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Successful melatonin therapy in a rare case of post clipping alopecia in golden retriever dog

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Abstract
The present article reports a rare case of post-clipping alopecia (PCA) in 3 year old golden retriever bitch presented to the Department of Veterinary Clinical Complex, COVAS, SVPUAT, Meerut. The case was presented with failure of hair growth for the last twelve months after clipping by the owner to ease the summer stress. Biochemical analysis reveals normal organ function and endocrine function (thyroid function) but there was no response to any dermatological treatment. Bitch was normally appetent, thirsty, and active. Clinical examination reveals normal physiological parameters, and skin scrapping was negative for any mite infestations. There was no evidence of flea dirt on combing and the case had been unresponsive to corticosteroid and fipronil therapy. Based on the history of failure of hair growth after clipping, normal thyroid function test, the disease was tentatively diagnosed as post clipping alopecia. Initially, the therapy was tried with levothyroxine for one month but no improvement was noticed then the case was tried with melatonin. After one month of melatonin administration, appreciable improvement become evident and after two months, alopecia was completely resolved. Hematology and biochemical profile were normal during the administration of melatonin and the drug was well tolerated by bitch.

Keywords: Post clipping alopecia, levothyroxine, telogen, melatonin

Introduction
Failure of hairs to regrow after clipping in canine is common manifestation of certain endocrine diseases like alopecia X, hypothyroidism, and hyperadrenocorticism (Mecklenburg, L. *et al*, 2009). Occasional cases with failure of hairs to regrow after clipping in canine has been recorded with normal endocrine function and are termed as post clipping alopecia (Diaz *et al*., 2004) [2]. Post clipping alopecia is also known as post clipping hair follicle arrest (Scott *et al*., 2012) [3]. Clipping is routinely performed in canines at venipuncture sites, ultrasound imaging, myelography, epidural anesthesia, excessive hair fall and to manage summer stress. Exact mechanism of pathology is not known but is often associated with clipping during catagen phase of hair cycle. Another theory credits it as a result of vasoconstriction induced decreased peripheral perfusion due to reduced skin temperature of clipped skin. (Anthony Yu, 2015) [4].

Post clipping alopecia is mostly observed in breeds with thick undercoats and guard hairs like Samoyed, Siberian husky, Alaskan malamute and Eskimo dogs. Such breeds are proposed to have telogen dominant hair cycle therefore they do not shed or regrow hair coat as a measure to conserve energy/heat in extreme cold condition. (Credille *et al*., 2001) [5]. Clinical manifestations of post clipping alopecia include failure of hair to regrow after clipping usually at dorsal pelvic region and lower back region often with hyperpigmentation (Anthony Yu, 2015) [4]. Diagnosis is made on the basis of failure of hairs to grow for months after clipping without any other clinical manifestation and absence of any endocrine pathology (Anthony Yu, 2015) [4]. Most cases require no treatment and hairs regrow back in 6-12 months (Cerundolo, 1999) [6]. Treatment options though not consistently successful include thyroxine, melatonin, pentoxifylline, or cyclosporine therapy (Anthony Yu, 2015) [4].

Material and Methods
History, Clinical examination and Diagnosis
A female golden retriever of age 3 years weighing around 35 kg was presented to department veterinary clinical complex with the chief complaint of generalized bilaterally symmetrical alopecia for the last twelve months. There was a history of clipping of hair of bitch by owner as summer management strategy but hairs failed to regrow post clipping.

Bitch was initially treated with antibiotic, antifungal, and corticosteroid therapy elsewhere. Bitch was clinically examined for a hint of any underlying primary disorder like myxedema and obesity for hypothyroidism, pot belly and epidermal choallertetes for hyperadrenocorticism. Biochemical findings were also investigated for indication of any primary underlying endocrine disorders. Skin scrapping and skin combing were performed to rule out mange and flea bite hypersensitivity. Most of the retained hair on examination were found in telogen stage indicating chances of post clipping alopecia. Endocrine findings were suggestive of normal thyroid function. Hemato-biochemical parameters and free T4 and TSH levels of affected dog on day 0 were in normal range that helped in establishing the diagnosis.

Based on history of failure of regrowth of hair after clipping, negative skin scrapping, dermatographism with most of retained hairs in telogen phase, endocrine profile negative for hypothyroidism, the condition was tentatively diagnosed as post clipping alopecia. Positive response to melatonin therapy is suggestive of post clipping alopecia.

Fig 1: Before Treatment

Fig 2: After Treatment

Treatment

Initial therapy was initiated with levothyroxine @ 0.02 mg/kg, BID, PO as per recommendation for the therapy of post clipping alopecia. With no evidence of improvement even after 4-6 weeks of levothyroxine administration, therapy was changed to melatonin @ 3 mg/kg, PO for 2 weeks. Bitch was monitored for blood count and organ function test after 7 days and then the treatment was repeated for the next 21 days with monitoring of blood count and biochemistry on day 21. After 21 days of therapy, bitch started to show growth of some hairs and the treatment was advised for one month till alopecia is completely resolved. Adjunctive treatment includes administration of syrup nutricoat advance @ 02 TSF PO, BID for maintaining the normal lipid profile of skin and multivitamin tablets nutrich @ 01 tab PO daily during the course of therapy.

Result and Discussion

Case start showing improvement in manifestation after 21 days of initiation of melatonin therapy and completely resolved within next 30 days. The hematobiochemical findings were screened on day of presentation, 7th day, 21st day and 42nd day of presentation and are presented in table 1. Clinical recovery on the basisi of improvement in manifestations was recorded on clinical sheet on day 0, day 21 and day 42 and is presented in table 2.

