

## **Alopecia X in dogs: report of seven cases**

**Alopecia X em cães: relato de sete casos**

**Alopecia X en perros: reporte de siete casos**

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### **Abstract**

Alopecia X (AX) is a non-inflammatory and non-pruritic skin disease characterized by progressive hair loss. The most commonly affected dogs are male Pomeranian, Chow-Chow and Poodles. Although there is a similarity with endocrinopathies that course with dermatological changes, AX does not bring systemic harm to affected dogs. The diagnosis is based on the exclusion of other diseases that lead to hair loss, in addition to systemic diseases. As it is a disease rarely reported in the literature, the objective of the present work is to make a retrospective study of seven cases of dogs with AX treated in clinical routine, from diagnosis to therapeutic results. At the time, the dogs received a similar therapeutic approach, which consisted of the orchiectomy process, followed by supplementation with omega-3 and vitamin complex. Only one dog was not neutered, due to constant platelet changes. Two dogs underwent the microneedling technique due to partial response to conventional treatment and only one of them showed complete repilation. From the above, it is considered that AX is a disease present in the dermatological routine of dogs and that the recognition of its lesion pattern is important for a better diagnostic and therapeutic direction. In addition, it was observed that, although all the therapies employed resulted in an improvement in hair growth, the therapeutic response was variable, so that some dogs may not show complete repilation. Further researches involving therapy comparison are encouraged in order to provide a better understanding of their efficiency.

**Keywords:** Alopecia; Hyperpigmentation; Hair cycle.

### **Resumo**

A Alopecia X (AX) é uma dermatopatia não-inflamatória e não pruriginosa caracterizada pela perda progressiva de pelos. Os cães mais comumente afetados são machos da raça Spitz Alemão, Chow-Chow e Poodles. Embora haja uma semelhança com endocrinopatias que cursam com alterações dermatológicas, a AX não traz malefícios sistêmicos aos cães afetados. O diagnóstico baseia-se na exclusão de outras enfermidades que cursem com a queda de pelos, além de doenças sistêmicas. Por se tratar de uma doença pouco relatada na literatura, o objetivo do presente trabalho é fazer um estudo retrospectivo de sete casos de cães com AX atendidos em rotina clínica, desde o diagnóstico até os resultados terapêuticos. Na ocasião, os cães receberam uma abordagem terapêutica semelhante, a qual consistia do processo de orquiectomia, seguido da suplementação com ômega-3 e complexo vitamínico. Apenas um cão não foi castrado, devido a alterações plaquetárias constantes. Dois cães foram submetidos à técnica de microagulhamento, devido à resposta parcial ao tratamento convencional. Desses, apenas um apresentou repilação completa. A partir do exposto, considera-se que a AX é uma doença presente na rotina dermatológica de cães e que o

reconhecimento do seu padrão de lesão é importante para um melhor direcionamento diagnóstico e terapêutico. Além disso, observou-se que, embora todas as terapias empregadas tenham resultado em melhora do crescimento piloso, a resposta terapêutica foi variável, de modo que alguns cães podem não apresentar completa repilação. Novas pesquisas envolvendo a comparação dos tratamentos são encorajadas, de modo a favorecer um melhor entendimento sobre sua eficácia.

**Palavras-chave:** Alopecia; Hiperpigmentação; Ciclo piloso.

### Resumen

La alopecia X (AX) es una enfermedad de la piel no inflamatoria y no pruriginosa caracterizada por la pérdida progresiva del cabello. Los perros más comúnmente afectados son los machos German Spitz, Chow-Chow y Poodles. Aunque existe una similitud con las endocrinopatías que cursan con cambios dermatológicos, AX no trae daño sistémico a los perros afectados. El diagnóstico se basa en la exclusión de otras enfermedades que conducen a la caída del cabello, además de las enfermedades sistémicas. Por ser una enfermedad poco reportada en la literatura, el objetivo del presente trabajo es realizar un estudio retrospectivo de siete casos de perros con AX tratados en la rutina clínica, desde el diagnóstico hasta los resultados terapéuticos. En ese momento, los perros recibieron un abordaje terapéutico similar, que consistió en el proceso de orquiectomía, seguido de suplementación con omega-3 y complejo vitamínico. Solo un perro no fue castrado, debido a los constantes cambios de plaquetas. Dos perros se sometieron a la técnica de microagujas debido a una respuesta parcial al tratamiento convencional. De estos, solo uno mostró una redepilación completa. De lo anterior, se considera que la AX es una enfermedad presente en la rutina dermatológica de los perros y que el reconocimiento de su patrón lesional es importante para una mejor dirección diagnóstica y terapéutica. Además, se observó que, aunque todas las terapias empleadas dieron como resultado una mejora en el crecimiento del pelo, la respuesta terapéutica fue variable, por lo que algunos perros pueden no mostrar una depilación completa. Se anima a realizar nuevas investigaciones que impliquen la comparación de tratamientos, con el fin de favorecer una mejor comprensión de su eficacia.

