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Micro needling Associated with Orchiectomy as a Treatment for Alopecia X in A German Spitz Dog

Case Report

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Abstract

This study aims to report the case of a male German Spitz canine patient and present the therapeutic approach of choice: micro needling associated with orchiectomy. Alopecia "X" is a common skin disease in dermatology, non- inflammatory and non-pruritic. In this, there is a racial and age predilection, since it most commonly affects animals of Nordic breeds, with double coat, especially German Spitz dogs, between one and five years of age. It qualifies for the gradual loss of coat, sparing only the head and final thirds of the limbs in its more evolved stages. The etiology and pathogenesis of alopecia X still remain unknown, but there are indications of genetic factors linked to this disease.

Keywords: Alopecia; Canine; Skin disease; Hair follicle; Micro needling

Introduction

Alopecia in dogs is a clinical sign that is frequently observed in the clinical care routine of veterinary dermatologists. Alopecia is defined as the absence of hair in areas that should be covered, due to various causes, and is commonly found in various dermatopathies [1]. Alopecia X is so named because the pathological mechanism by which it develops remains unclear [2,3]. The most commonly used treatments today are castration, administration of melatonin and administration of trilostane. Treated patients present hair loss with rates that vary between 40 and 85%. Another form of treatment that has been used is microneedling with repilation rates that can reach up to 90% [4].

This work aims to report a case of alopecia X in a male canine, German Spitz breed, whose treatment of choice was an association between microneedling and orchiectomy and had 100% regrowth.

Clinical Case Report

A male, non-neutered, German Spitz canine, 2 years and 4 months old, weighing 2.8 kg, was seen at home on December 5, 2019, with a history of dermatological complaints for 10 months (beginning in February of 2019). On physical examination, the patient was active, normocolored mucous membranes, normohydrated. No pain on abdominal palpation and non-reactive lymph nodes. A vast alopecic area was observed throughout the body, sparing only the head and the distal region of the limbs (Figure 1). Presence of large amounts of crusts in the lumbosacral region and at the base of the tail, as well as a darker appearance of the skin in the neck region (melanoderma). Erythematous ear pinna, with moderate amount of yellowish secretion and characteristic odor of otitis. Tutor reported that, in April 2019, the animal had an injury in the dorsal region where it was already alopecic. He treated the site with veterinary dermatological ointment (based on Miconazole Nitrate 0.40g, Gentamicin Sulfate 0.04g, Betamethasone Valerate 0.02g and Excipient q.s.p 20.00g) and, after healing of the lesion, growth of the hair on the spot. After evaluation, complementary tests were requested and authorized: complete blood count, ehrlichia serology, TSH (chemiluminescence), total T4 and free T4, ear cytology, skin scrapings, skin cytology and fungal culture (Table 1). A skin biopsy was requested, but was denied by the tutor. Prescrito, inicialmente:

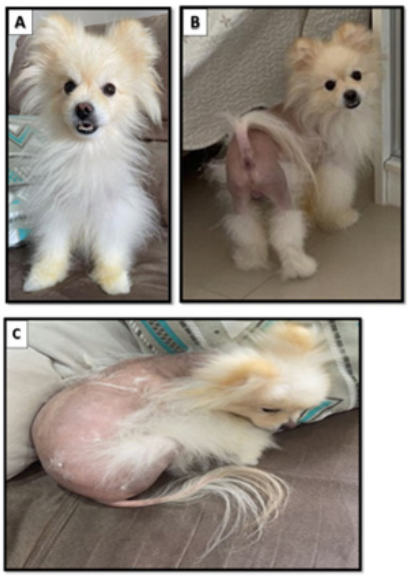

Figure 1 (A,B,C): Cutaneous appearance at the first consultations of the canine John Kelvin, German Spitz, 2 years and 4 months old.

Table 1: Hematological and sérum biochemical exams of the patient John Kelvin, German Spitz, 2 years and 4 months old, carried out by the VETINLAB laboratory – Salvador/Bahia/Brazil.