Table 1: Pre and post therapy Hematological analytes and biochemical parameters

Erythrogram analytes				
Parameters	**0 Day**	**21 Day**	**42 Day**	**References range**
TEC (× 10 6 /µl)	5.68	5.46	5.04	5.5-8.5
HB (gm/dl)	11	11	13	12-18
PCV (%)	36	35	38	37-55
MCV (%)	73	71	72	62-77
MCH (Pcg)	25	28	26	21-26.2
MCHC (gm/dL)	34	32	36	32-36

Leucogram analytes				
Parameters	0 Day	21 Day	42 Day	References range
WBC (/µL)	12000	14500	13200	6000-17000
Neutrophils (%)	72	65	69	62-80
Lymphocytes (%)	18	23	23	10-28
Monocytes (%)	5	8	4	3-9
Eosinophils (%)	5	4	2	2-12
Basophils (%)	0	0	2	0-2

Biochemical parameters				
ALT (U/L)	54	48	64	60
AST (U/L)	44	65	42	50
ALP (U/L)	120	110	88	150
Total protein (g/dL)	5.6	5.7	5.6	6-8
Albumen (g/dL)	2.4	1.9	2.5	5-6
Globulin (g/dL)	3.2	3.8	3.1	3-5
Total Bilirubin (mg/dL)	0.52	0.5	0.48	0.07-0.061
Direct Bilirubin (mg/dL)	0.22	0.23	0.22	0.06-0.012
Indirect Bilirubin (mg/dL)	0.30	0.27	0.24	0.01-0.049
T4 (nmol/L)	39.3	38.5	28.8	19-58
TSH (nmol/L)	0.061	0.072	0.065	0.04-0.35
BUN (mg/dL)	29.8	36.0	24.6	10-20
Creatinine (mg/dL)	1.1	0.95	0.65	0.5-1.5

Table 2: Clinical case evaluation sheet

Recovery parameters	**0 day**	**21 day**	**42 day**
Hyperpigmentation of skin	++	+	--
Hair growth	----	++	++++
Thickness of skin	++	+	-

Alopecia refers to complete absence of hair coat. Alopecia in dogs can be due to excessive shedding of hairs or due to deficient production of new hairs. Excessive shedding of hair in canine is usually associated with skin infections, immune mediated disorders and certain toxicants. Deficient production of new hairs is usually associated with dietary deficiencies and hormonal disorders. Hormonal disorders can be sex hormone disorders or thyroid or adrenal hormone disorders. Non-hormone dermatosis associated with deficient production of hairs even in the absence of any dietary deficiency or hormonal disturbances are also common in veterinary clinical practice. Non-hormone dermatosis include cyclical flank alopecia, pattern baldness alopecia, post clipping alopecia, follicular dysplasia and post injection alopecia.

Post clipping alopecia is one of the most ignored alopecia observed in canines. There are rarely any scientific research and case reports on post clipping alopecia and its management. (Diaz *et al*., 2004) [2] (Scott *et al*., 2012) [3] Clinical manifestations of hair loss from dorsal pelvic region and lower back with hyperpigmentation are also recorded by earlier authors (Anthony Yu, 2015) [4]. Most commonly employed therapeutic strategies include administration of levothyroxine or melatonin. Levothyroxine is known to stimulate anagen phase of hair cycle. Other strategies include administration of pentoxifylline and cyclosporine. Pentoxifylline a phosphodiesterase inhibitor is known to increase the blood flow to the hair follicles. Cyclosporine stimulates growth of hair follicles by inhibiting protein kinase C expression resulting in prolongation of anagen phase (Takahashi *et al*., 2001) [22].

This case was successfully treated with melatonin therapy. Similar success has been reported for treatment of canine recurrent flank alopecia with melatonin (Paradis M., 2009) [21]. Even Implants of melatonin has been successfully used in the prophylaxis of further episodes of canine recurrent alopecia (Paradis, 2000) [20]. Melatonin is a methoxyindole produced in pineal and extrapineal sites in mammalian body (brain, eye, bone marrow, immune cells gonads and skin). (Slominsky *et al*., 2005, Pandi-Perumal *et al*., 2006 Tan *et al*., 2007) [8, 9]. Chemically Melatonin is N-Acetyl-5 Methoxytryptamine. Melatonin is considered as circadian rhythm regulator which possess direct radical scavenging and indirect antioxidant property (Sener *et al*., 2002) [13]. Melatonin is known to possess more strong property of radical scavenging and suppressing reactive oxygen species formation as compared to vitamin C (Fischer *et al*., 2002). Melatonin is also reported to inhibit formation of nitric acid, polyamine and peroxidation of lipids. (Kim *et al*., 2011) [11]. Melatonin stimulates important endogenous antioxidants like catalase, superoxide dismutase and glutathione peroxidase (Gurlek *et al*., 2004) [12]. Exogenous administration of melatonin is also reported to inhibit production and deposition

of dermal collagen as well as apoptosis of dermal fibroblast apoptosis (Drobnik and Dabrowski, 1999) [14], (Slominski *et al*., 2003) [15]. Melatonin has been explored in the treatment of androgenic alopecia (Fischer *et al*., 2004) [18] cancer, & sleep disorders (Reiter *et al*., 2002) [16], (Haredeland *et al*., 2012) and atopic dermatitis (Gitto *et al*., 2009) [19]. No adverse effect was noticed in behavior and hemato biochemical findings during the melatonin therapy and it was in accordance to the findings by Kerem *et al*., (2015) [23].

Conclusion

From the findings of the present study, it is concluded that melatonin is well tolerated by canine and is effective and safe therapeutic strategy for canine post clipping alopecia.

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