**Palabras clave:** Alopecia; Hiperpigmentación; Ciclo del cabello.

## 1. Introduction

Alopecia is a common sign in dogs and can be present in most dermatological diseases. Although it may not be uncomfortable for animals, it can be a cause of aesthetic and emotional concern for owners who often select a breed considering its coat type (Patterson, 2013). According to Paradis and Cerundolo (2003), the main causes of alopecia in dogs are induced traumatic alopecia, parasitic alopecia, infectious and inflammatory or non-inflammatory alopecia. Among the diseases that course with non-inflammatory alopecia in dogs, alopecia X (AX) is highlighted in previous researches (Carvalho et al., 2020).

AX is a skin syndrome that affects dogs and it is characterized by causing symmetrical, non-pruritic and non-inflammatory bilateral alopecia in the neck, tail, perineum and trunk. Head and distal extremity of the limbs are usually spared (Miller et al., 2013).

Its pathogenesis is still not well understood, but it is known that changes in the levels of different hormones (growth hormone, sex hormones and adrenal steroid hormones) contribute to this condition and treatments aimed at correcting these changes can improve the clinical picture (Frank et al., 2004; Huang et al., 2009; Frank, Watson, 2013; Albanese et al., 2014; Cunha, 2015). The diagnosis of AX is made by excluding other diseases that cause the hair cycle to be interrupted – such as hypothyroidism, hyperadrenocorticism and disorders of sex hormones in uncastrated animals – since its pathological mechanism remains unknown (Frank, 2017).

Since AX is an uncommon disease in dermatological veterinary clinical practice, the aim of this study is to report a case series of this disease in dogs.

## 2. Methodology

The present research comes from an analysis of seven cases of a private clinics in Fortaleza/CE from January to December/2021. Seven patients with a suggestive diagnosis of Alopecia X, which were able to follow all research stages, from suspicion to the diagnostic conclusion, were part of this retrospective study. All dogs were submitted to clinical and

dermatological evaluation and the diagnosis of Alopecia X was established after screening and exclusion of other non-inflammatory alopecic skin diseases. In addition, animals with clinical lesions suggestive of ear and skin infection were included in the present study. Such dogs were submitted, during the clinical-dermatological observation, to skin exams in order to confirm and/or exclude other cutaneous disorders (Ferreira et al., 2022). The methods are described below.

## 2.1 Diagnosis of Alopecia X

The evaluated dogs were confirmed with AX diagnosis based on clinical history and progression, lesion pattern and exclusion of additional non-inflammatory skin alopecic diseases. The cutaneous alterations are indicated in figures 1, 2 and 3. The dogs went through exclusion of clinical history/signs associated with hyperadrenocorticism and hypothyroidism. Futhermore, cutaneous parasitological exam was carried out to rule out demodectic and sarcoptic manges, and cytological exam was performed to observe the presence/absence of skin infections.

**Figure 1.** Non-inflammatory alopecia in a chow-chow dog (A1). (A) and (C) Lesion aspect with the presence of lateral alopecic areas that extend from the limb to the trunk without signs of inflammation at first consultation. (B) and (D) Skin aspect 60 days after the initial therapy, with evident repilation.



Source: Authors.

**Figure 2.** Alopecia X in a pomeranian dog (A3). (A) and (C) Initial skin lesions with the presence of epidermal collars and alopecic areas in trunk. (B) and (D) Skin aspect after 60 days of therapy, with evident hair growth and infection control.



Source: Authors.