Hemograma	**Results**	**Reference Values***
Red Cells	7,00 millions/ mm3	5,7 – 7,4
Hemoglobin	15,6 g/dL	14,0 – 18,0
Hematocrit	47,4%	38 - 47
V.C.M.	67,7 fL	63,0 – 77,0
C.H.C.M	32,9 g/dL	32,0 – 36,0
Platelets	217.000 /mm3	175.000 – 500.000
Leukocytes	11.600 /mm3	6.000 – 16.000
Rod	0 /mm3	0 - 200
Segmented	7.656 / mm3	3.300 – 12.800
Eosinophils	464 /mm3	50 – 1.200
Lymphocytes	3.132 / mm3	1.000 – 6.800
Basophils	0	0 - 50
Monócitos	348 /mm3	150 – 1.350
PPT	7,00g/dL	6,0 – 8,0
Biochemistry	**Results**	**Reference Values***
Total cholesterol	246,8 mg/dl	135 – 270
hormones	**Results**	**Reference Values***
Free T4	1,22ng/dl	0,60 – 2,00
Total T4	2,27mcg/dL	0,85 – 4,66
TSH	0,24ng/mL	0,01 – 0,60
Serology	**Results**	
Canis Ehrlichia	Non-reactive	***

*Reference values provided by Vetinlab Laboratory.

a. Queranon 3,4g (for details, see Queranon Cápsulas Avert Animal Health): 01 Capsules every 12 hours for 60 days. After 60 days, 01 capsule Every 24 hours until new recommendations.

b. Dermogen oto (for details, see Dermogen Oto Auricular Cleanser Agener Saúde): Instill 10 drops in each ear, Every 12 hours, for 10 days.

c. Cloresten (for details, see Cloresten Agener): Bathe the whole body, once a week, for 06 weeks.

d. Douxo Calm Spray (for details see Douxo Calm Spray Ceva Microemulsion): Apply all over the body, twice a week, until further notice.

e. Clorhexidine 2% wipes (manipulated): Gently rub the base of the tail and lumbosacral region, once a day for 20 days.

The skin scraping was negative by the direct method. Skin cytology with cytological findings compatible with septic suppurative inflammatory dermatopathy. Culture for fungi negative. Tutor did not return for revisions. On August 6, 2020, the tutor decided to perform a skin biopsy. A fragment was removed from the dorsal region, close to the shoulder blade. Sent to Werner and Werner lab. The examination result concluded follicular inactivity and irregular and exacerbated tricholemal istimal follicular keratinization. Also, in the comments on the examination, it was said that the clinical histopathological pattern is quite compatible with the clinical suspicion of alopecia X. However, it is not possible to completely rule out the possibility of another endocrine dermatopathy (hyperadrenocorticism due to topical or systemic corticosteroid therapy, hypothyroidism, hyperestrogenism). In view of the result, the tutor was asked to perform the suppression test with a low dose of dexamethasone (two doses).

This was performed on April 12, 2021. The test result showed that the patient had no indication of endocrinopathy (Table 2). Once again, the exams took us suspect Alopecia X. Given the clinical picture and the test results, we were able to make a diagnosis of Alopecia X. Microneedling and orchiectomy was indicated for the patient, authorized by the tutor.

Table 2: Exam result Low-dose Dexamethasone Suppression Test (two doses).

Low-dose Dexamethasone Suppression Test (two doses).	**Results**	***Reference values**
Basal Cortisol	19,90 ng/ mL	10,0 a 46,0ng/ mL
Cortisol – 2nd collection	0,50 ng/mL	< 9,0ng/mL 4h/8h after dexametasona - Normal

* Reference values provided by Vetinlab Laboratory.

* Examination performed at vetinlab Laboratory in Salvador/Bahia. Brazil.

Microneedling

The patient was referred for microneedling to treat a condition of Alopecia X. Before the session, the patient was instructed to perform a preparation 30 days before the procedure, so that the skin was hydrated and without any focus of cutaneous dysbiosis. We started this preparation on August 24, 2021.

Was prescribeb:

i. Ograx Derme 10mg (for details, see Ograx Derme 10mg Avert Saúde Animal) – 1 capsule/ SID (once a day) / VO (oral), until the day of the procedure.

ii. Queranon for animals 3.4mg (for details, see Queranon Cap-

sules 3.4 mg Avert Saúde Animal) – 1 capsule /PO, until the day of the procedure.

iii. Noxxi Wall Moisturizing Spray (for details, see Noxxi Wall spray Avert Saúde Animal) applications in all alopecic areas (twice a day), until the day of the procedure.

iv. Manipulated shampoo composed of Minoxidyl 5% + Hidroviton 7% - performing 1 bath every 3 days, with 10-minute massages, until the day of the procedure.

