

## CASE REPORT

# Putative *erythema annulare centrifugum* in two Peruvian hairless and one Chinese crested dog

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## Abstract

*Erythema annulare centrifugum* (EAC) is an inflammatory skin condition characterised in humans by distinctive annular erythematous lesions. Three hairless dogs were examined with clinical and histological features suggestive of EAC. Oral or topical glucocorticoid administration led to complete clinical resolution.

## INTRODUCTION

In humans, *erythema annulare centrifugum* (EAC) is characterised by annular erythematous lesions that appear as urticaria-like papules and enlarge centrifugally, then clear centrally, sometimes with fine scale at the inner edge of the advancing border.<sup>1</sup> EAC can appear at any age without sex predisposition, predominantly affecting the trunk and proximal extremities.<sup>1</sup> Many factors have been associated with EAC, such as infections, drug eruptions or inflammatory diseases, yet direct causality is difficult to prove, and in most cases, EAC is considered idiopathic.<sup>2</sup> Diagnosis is made clinically with histological analysis to exclude common differential diagnoses.<sup>2</sup> The histopathological findings of EAC vary according to its type (superficial or deep) and may be nonspecific with mild spongiosis, microvesiculation, focal parakeratosis, epidermal hyperplasia, minimal superficial perivascular infiltration or papillary dermal oedema.<sup>3,4</sup> To the best of the authors' knowledge, EAC has not been reported previously in dogs. This study describes clinical and histopathological findings suggestive of EAC in three hairless dogs.

## CASE 1

An 11-year-old, castrated male Peruvian hairless dog was presented with a 3-month duration of moderately

pruritic dermatitis. The dog was otherwise healthy. A first veterinary surgeon had prescribed oclacitinib (0.5 mg/kg twice daily for 2 weeks then once daily for 2 weeks; Apoquel, Zoetis), terbinafine (35 mg/kg/day for 1 month; Terbinafina, Genfar) and weekly baths with 2% miconazole/chlorhexidine shampoo (VetproDermacare; Petmedica) with no response. The dog received fluralaner (33 mg/kg every 3 months; Bravecto, MSD). On dermatological examination, bilaterally asymmetric, 1–15 cm wide annular and polycyclic erythematous plaques, with a scaly and raised periphery and central hypopigmentation, were found on the trunk and proximal extremities (Figure 1a,b). Differential diagnoses included dermatophytosis and superficial pyoderma. Impression smears performed under the scaly edge revealed neutrophilic inflammation with no microorganisms; skin scrapings, Wood's lamp examination and fungal culture were all negative. Cutaneous biopsies were performed and processed routinely. Lokivetmab (2 mg/kg subcutaneously; Cytopoint, Zoetis) was administered, unsuccessfully, for itch management. Histological examination of skin biopsy samples revealed moderate superficial perivascular to interstitial lymphocytic and neutrophilic dermatitis with mild superficial oedema, and epidermal hyperplasia with focal spongiosis, neutrophilic exocytosis and serocellular crusts (Figure 2). Gram staining was negative for bacteria (see Figure S1). Based on the dog's history and clinical signs, and taking together the



**FIGURE 1** Macroscopic pictures of Case 1. Lateral (a) and dorsal (b) photographs at initial presentation. Presence of annular and polycyclic erythematous plaques with scaly and raised periphery and central depigmentation. Lateral (c) and dorsal (d) photographs of Case 1 after treatment with oral prednisolone showing resolution of the lesions.