**Figure 3.** Non-inflammatory alopecia in a pomeranian dog (A6). (A) and (C) Initial skin lesion appearance, with large alopecic areas in dorsum, flank and limbs. (B) and (D) Skin aspect after 60 days of therapy, with partial repilation.



Source: Authors.

## 2.2 Skin parasitological exam

The cutaneous parasitological exam was done with skin scraping using a scalpel blade. Five random lesions were chosen and, from these lesions, skin material was collected to rule out demodectic and sarcoptic manges. This material was placed on a glass slide and evaluated with a microscope to exclude mites.

### **2.3 Skin cytological exam**

Aiming at confirming/excluding the cutaneous infectious processes, skin samples from different sites were collected at the first dermatological analysis. Cutaneous samples were collected from alopecic areas, epidermal collars or pustules when they were present by scarification and imprinting. These materials were fixed on microscope slides, stained with Quick-Diff and evaluated with microscopy to identify microbes associated with superficial pyoderma, cutaneous malasseziosis or dermatophytosis.

### **2.4 Fungal culture**

The fungal culture examination was performed by collecting hair using sterile gloves. The material was seeded on a plate containing DTM agar and a period of 30 days was allowed for the growth of colonies compatible with dermatophyte fungi. A positive result was considered when the agar plate changes color and the growth of cotton-wool colonies suggestive of dermatophytes is observed.

### **2.5 Histopathological analysis**

For histopathological analysis, skin biopsies were collected from alopecic areas using a 5mm punch. Papules and pustules, if present, were avoided. The samples were fixed in 10% buffered formalin and further processed by conventional histological techniques. Histological sections were stained with Hematoxylin and Eosin (HE) for analysis of histological changes. The analyzes were performed under light microscope with magnification of 200x and 400x.

### **2.6 Blood sampling and hemato-biochemical analysis**

Blood samples were collected by jugular venipuncture and stored in EDTA and non-anticoagulant tubes for evaluation of systemic parameters and exclusion of systemic diseases. The following parameters were evaluated: complete blood count, serum albumin, total bilirubin, alanine aminotransferase (ALT), creatinine, alkaline phosphatase, thyroid stimulating hormone (TSH) and free thyroxine (FT4).

### **2.7 Treatments and clinical follow-up**

The dogs were initially submitted to castration (n=6/7). After the surgical procedure, all dogs initiated the same therapy protocol: Ograx-3® (one capsule/SID), Queranon® (1 capsule/SID) and Melatonin (6mg/kg/BID). Only one dog (N=1/7) was not able to be castrated due to platelet abnormalities. Two dogs received the microneedling treatment due to partial poor resolution of alopecia within 30 days of treatment. The therapy was sustained for sixty days, when the dogs went to follow-up. The individual therapeutic approach was shown in Table 1.

**Table 1.** Therapeutic approach of dogs with Alopecia X. The treatment was established at D0 and the revaluation was done at D60.

Case	Treatment	Comments
A1	Castration, Queranon®, Ograx-3® and Melatonin.	Complete repilation.
A2	Castration, Queranon®, Ograx-3®, Melatonin and microneedling.	Partial repilation.
A3	Castration, Queranon®, Ograx-3® and Melatonin.	Complete repilation.
A4	Castration, Queranon®, Ograx-3® and Melatonin.	Complete repilation.
A5	Castration, Queranon®, Ograx-3® and Melatonin.	Complete repilation.
A6	Queranon®, Ograx-3® and Melatonin.	Partial repilation.
A7	Castration, Queranon®, Ograx-3®, Melatonin and microneedling.	Complete repilation.

Source: Authors.