Three days before the procedure, preventive antimicrobial therapy was started with Amoxicillin + Potassium Clavulonate (for details see Agemoxi CL 50 mg Agener) – 10mg/kg/BID, which was maintained for another 7 days after microneedling and, on the day of the procedure, a bath with 3% Chlorhexidine-based shampoo to proceed with asepsis of all regions that would be microneedled. On October 4, 2021, the patient underwent preoperative medication with Tramadol – 2mg/kg/IM (intramuscular) and induction with Proporfol – 6mg/kg/IV and maintained under inhalatory anesthesia with Isoflurane (Figure 2).

Figure 2: Animal already anesthetized and prepared to start the microneedling procedure.

In cases of microneedling, anti-inflammatory medications are contraindicated because they interfere with the process of formation and activation of new hair follicles. With the animal already anesthetized, a spray of Chlorhexidine 0.5% alcoholic solution was applied and soon after starting microneedling, with Dermoroller: which consists of a roller with 540 microneedles measuring 0.5 mm in length, rolling about 40 times, in each square centimeter of alopecic skin, in several directions so that all areas are stimulated (Figure 3). This process causes micro injuries to the skin, generating an extravasation of blood and activation of platelet aggregation factors, so that clotting can occur. These platelets release factors that stimulate new keratinocytes, fibroblasts and, with that, generate capillary growth, in addition to stimulating the growth factor of the vascular endothelium, which help in hair growth. After microneedling, the animal underwent orchiectomy, using the same anesthesia. After the procedure was prescribed for therapy at home:

Figure 3: Dermoroller (Figure taken from the americanas.com website to demonstrate the type of Dermoroller used in the procedure).

a) Dipyrone – 25mg/kg/TID (three times a day) for 3 days;Dipirona – 25mg/kg/TID (três vezes ao dia) por 3 dias

b) Maintenance of all supplesments that were indicated in the preparations for microneedling

c) Noxxi Wall Moisturizing Spray– applications in all alopecic areas/BID (twice a day)

d) Manipulated shampoo composed of Minoxidyl 5% + Hidroviton 7% - performing 1 bath every 3 days, with 10-minute massages, until new recommendations

e) Amoxicillin + Potassium Clavulonate (for details see Agemoxi CL 50 mg Agener) – 10mg/kg/BID – 7 days.

The baths were only released after seven days of the procedure, so as not to interfere with the cutaneous inflammatory process, which is necessary for the success of the therapy. One day after the procedure, the animal was already very comfortable, showing no pain, eating and drinking normally (Figure 4). Daily dressings were performed only in the scrotal region, where the orchiectomy was performed, with application of Rifamycin at the site of the stitches. The removal of the stitches was performed fifteen days after the procedure. Twenty-four days after the procedure, we could already see the hair shafts appearing (Figure 5). Thirty-two days after the session, the animal already showed hair growth, but still with many thinning areas (Figure 6). After seventy-two days, he already had more voluminous hairs with few areas of hair thinning (Figure 7). After eighty-six days of microneedling, the patient returned for the revision, where it was observed that he already had good coverage of his coat, but the tail region and hind limbs still had a large area of alopecia (Figure 8).

Figure 4: Patient one day after the procedure.

Figure 5: First hair shafts appearing.

The patient returned after 171 days, where we could see a voluminous coat, the whole body covered, only the tail had little volume, but

with the presence of hair in its entirety (Figure 9). During the entire recovery, we maintained the maintenance prescription for all the supplements, the Noxxi Wall moisturizing spray, the baths with the manipulated shampoo composed of Minoxidyl 5% + Hidroviton 7% every three days and, after five months, we switched to weekly baths. After two hundred and ninety days (9 months and 20 days), 100% of the hairs were already restored (Figure 10). After this last review, we suspended the use of Noxxi Wall and the compounded shampoo, maintaining only the maintenance of supplements (Ograx Derme and Queranon).

Figure 6: Hair growth after 32 days of the procedure, still with many thinning areas.

Figure 7: After 72 days of the procedure, more voluminous hair and few areas of hair thinning.

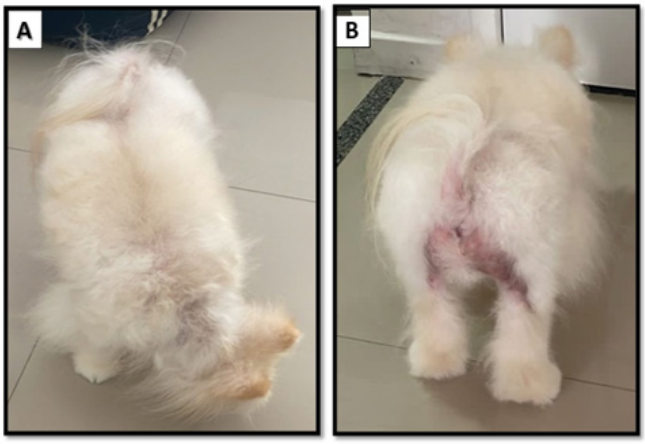

Figure 8 (A,B): After 86 days of microneedling, the patient already had good coverage of his coat, but the tail region and hind limbs still had a large area of alopecia.

