

# A New Canine Skin Disorder Resembling Granular Parakeratosis

## Clinical and Pathological Features of 3 cases

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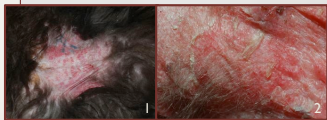


### Case 1

**Signalment**  
Seven-year-old female neutered Dwarf Spitz

**History**  
Severe pruritic skin lesions in the inguinal and perianal area since 6 months. A presumptive diagnosis of pruritic dermatitis caused by *Aectromyobia cutonomis* was made few months ago and topical treatment was prescribed (Table 1).

**Clinical examination**  
Erythema, erosions and large white scales in perianal and ventral (Fig. 1 and 2) and perineal area. Superficial fissures and erosions were also present on the abdomen.



**Differential diagnoses** included allergic or irritant contact dermatitis, drug adverse reaction, steroid-induced cutaneous atrophy, superficial pyoderma, muco-cutaneous T cell lymphoma and dermatophytosis.

**Diagnostic procedures**  
The results of haematology and biochemistry were all within normal limits. Skin scrapings, acetate tape impression smears and a fungal culture were negative for parasites, bacteria and fungi. Four 8 mm skin biopsies from different body regions were taken under local anaesthesia for histological examination (results described in Histology section).

**Treatment**  
All topical treatments were stopped due to a very likely irritant contact reaction. To prevent a possible secondary bacterial infection cefovecin (Convenia, Pfizer) was administered subcutaneously.

**Outcome**  
Two weeks later the pruritus and the lesions had greatly improved (Fig 3). Complete resolution and hair regrowth had occurred 30 days after the initial examination.



### Case 2

**Signalment**  
Six-year-old male intact Miniature Poodle

**History**  
Pruritic, erythematous perianal dermatitis 24 hours after grooming persisting for 6 weeks. Various topical treatments had been used without improvement (Table 1).

**Clinical examination**  
Erythema, erosions and large white scales in perianal and ventral tail area (Fig.4).



**Diagnostic procedures**  
Skin surface cytology and fungal culture were negative for bacteria and fungi. Cytological examination revealed numerous keratinocytes and some cornocytes with numerous keratohyaline granules. Pathohistological examination: see Histology section.

**Treatment**  
As contact dermatitis was suspected all topical treatments were discontinued and no other treatment was administered.

**Outcome**  
After 2 weeks, the pruritus had resolved and the lesions substantially healed. There was complete resolution of all signs by day 30 with no additional treatment.

Table 1. Prescribed topical medications in cases 1, 2 & 3

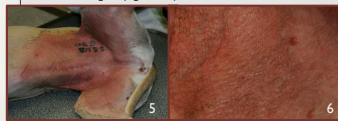
Product name	Main components	#1	#2	#3
<b>Topical antimicrobial</b>				
Banivone	Rufinone, chlorhexidine		X	
Neopogonamine	Boric acid, numerous homeopathic extracts		X	
Ceraton	Ceramide		X	
Déodorant	Polidocanol, Benzoinum		X	
<b>Topical moisturiser (petrol)</b>				
Humidum spray	Propylene glycol, urea, glycerol, lactic acid		X	
<b>Shampoos</b>				
Milermil shampoo	Cocamidopropylbetaine, sodium lauryl sulfate, sodium allyl ether sulfate, propylene glycol, PEG-6 glyceryl lauryl ether, propylene glycol laurate, vitamin E, tocopheryl acetate, pantothenic acid, L-lysine, chlorhexidine gluconate		X	
<b>Antibiotic</b>				
Prionoxone	Phenoxone olamine, ammonium lactate		X	
Alérolane	Chlorhexidine acetate, glycerol		X	
Pyoderma	Chlorhexidine		X	
<b>Topical steroids &amp; antipruritics</b>				
Stromer	Hydrocortisone, gentamicin, chlorhexidol		-	X
Cortibaine	Hydrocortisone, neomycin		X	
Contance	Hydrocortisone aceponate, propylene glycol		X	X

### Case 3

**Signalment**  
Six-year-old female neutered Whippet

**History**  
The owner reported a pruritic erythematous dermatitis of a 6 week duration, partially responsive to oral and topical antibiotics. A progressive worsening was observed after addition of daily topical treatment with hydrocortisone aceponate and a shampoo (Allercam, Virbac) 4 weeks before presentation.

**Clinical examination**  
The patient exhibited severe pruritus and the lesions consisted of bright red erythema and peripheral scaling localized to ventrum and groin (Fig 5 and 6).

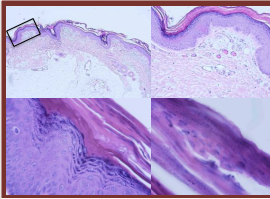


**Diagnostic procedures**  
Skin surface cytology showed numerous keratinocytes with keratohyaline granules and no bacteria, fungi nor inflammatory cells.

**Histopathologic changes** see – Histology section.

**Treatment**  
As contact dermatitis was suspected all topical treatments were discontinued. No treatment was administered.