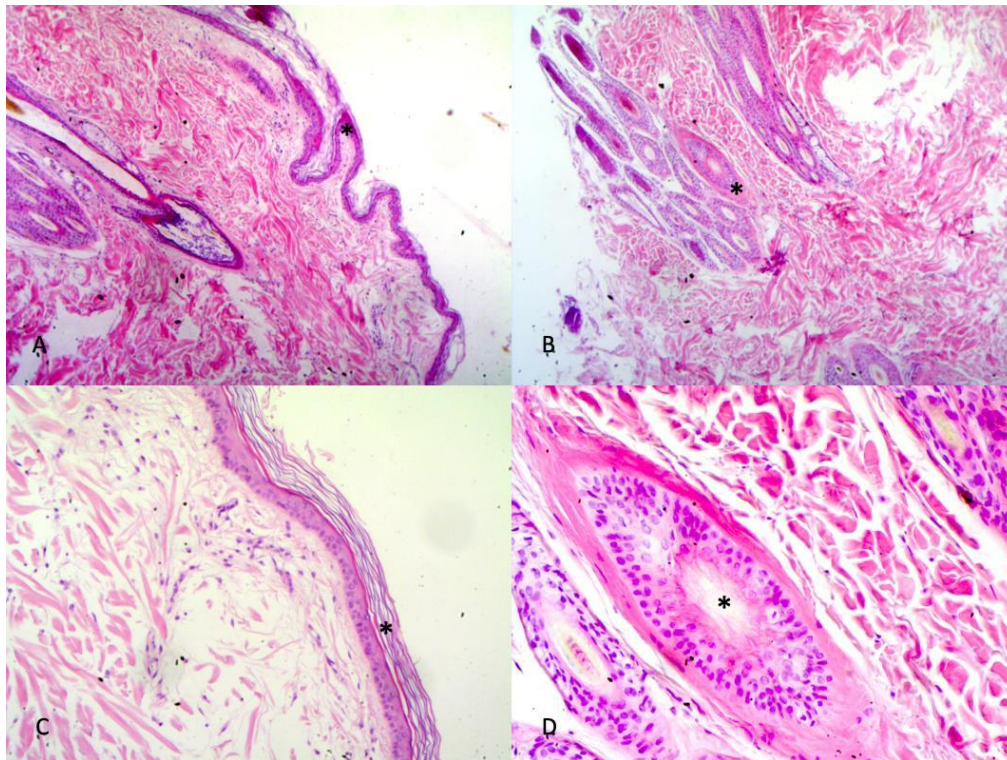
### 3. Results

The individual clinical and histopathological data of dogs are described in Table 2. Seventy one percent (n=5/7) of the dogs were Pomeranians, while twenty nine percent (n=2/7) were Chow-Chows. All dogs were uncastrated males and adults.

Hemato-biochemical analysis (complete blood count, serum albumin, total bilirubin, ALT, creatinine, alkaline phosphatase, TSH and FT4) showed no alterations in eighty five percent of the animals (n=6/7). One dog had persistent thrombocytopenia, which impaired its castration procedure. Twenty eight percent (n=2/7) of the dogs were diagnosed with concomitant superficial pyoderma (Figure 2). Fungal infection was not detected in all dogs. Skin biopsy was performed in four dogs and revealed trichilemmal keratinization, orthokeratosis and epidermal atrophy. Histopathological data are disposed in Figure 4 and Table 2.

Regarding the treatment, good clinical resolution of alopecia was observed in all animals within a period of 60 days of therapy. However, two dogs still remained with mild/moderate alopecia areas despite the adopted therapy. After the initial approach, maintenance treatment was carried out, consisting of Ograx-3®, Queranon® and Melatonin. The individual therapeutic approach is shown in Table 1, and the results of the therapies are shown in Figures 1, 2 and 3.

**Figure 4.** Histopathology of lesions in Alopecia X. (A), (B) and (C) revealing epidermis with thinning of the epidermal layers (atrophy) and foci of orthokeratosis that sometimes extends to the follicles. Asterisks reveal epidermal thinning in (A), flame follicle in (B) and (D) and orthokeratosis in (C). There are rare foci of perivascular lymphoplasmacytic inflammation in the dermis. (D) Hair follicles with trichilemmal keratinization and perifollicular fibrosis. (A) and (B) 40x magnification. (C) 100x magnification. (D) 400x magnification. Hematoxylin and Eosin.



Source: Authors.

**Table 2.** Clinical data and histopathology of dogs with Alopecia X. NP = not performed; TK = trichilemmal keratinization; OK = orthokeratosis; EA = epidermal atrophy.