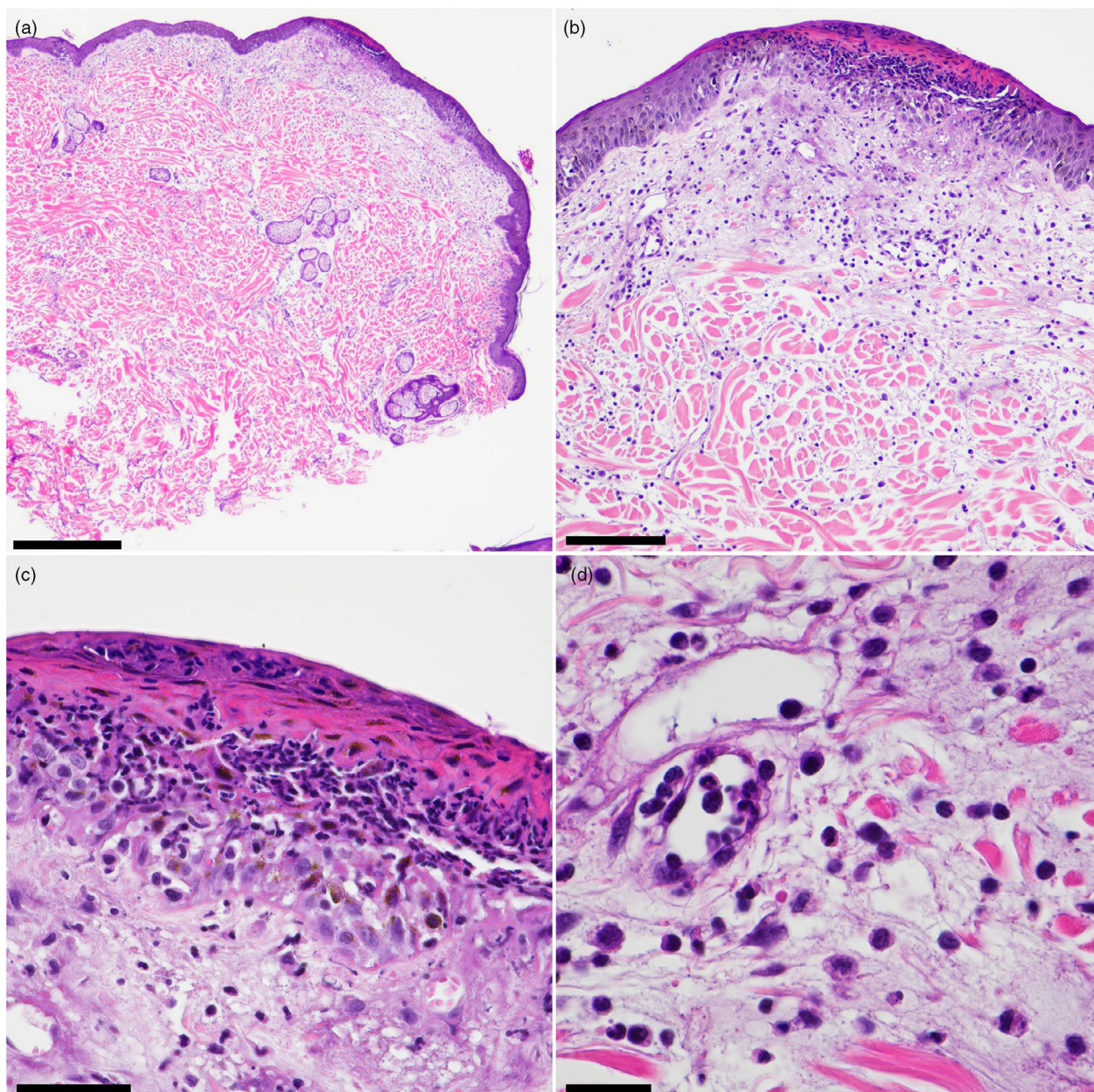
results of the ancillary tests, EAC was considered the most likely diagnosis. Prednisolone (1 mg/kg once daily for 5 days, followed by a tapering regimen of 1 mg/kg every other day for 5 days, then 1 mg/kg every third day for 10 days before discontinuation; Prednovet, Zoovet) led to rapid resolution (Figure 1c,d) within 4 weeks. Twelve months after the initial diagnosis, there had been no relapse.

## CASE 2

A 3-year-old, spayed female Chinese crested dog was presented with severely pruritic and erythematous

pododermatitis that had been present for 2 years. The dog's general health was good, and the dog had been receiving sarolaner once monthly (3.2 mg/kg; Simparica, Zoetis). On dermatological examination, pododermatitis of all 4 paws, erythema of the flexural elbow and axillary folds, mild blepharitis, cheilitis and numerous comedones were observed. On the left lateral thorax, a 2 cm diameter annular plaque with raised erythematous periphery and central hypopigmentation was observed (Figure S2a). Cytological examination of interdigital skin revealed mild *Malassezia* overgrowth. Atopic dermatitis (AD) with secondary *Malassezia* pododermatitis was considered the most likely diagnosis explaining the clinical signs and pruritus. An elimination diet trial was