**Outcome**  
After 2 weeks, the pruritus had resolved and the lesions healed (Fig. 7). There was complete resolution of all signs by day 30 with no additional treatment.



**Histology**

There was a diffuse severe epidermal hyperplasia with a prominent granular cell layer and rete ridges formation. The most striking finding was the presence of a, focally alternating, parakeratotic stratum corneum, showing simultaneous occurrence of preserved nuclei and large amounts of keratohyalin granules. The follicular infundibula showed similar changes. A marked vascular dilatation and multifocal mild superficial perivascular mononuclear infiltrate were observed in the superficial dermis. PAS stain was negative for fungi.

### Discussion

Granular parakeratosis was first described in 1991 in humans as an erythematous or hyperpigmented papular eruption, confined classically to intertriginous areas (axillae, groin, mammary, perianal and abdominal).<sup>1</sup> It is more often seen in middle aged women (female-to-male ratio 25:1)<sup>2</sup> and rarely in young children in diapered regions.<sup>3,4</sup> Patients typically describe sensations such as itching, burning or stinging.<sup>5</sup> Clinically two different patterns are discerned: red-brown slightly hyperkeratotic (lichen planus-like) or scaly shiny papules, which can coalesce into plaques.<sup>6</sup> The clinical presentation in these three dogs was uniform with bright, in two cases shiny, red papular erythema and scaling. Additionally, erosions and superficial fissures were observed.

In human medicine the final diagnosis is based on distinct histopathological features, such as epidermal hyperplasia with marked compact parakeratosis and retention of keratohyalin granules<sup>1,2</sup>, and is identical to the reported canine cases. In about 20 % of patients a hypergranulosis, as seen in these cases, with focal vacuolization can be observed.<sup>6</sup> Additional dermal changes include marked vascular dilatation but minimal dermal inflammation<sup>1,2</sup>, also described in our cases.

The etiology and pathogenesis of granular parakeratosis are uncertain, however most cases are associated with application of deodorants, antiperspirants, paste containing zinc oxide.<sup>6</sup> Physical factors such as obesity, hyperhidrosis and friction presumably contribute to disease evolution.<sup>6</sup> An impaired conversion of proflaggrin into flaggrin units is suspected to be the basic pathogenic abnormality and pointing toward an unusual form of retention hyperkeratosis.<sup>7</sup>

In our dogs, the dermatitis was associated with the repeated (ab)use of various topical medications. No link with a particular drug or drug component could be identified, although hydrocortisone aceponate spray was used in two cases, but was always associated with other medications. We suspect that these medications were overused (applications of large amounts, every day or twice daily for several weeks). All patients received simultaneously multiple topical medications and a 'crossover phenomenon' could be implicated.<sup>10</sup>

Comparably to humans, these three dogs recovered spontaneously within one month once the topical medications were discontinued. However, refractory cases of granular parakeratosis do exist.<sup>3</sup> In such cases topical retinoids, vitamin D derivatives or topical salicylic acid lead to complete remission.<sup>8,11</sup> Topical glucocorticoids, antifungals, antibiotics<sup>12</sup>, ammonium lactate<sup>13</sup> and cryotherapy<sup>14</sup> were used with variable results.

The incidence of granular parakeratosis in the dog is unknown, because it is uncommon to biopsy suspected pruritic or irritant contact dermatitis. We propose to be considered in cases featuring scaly or hyperkeratotic papulovesicular lesions confined to intertriginous areas and a history of intensive topical treatment. These cases highlight the need for close follow up of topical treatment, clear medication prescription (dose, frequency, duration) and regular checks.

### Summary

A new canine skin abnormality characterized by refractory pruritus, marked erythema and papules covered with large scales occurred in three privately owned dogs (7-years-old female neutered Dwarf Spitz, 3-years-old male Miniature Poodle and 6-years-old female neutered Whippet). The lesions were limited to the ventrum and perianal area. Two dogs exhibited also superficial fissures on the abdomen. In all dogs a deterioration, associated with different topical treatment formulations, containing chlorhexidine, glycerin, boric acid, zinc oxide and steroids, was observed. The major histopathologic findings involved the epidermis. There was a severely thickened stratum corneum with marked diffuse retention of keratohyaline granules and parakeratosis. In all dogs a spontaneous cure was observed within two to four weeks after discontinuation of the topical treatment. A one to four years follow up did not reveal further skin changes.

The clinical and histopathologic findings in these dogs represent those seen in granular parakeratosis, a human keratinization disorder of unknown etiology. Typical clinical signs in humans include brown or red keratotic or scaly, occasionally pruritic papules which often coalesce to plaques and are generally confined to intertriginous areas, as in our cases. A defective proflaggrin-flaggrin pathway is hypothesized to be involved in the pathophysiology of this disease. Therapeutic responsiveness is ambiguous; however, spontaneous clearance appears to be the rule in most cases. It remains unclear whether granular parakeratosis is a disease entity or whether it is just a reaction pattern to unknown stimuli.

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