Case	Breed	Age	Sex	Age of clinical onset	Skin infection	Histopathology
A1	Chow-Chow	7 years	Male	6 years	Absent	TK, OK, EA.
A2	Pomeranian	3 years	Male	3 years	Absent	NP.
A3	Pomeranian	6 years	Male	4 years	Superficial pyoderma	NP.
A4	Pomeranian	3 years	Male	3 years	Absent	TK, EA.
A5	Chow-Chow	4 years	Male	3 years	Superficial pyoderma	NP
A6	Pomeranian	8 years	Male	6 years	Absent	TK.
A7	Pomeranian	4 year	Male	4 years	Absent	TK, OK, EA.

Source: Authors.

#### 4. Discussion

The term alopecia X encompasses a number of dysplastic follicular conditions that potentially have many underlying pathogenic mechanisms that are not fully understood but that result in disruption of the follicular cycle (Yu, 2015). Recent studies have sought to elucidate aspects of its etiopathogenesis in order to better understand its mechanisms of occurrence.

Baptista and Marco (2020), carried out a survey of the history of 171 dogs of the German Spitz breed diagnosed with AX and found that 93% of the animals in the study failed to change the infant coat (they did not change the coat or performed it lightly), which occurs around 4 months of age. This finding could be an early alteration of the hair follicle and act as a predictive factor in the diagnosis of the disease.

AX is a disease that mainly affects dogs of Nordic breeds, such as the German Spitz, and is associated with abnormalities in the hair cycle (Patterson, 2013). In these animals, the hair remains stagnant in the telogen phase, which prevents its growth (Frank, 2005). Affected dogs are healthy but have progressive hair loss, bilaterally, symmetrically and not pruriticly, with variations in the degree of skin hyperpigmentation (Cerundolo et al., 2004).

Initial and screening tests for the diagnosis included skin scraping and cytology in order to rule out other diseases that cause alopecia such as demodectic mange and dermatophytosis (Ferreira et al., 2022). Although AX is a non-inflammatory and non-pruritic disease, alopecic areas can become hyperpigmented, thin and mild secondary seborrhea and superficial pyoderma can manifest (Keith, 2012). Secondary bacterial infections have already been reported in other cases (Frank, 2017; Talarico, 2020) and may be present in AX, since the skin has lost its coverage and protection.

The diagnosis of AX is based on the clinical history of the animal, physical examination findings, absence of systemic changes, in the exclusion of other pathologies, especially those of an endocrine nature - hypothyroidism, hyperadrenocorticism, gonadal neoplasms, telogen effluvium and follicular dysplasias -, in the histopathological examination of the skin biopsy and in the therapeutic response (Venâncio et al., 2016). The evaluation of gonadal and adrenal sex hormones pre and post stimulation with ACTH has questionable value, however, they are generally recommended according to the therapy chosen to be adopted (Yu, 2015).

The histopathological examination of the alopecic and unaffected areas generally presents characteristics common to other endocrinopathies, such as superficial and infundibular hyperkeratosis and comedone formation. However, a study carried out by Rest et al. (2004) in dogs whose history and clinical manifestations, as well as complementary exams, led to suspicion of AX, catagenization with the formation of the hair follicle in flame was a striking feature in 90% (20/22) of the animals. In cases where there is a clinical suspicion of the disease, a skin biopsy is recommended, which may contribute to the diagnostic screening. Despite this, histopathological examination does not allow to differentiate AX from other non-inflammatory alopecias (Frank, 2017; Gondim, 2020), being necessary to exclude other causal factors that lead to alopecia.

The therapeutic response is one of the forms of diagnosis, although some animals show improvement with a certain active ingredient and others do not. There are also cases that do not respond to any therapy, whether medical or surgical (orchietomy/OH) (Cerundolo et al., 2008). In this case, therapy was instituted and, due to the positive therapeutic response presented by the animal, the tutor chose not to perform histopathological examination. Since AX is a disease with low impact on animal health (Brooks, 2003), some dogs were submitted to biopsy exam, since it would be an invasive exam and it would not bring a definitive diagnosis.

The pathogenesis of AX is not well understood and, therefore, there is no specific treatment. Given the variety of therapeutic responses to resolve AX, different approaches have been taken (Baptista, 2018). Among the treatments already described are castration, melatonin, trilostane, deslorelin and microneedling (Cerundolo, 2004; Frank & Watson, 2013; Adamo, 2018). Although there are several studies reporting the adoption of these, often the results with hormonal therapies are inconsistent (Bourguignon et al., 2013).