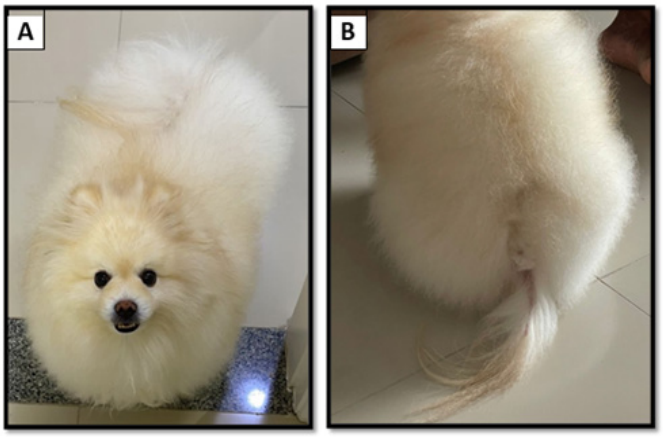

Figure 9 (A,B): After 171 days, voluminous hairs, only the tail with little volume, but already completely covered.

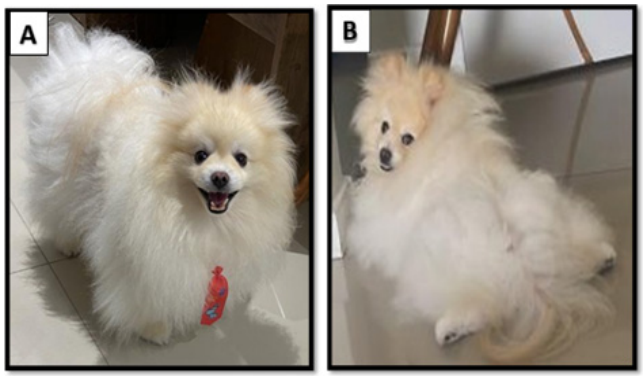

Figure 10 (A,B): After 290 days of microneedling, 100% of the hairs were restored.

Results and Discussion

Alopecia is the absence of hair in areas that should be covered, due to various causes, and is commonly found in various dermatopathies [1]. Alopecia X is a dermatopathy that affects dogs, being more commonly observed in Nordic breeds, non-inflammatory, bilateral, symmetrical, non-pruritic and of unknown etiopathogenesis. In addition to these clinical findings, the affected animal may have a dry, dull coat that comes off easily from the skin, melanoderma, in addition to other nonspecific clinical alterations, with a picture similar to that of several endocrine diseases that also cause alopecia, but without systemic signs [1,5-7].

Usually, alopecia X is observed in adult animals, young, on average, between 1 and 5 years old, mostly males, not castrated [1,3,8]; however, it can occur in both sexes, regardless of whether the animal is castrated or not [1,9]. Predisposed breeds are those with a dense, double coat, such as Pomeranians or German Spitz, Chow chows, Keeshonds, Samoyeds and Alaskan Malamutes, and also Miniature Poodles [10-12].Although some authors describe alopecia X as an aesthetic disease, dogs that develop alopecia suffer from constant thermal stress, as they do not have sweat glands and subcutaneous fat layer developed enough to exercise thermoregulation efficiently, in addition to losing their protection that the coat provides [13]. It should also be noted that alopecic skin is more subject to the development of bacterial and fungal infections [13].This dermatopathy is so named because the pathological mechanism by which it develops remains unclear [2,3]. It is believed that the etiology is related to a genetic predisposition that results in failure in hormone production or in a deficient hormonal action on the hair follicle [3,9,14].

Some studies support the hypothesis that a deficiency in the production of sex hormones may be the cause of alopecia X, given the

fact that hair grows in dogs after castration or after subjecting them to treatments with active ingredients that affect the production of hormones. And, which decrease hormone levels [2-4]. Studies also indicate that the disease is hereditary because there is a greater predisposition in Nordic breeds for alopecia X, taking into account the relatively early clinical manifestation and genealogical analysis of these dogs, however the mode of hereditary transmission has not yet been elucidated. It should be mentioned that few significant changes were observed in the genes of carrier animals [4]. The development of the disease is initially slow and the animal only loses the primary hairs, retaining the secondary hairs, mainly in areas of greater friction such as around the neck, tail, dorso-caudal region, perineum and caudal area of the thighs. After a while, alopecia progresses and the hair in these regions completely falls out, with large alopecic areas appearing [13].

