Generalized vitiligo in a pure-bred Rottweiler: case report

Vitiligo generalizado em um cão da raça Rottweiler: relato de caso

Gabrielle Márcia Marques Cury,* e Adriane Pimenta da Costa Val**

Resumo

Vitiligo é uma desordem adquirida causada pela perda progressiva de melanócitos. O vitiligo canino localizado (VL) é uma doença relativamente comum em cães adultos jovens que normalmente apresentam despigmentação da pele, pelo, focinho, lábios e mucosas oral e oculares, embora unhas e coxins também possam ser afetados. O vitiligo generalizado (VG), por outro lado, é raramente reportado em cães. O presente artigo descreve a primeira ocorrência do VG em um cão puro da raça Rottweiler com 18 meses de idade e histórico de despigmentação progressiva das áreas de pelos pretos.

Palavras-chave: despigmentação, pele, cão, melanócito.

Abstract

Vitiligo is an acquired depigmentation disorder caused by the progressive destruction of melanocytes. Canine localised vitiligo (LV) is a relatively common disease that is expressed in young adult dogs, normally as a discoloration of the skin, hair, muzzle, lips, and oral and facial mucosa, although the elbows and nails may also be affected. Generalised vitiligo (GV), on the other hand, has very rarely been reported in dogs. The present sudy describes for the first time the occurrence of GV in a black and nut-brown pure bred Rottweiler with an eighteen month history of progressive discoloration in the black-haired, but not brown-haired, areas.

Keywords: depigmentation, skin, dog, melanocyte.

Introduction

Vitiligo is an acquired depigmentation disorder (Dell'ana e Picardo, 2006; Fain et al., 2003) that has been known for more than 3000 years (Nair, 1978). The disease is caused by the chronic and progressive destruction of melanocytes (Dell'ana e Picardo, 2006), and is characterised by the emergence of areas presenting leukoderma and leukotrichia (Fain et al., 2003). Human vitiligo is classified as localised (LV) and generalised (GV). The former is normally unilateral, whereas the latter is symmetric with lesions occurring near the mouth and eyes (Taïeb, 2000).

The diagnosis of GV is based on the history of the patient together with clinical and histopathological examinations of the lesions. Old lesions are characterised by relatively normal dermis and epidermis, except for the absence of melanocytes, whereas recent lesions are characterised by the moderate presence of lymphocytes, as well as melanocytes presenting signs of degeneration such as cytoplasmic vacuolisation, melanosome aggregation, lipid degeneration and pyknosis (Scott et al., 2001).

On the basis that human GV is more frequent in individuals with a positive family history, it has been proposed that the disease is a polygenic trait (Rezaei et al., 2007) and that some of these multiple genes may be linked to others coding for GV-associated autoimmune diseases (Fain et al., 2003). The polygenic hypothesis is supported by segregation studies involving GV-affected families (Majumder et al., 1993; Nath et al., 1994).

The destruction of melanocytes in vitiligo has been explained by three different mechanisms, namely, the autoimmune, the self-toxicity and the neurological hypotheses (Le Poole et al., 1997; Taïeb, 2000; Scott et al., 2001). The first of these suggests a non-inflammatory response from T-lymphocytes against melanocytes (Ongenae et al., 2003; Le Poole, 2004), while the second assumes that the melanocytes are susceptible to toxic intracellular metabolites (particularly hydrogen peroxide and free radicals) produced during melanogenesis (Agrawal et al., 2004; Hasse et al., 2004; Pelle et al., 2005; Schallreuter et al., 2008). The third hypothesis explains the distribution of the disease in terms of the injury of peripheral nerve endings (Scott et al., 2001). This proposal, which is more related to LV, has received less support than the other two hypotheses.

The main treatments available for human GV include systemic photochemotherapy with psoralen plus ultraviolet A (PUVA) and phototherapy with narrow-band ultraviolet B (NB-UVB), but these do not confer a complete cure. The active principle of PUVA has been used in dermatological treatment for more than 2500 years (Fitzpatrick e Pathak, 1959), whereas NB-

---

* Post Graduation Programe, Veterinary School, UFMG, Avenida Antonio Carlos, 6627, Belo Horizonte, MG, gabriellecury@gmail.com

** Veterinary School, UFMG, Avenida Antonio Carlos, 6627, 31270-901, Belo Horizonte, MG.

A quem enviar correspondência: adriane@ufmg.br

UVB therapy was only introduced in 1997 (Westerhof e Krobotova, 1997). The response to treatment varies according to the areas affected: hands and feet show little or no repigmentation (Brazzelli et al., 2007; Lee et al., 2007).Other GV therapies involve topical photochemotherapy with khellin plus ultraviolet A (KUVA), application of topical macrolide immunomodulators, vitamin D_3 analogues (ex. calcipotriol), glucocorticoids or L-phenylalanine, excimer laser and surgical procedures (Forschner et al., 2007).