The first therapeutic option in cases of fertile animals is castration (orchietomy and OH), which results in the growth of new hair (Huang et al., 2009; Cunha, 2015; Talarico, 2020). Many dogs may experience hair regrowth permanently or from months to years after surgery, just by controlling serum hormone concentrations. Females can also benefit from this procedure, although to a lesser extent (Venâncio et al., 2016). The patients in this report were fertile dogs, so the owners were instructed,



right on the first visit, about the possibility of alopecia being influenced by hormonal factors and that the performance of castration could bring benefits to the animal. In addition, a therapeutic protocol was started with melatonin (6mg every 12 hours) in order to improve the treatment for the AX condition.

In neutered animals, melatonin has been considered the treatment of choice by most veterinary dermatologists (Gondim & Araujo, 2020). The administration of melatonin generally contributes to the hair growth of affected dogs, albeit partially. However, the mechanism of action involved is not fully understood and may be related to its inhibitory action on 21-hydroxylase and aromatase enzymes, which are involved in the synthesis of sex and adrenal hormones (Frank, 2013), cortisol production and blockade of receptors of estrogen at the hair follicle level (Koch, 2012). In another case report, oral therapy with melatonin was also performed before castration with good results of hair loss that obtained an improvement in the condition, even more evident, after castration (Talarico, 2020). Its advantage over other hormonal therapies in dogs is its safety, which allows its administration without causing important adverse effects (Koch, 2012).

A study showed that the use of melatonin at a dose of 3 to 6 mg per animal promoted hair regrowth in about 40 to 60% of dogs diagnosed with AX. Treatment for a minimum period of 3 months is recommended, although longer treatments (6 to 9 months) generally increase the possibility of positive results. Adverse effects of melatonin use include sedation and possibly insulin resistance, and because of this, higher doses (>9mg) are generally not prescribed as they result in profound sedation of the animals (Frank et al., 2004). No changes related to this aspect have been reported by the tutors within 60 days of therapy. In order to contribute to the development of the coat, nutritional supplements, Queranon® and Ograx-3® were also associated with the treatment, with the objective of helping the coat development and restoring its quality.

Hair growth in trauma areas is common (Yu, 2015) and, due to this response, the microneedling technique has been used in cases where the animal does not obtain clinical improvement with oral therapy (Carvalho et al., 2020). This technique consists of an alternative procedure in which a dermal roller or dermal pen consisting of numerous microneedles is used that will cause microtraumas in the dermis and, through stimulation, can promote the repilation of alopecic areas (Stoll et al., 2015). Two dogs in this report had a history of hair regrowth in regions that were injured. Therefore, it is likely that they could respond to the microneedling technique in areas where repilation did not occur after castration and oral therapy. However, only one of the dogs that were submitted to microneedling have a good repilation. The other one had partial hair growth and other therapies should be considered to achieve the complete repilation.

Although there are different ways to treat AX, hair regrowth can occur incompletely or temporarily. It is expected that, after instituting treatment, the start of new hair growth will occur between 6 to 8 weeks. If there are no responses after 3 months of treatment, another therapeutic option should be considered (Carvalho et al., 2020).

According to Frank (2017), new hairs are rarely permanent and often disappear again within a few months or years. In view of this, it is recommended that any treatment be discontinued once hair growth has taken place and, when the patient develops alopecia again, the treatment can be reinstated or another treatment can be considered.

Regarding these cases, the dogs kept the hair that grew after the therapy for six months, which was the follow up period until this research was done. In addition, there was a reduction in skin pigmentation after hair growth. It is emphasized here, the importance of maintaining the patient's follow-up to monitor the use of the medication - dose reduction and/or interruption after stabilization of the condition - as well as its long-term systemic effects through complementary exams, always seeking to maintain the quality of life and animal welfare.

## 5. Conclusion

From the above, it is concluded that Alopecia X is a skin disease present in clinical practice and due to its uncertain etiology and inconsistent therapeutic responses, it is necessary for the veterinarian to have knowledge of the disease in order to

clarify the path to be followed, from diagnosis to treatment, and that, in many situations, therapy may not be fully effective. In addition, further researches involving the comparison between different therapies are encouraged in order to provide a better understanding of their efficiency.

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