In some patients, primary hair loss on the trunk and head is also observed, and the distal extremities of the limbs are preserved, which is an almost pathognomonic condition of the disease [9,12,15,16] An interesting clinical feature is hair regrowth in areas of trauma or skin biopsy [15-18]. Another important aspect to be observed is that these animals are absolutely healthy, without any systemic alteration, however, as the lesion pattern of the disease is similar to that presented in animals with endocrine diseases, one should always investigate and exclude the endocrinopathies that cause alterations dermatological disorders such as hypothyroidism, hyperadrenocorticism and gonadal disorders, with exclusion being the diagnosis of alopecia X [4].

The diagnosis of alopecia X is made by excluding other diseases that can cause a similar dermatological condition, such as hypothyroidism, hyperadrenocorticism (natural or iatrogenic), sexual hormonal imbalances, sebaceous adenitis, among others [18]. The patient's history must always be taken into account, as well as the predisposed race (Nordic breeds), age (generally between one and five years), location of the alopecic areas (sparing the head and distal extremities of the limbs) and the non-manifestation of other systemic signs that characterize endocrinopathies, for example [3,9,18].

According to Cerundolo, et al. [3] the response to therapy consists of a form of diagnosis, even though some animals show improvement with a certain active principle and others do not; and there are still those who do not respond to any medical or surgical therapy (orchiectomy/OSH). More recent studies [19-21], have shown that micro trauma caused by microneedling can stimulate hair growth. Suggested mechanisms are increased release of platelet-derived growth factors, epidermal growth factors via platelet activation and tissue repair mechanisms, activation of hair bulb stem cells and hyperexpression of hair growth genes, "Vegf", B-catetin and "Wnt'. This hypothesis is supported by a study that demonstrated the hypo-expression of genes that encode "Wnt", and its B-Catenin receptors, in addition to the hyper-regulation of "Wnt" antagonists in dogs with alopecia X [22].

Swiss researchers applied microneedling with a dermal roller to two four-year-old German Spitz females, littermates, diagnosed with alopecia X (apparently with moderate/mild hair loss). In three months, the patients showed hair regrowth of about 90% and maintained the coat after one year of treatment [23,24]. The canine patient John Kelvin had all the characteristics of an animal with Alopecia X and, after discarding the possibilities of other diseases that could present a similar dermatological condition, the diagnosis of Alopecia X was closed. The treatment of choice for the canine John Kelvin was an association between microneedling and orchiectomy. Microneedling was performed with a dermal roller, with stainless microneedles arranged in a cylinder coupled to a handling rod. All needles have a single length that can vary between 0.5 and 3mm. When applying the roller to the skin (or rolling), thousands of microperforations are made [24].

We associated the following prescription with the treatment: Ograx Derme 10mg – 1 capsule/SID/VO (orally); Queranon for animals up to 5Kg – 1 capsule /PO; Noxxi Wall Moisturizing Spray – applications on all alopecic areas/BID (twice a day); Manipulated shampoo composed of Minoxidyl 5% + Hidroviton 7% - performing 1 bath every 3 days, with 10-minute massages. This prescription began thirty days before microneedling. Still three days before the procedure, we started antibiotic therapy with Amoxicillin + Potassium Clavulonate (Agemoxi CL) – 10mg/kg/BID. After the procedure, we kept the prescription, plus the antibiotic. After thirty days of treatment, it was already possible to observe hair growth all over the body. After ninety days, the patient already had good coverage of his coat and, after nine months and twenty days of microneedling, 100% of the hair was already restored. On October 4, 2022, the patient completed 01 year of the procedure, and still has a voluminous coat and 100% coverage.

Conclusion

Alopecia X has been increasingly found in veterinary dermatological consultations, due to the great popularization of Nordic breeds, in particular, the German Spitz. As the cause of the disease is not yet well defined, there is no specific treatment for it. What we see in practice is a great diversity of treatments that can be used, and their responses are very variable. Even those treatments that present complete hair regrowth are subject to relapse [24]. The treatment of choice for John Kelvin was microneedling associated with orchiectomy, which proved to be effective and with very satisfactory results [25-27].

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