N.A.; CUNNINGHAM, E.T. Vogt-Koyanagi-Harada disease. **Current Opinion in Ophthalmology**, Philadelphia, v. 11, n. 6, p. 437-442, 2000.
- READ, R.W.; RECHODOUNI, A.; BUTANI, N.; JOHNSTON, R.; LABREE, L.D.; SMITH, R.E.; RAO, N.A. Complications and prognostic factors in Vogt-Koyanagi-Harada disease. **American Journal of Ophthalmology**, New York, v. 131, n. 5, p. 599-606, 2001b.
- ROMATOWSKI, J. Uveodermatological syndrome in an Akita dog. **Journal of the American Animal Hospital Association**, Lakewood, v. 21, p. 777-80, 1985.
- SLINCKX, J.; FONTAINE, J. [A case of solar dermatological syndrome resembling Vogt-Koyanagi-Harada in a fox terrier dog.]. **Point Veterinaire**, Maisons-Alfort, v. 30, n. 198, p. 243-7, 1999.
- TACHIKAWA, S.; TACHIKAWA, T.; NAGATA, M. Uveodermatological (Vogt-Koyanagi-Harada-like) syndrome with sloughing of the claws in a Siberian Husky. **Journal of Veterinary Medicine**, Berlin, v. 48, n. 7, p. 559-61, 1990.
- VERCELLI, A.; TARAGLIO, S. Canine Vogt-Koyanagi-Harada-like syndrome in two Siberian Husky dogs. **Veterinary Dermatology**, Oxford, v. 1, n. 3, p. 151-8, 1990.
- WARMOES, T. [Canine model of Vogt-Koyanagi-Harada syndrome.]. **Point Veterinaire**, Maisons-Alfort, v. 30, n. 198, p. 249-54, 1999.
- YAMAKI, K.; GOCHO, K.; HAYAKAWA, K. Tyrosinase family proteins are antigens specific to Vogt-Koyanagi-Harada disease. **Journal of Immunology**, Bethesda, v. 165, n. 12, p. 7323-9, 2000.

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