In dogs, LV is fairly common amongst the breeds German Shepard, Collie, Rottweiler, Doberman, Giant Schnauzer, Bull Mastiff, Sheepdog and Dachshund. Normally, the disease is expressed in young adult dogs as a discoloration of the skin, hair, muzzle, lips, oral and facial mucosa, although the elbows and nails may also be affected (Scott et al., 2001). In contrast to LV, reports of GV are extremely rare in dogs. The present paper describes for the first time the occurrence of GV in a pure bred Rottweiler.

Material and methods

A 4 year old, bicolour (black and nut-brown) male Rottweiler was referred to the Dermatology Service of the Veterinary Hospital of the Universidade Federal de Minas Gerais, Brazil, with an 18 month history of progressive discoloration in the black-haired areas (Fig. 1A). Clinical and dermatological examination revealed depigmentation of the skin (Fig. 1B and Fig. 1C) and hair in 90% of the areas that had formerly been covered by black hair. Interestingly, however, the brown haired areas were normal (Fig. 1A). Since no other dermatological or systemic abnormalities were detected, skin biopsies from the face, superior lip, and dorsum were performed and the samples were submitted for histopathological analysis.

Results

Examination revealed spots with hypopigmented epidermis (hypomelanosis), focal intradermic invasion of peripheral blood mononuclear cells, and melanin deposits within subepithelial stroma (melanin incontinence). The skin fragments removed from the brown-haired areas were completely normal. No treatment was prescribed for the dog.

Discussion and conclusion

The pure-bred Rottweiler is considered to be predisposed to LV (Ackerman, 2008), although there are no reports in the literature relating to GV-affected animals or to dogs presenting vitiligo in black-haired areas concomitant with healthy brown areas. Since eumelanin generates black to dark-brown pigments while pheomelanin produces yellow to red pigments, it is possible that the destruction of melanocytes may be associated in some manner with the former but not with the latter, although the mechanism involved is not known. In this context, however, it has been reported that 4-tert-butylcatechol (TBC) promotes the destruction of eumelanin in human melanocytes (Yonemoto et al., 1983). TBC, a depigmenting chemical used in the manufacture of carpets, has been implicated in a case of occupational vitiligo developed by a worker in a polyester resin plant (Gellin et al., 1970).

Figure 1: (**A**) Rottweiler affected by generalised vitiligo. Leukoderma and leukotrichia can be observed in the black-haired areas whereas the brown-haired areas are normal. (**B**) Close-up view of the eye area showing the affected skin and hair. (**C**) Close-up view of the muzzle showing the affected skin and mucosa.

Although vitiligo does not represent a serious health problem per se, GV-affected humans may develop dermatosis in those areas where melanin is absent following exposure to sun light (Gül et al., 2007). It is possible that this type of dermatosis may also emerge in GV-affected dogs.

The subject of this case study has not exhibited other associated diseases. Although the animal has not received any medication so far, treatment is under consideration.

References

ACKERMAN, L. Immunologic skin disorders. In:_____. (Ed.) *Atlas of small animal dermatology*. Buenos Aires: Inter-médica, 2008. p. 135-226.

AGRAWAL, D.; SHAJIL, E.M.; MARFATIA, Y.S. et al. Study of the antioxidant status of vitiligo patients of different age groups in Baroda. *Pigment Cell Res.,* v. 17, p. 289-294, 2004.

BRAZZELLI, V.; ANTONINETTI, M.; PALAZZINI, S. et al. Critical evaluation of the variants inuencing the clinical response of vitiligo: study of 60 cases treated with ultraviolet B narrow-band phototherapy. *J. Eur. Acad. Dermatol. Venereol.,* v. 21, p. 1369-1374, 2007.

DELL'ANA, M.L.; PICARDO, M. A review and a new hypothesis for non-immunological pathogenetic mechanisms in vitiligo. *Pigment Cell Res.,* v. 19, p. 406-411, 2006.

FAIN, P.R.; GOWAN, K.; LABERGE, G.S. et al. A genomewide screen for generalized vitiligo: confirmation of *AIS1* on chromosome 1p31 and evidence for additional susceptibility loci. *Am. J. Hum. Genet.,* v. 72, p. 1560-1564, 2003.

FITZPATRICK, T.B.; PATHAK, M.A. Historical aspect of methoxsalenand other furocoumarins. *J. Invest. Dermatol.,* v. 32, p. 229-231, 1959.

FORSCHNER, T.; BUCHHOLTZ, S.; STOCKFLETH, E. Current state of vitiligo therapy – evidence-based analysis of the literature. *J. of the German Society of Dermatol.,* v. 5, p. 467-476, 2007.

GELLIN, G.A.; POSSICK, P.A.; PERONE, V.B. Depigmentation from 4-tertiary butyl catechol-an experimental study. *J. Invest. Dermatol.,* v. 55, p. 190-197, 1970.

GÜL, U.; KILIC, A.; TULUNAV, O. et al. Vitiligo associated with malignant melanoma and lupus erythematosus. *J. Dermatol.,* v. 34, p. 142-145, 2007.

HASSE, S.; GIBBONS, N.C.J.; ROKOS, H. et al. Perturbed 6-tetrahydrobiopterin recycling via decreased dihydropteridine reductase in vitiligo: more evidence for H_2O_2 stress. *J. Invest. Dermatol.,* v. 122, p. 307-313, 2004.

KANWAR, A.J.; DOGRA, S. Narrow-band UVB for the treatment of generalized vitiligo in children. *Clinical and Experimental Dermatol.,* v. 30, p. 332-336, 2005.

LE POOLE, I.C.; VAN DEN WIJINGAARD, R.M.; WESTERHOF, W. et al. Tenascin is overexpressed in vitiligo lesional skin and inhibits melanocyte adhesion. *Br. J. Dermatol.,* v. 137, p. 171-178, 1997.

LE POOLE, I.C.; WANKOWICZ-KALINSKA, A.; DEN WIJNGAARD, R.M. et al. Autoimmune aspects of depigmentation in vitiligo. *J. Invest. Dermatol. Symp. Proc.,* v. 9, p. 68-72, 2004.

LEE, Y.; SEO, Y.J.; LEE, J.H. et al. High-dose prednisolone and psoralen ultraviolet A combination therapy in 36 patients with vitiligo. *Clinical and Experimental Dermatol.,* v. 32, p. 499-501, 2007.

MAJUMDER, P.P.; NORDLUND, J.J.; NATH, S.K. Pattern of familial aggregation of vitiligo. *Arch. Dermatol.*, v. 129, p. 994-998, 1993.

NAIR, B.K. Vitiligo: a retrospect. *Int. J. Dermatol.,* v. 17, p. 755-757, 1978.

NATH, S.K.; MAJUMDER, P.P.; NORDLUND, J.J. Genetic epidemiology of vitiligo: multilocus recessivity cross-validated. *Am. J. Hum. Genet.,* v. 55, p. 981-990, 1994.

ONGENAE, K.; VAN GEL, N.; NAEYAERT, J.M. Evidence for an autoimmune pathogenesis of vitiligo. *Pigment Cell Res.,* v. 16, p. 90-100, 2003.

PELLE, E.; MAMMONE, T.; MAES, D. et al. Keratinocytes as a source of reactive oxygen species by transferring hydrogen peroxide to melanocytes. *J. Invest. Dermatol.,* v. 124, p. 793-797, 2005.

REZAEI, N.; GAVALAS, N.G.; WEETMAN, A.P. et al. Autoimmunity as an aetiological factor in vitiligo. *J. Eur. Acad. Dermatol. Venereol.,* v. 21, p. 865-876, 2007.

SCHALLREUTER, K.U.; BAHADORAN, P.; PICARDO, M. et al. Vitiligo pathogenesis: autoimmune disease, genetic defect, excessive reactive oxygen species, calcium imbalance, or what else? *Exp. Dermatol.,* v. 17, p. 139-160, 2008.

SCOTT, D.W.; MILLER, W.H.; GRIFFIN, C.E. Pigmentary abnormalities. In:_____. *Muller & Kirk's Small animal dermatology*, 6th ed. Philadelphia: W.B. Saunders, 2001. p. 1005-1024.

TAÏEB, A. Intrinsic and extrinsic pathomechanisms in vitiligo. *Pigment Cell Res.,* v.13, p. 41-47, 2000. Suplementum 8.

WESTERHOF, W.; KROBOTOVA, L.N. Treatment of vitiligo with UV-B Radiation vs topical psoralen plus UVA. *Arch. Dermatol.,* v. 133, p. 1525-1528, 1997.

YONEMOTO, K.; GELLIN, G.A.; EPSTEIN, W.L. et al. Reduction in eumalanin by the activation of glutathione reductase and gamma-glutamyl transpeptidase after exposure to a despigmenting chemical. *Biochem. Pharmacol.,* v. 32, p. 1379-1382, 1983**.**