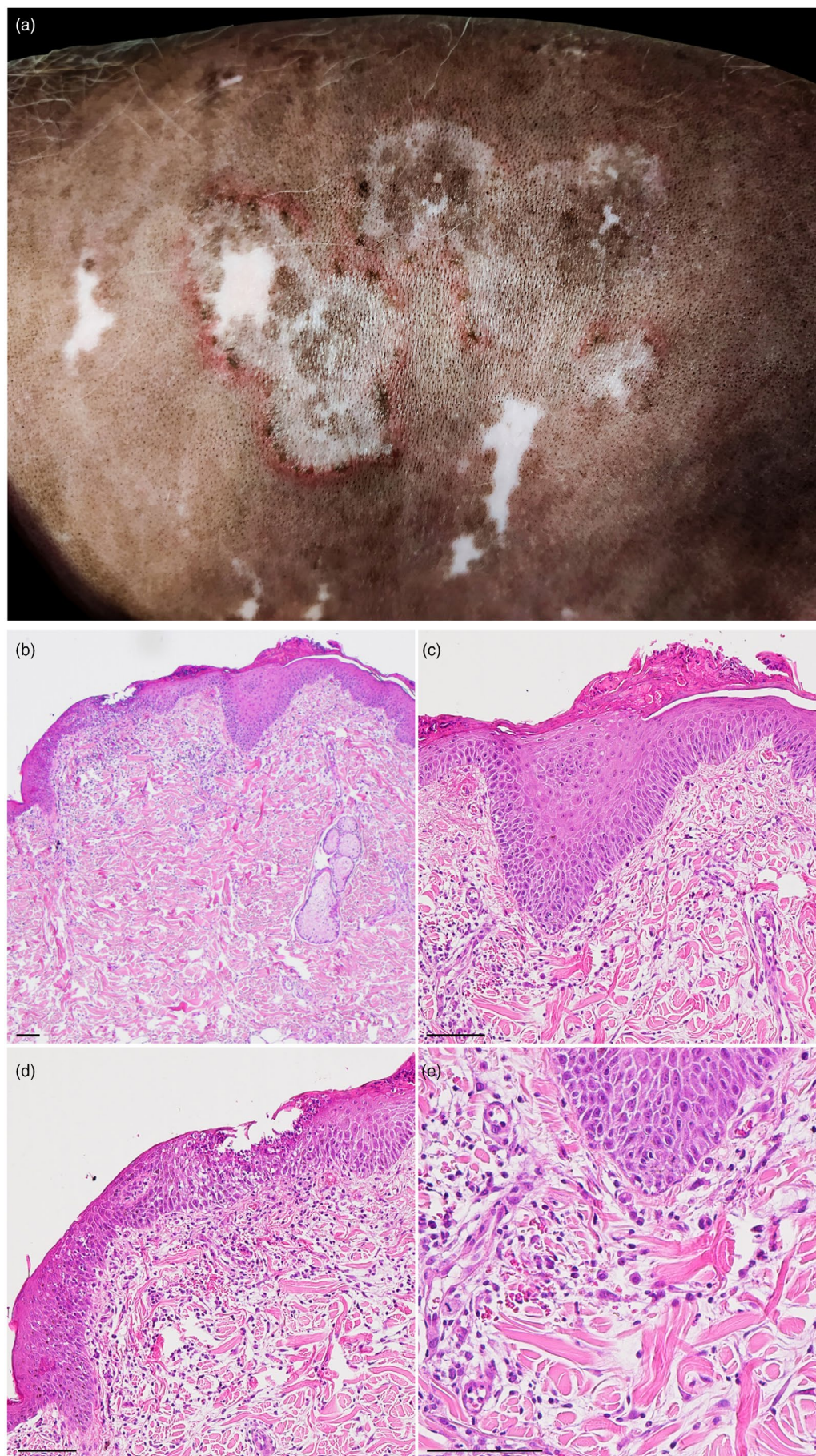
**FIGURE 2** Histopathological findings of skin biopsy samples in Case 1 (haematoxylin and eosin). (a) Superficial perivascular dermatitis with severe dermal oedema, and regular and diffuse epidermal hyperplasia; bar=500µm. (b) Close-up of superficial dermis and epidermis; bar=200µm. (c) Spongiosis and neutrophilic exocytosis with formation of serocellular crust; bar=50µm. (d) Close-up of the superficial mixed inflammatory infiltrate; bar=25µm).

started to investigate food-induced AD. An injection of lokivetmab at 1.4mg/kg s.c. (Cytopoint; Zoetis) was given, and 2% chlorhexidine/2% miconazole shampoo (Malaseb; Dechra) was prescribed for distal extremities twice weekly. Impression smear of the annular lesion revealed neutrophils with no bacteria. Because the lesion was nonpruritic and the owners thought that it was an area of trauma, no specific treatment was prescribed.

At the follow-up visit, 5 weeks later, pruritus and lesions associated with AD were markedly improved. However, the left lateral thorax lesion had progressed to multifocal plaques with polycyclic and serpiginous raised erythematous and scaly borders with irregular central depigmentation (Figure 3a). Differential diagnosis included dermatophytosis, superficial pyoderma,

generalized cutaneous discoid lupus, contact dermatitis, and EAC. Fungal culture was negative, and no bacteria were observed in the cytological samples. Biopsy of the plaques was performed, and samples were processed routinely. Superficial perivascular lymphocytic and neutrophilic dermatitis associated with severe epidermal acanthosis and focal areas of spongiosis, lymphocytic and neutrophilic exocytosis, and focal parakeratosis were observed on histological examination (Figure 3b–e). Gram staining was negative for bacteria (Figure S3). Erythema annulare centrifugum was considered the most likely diagnosis. Daily local application of betamethasone 0.05% cream (Diprosone; Organon) led to complete resolution of lesions within 15 days (Figure S2b). At 2 years after initial diagnosis, there had been no relapse of EAC lesions.





**FIGURE 3** Photograph of Case 2 and the corresponding histopathological findings (haematoxylin and eosin). (a) Multifocal arciform to polycyclic lesions with elevated erythematous and scaly borders, and central depigmentation. (b) Superficial perivascular dermatitis with severe irregular epidermal hyperplasia, serocellular crust, and focal parakeratosis; bar=100µm. (c) Close-up of superficial dermis and epidermis, note epidermal spongiosis; bar=100µm. (d) Marked spongiosis and neutrophilic exocytosis with formation of micro-vesicles; bar=100µm. (e) Mixed perivascular inflammatory infiltrate with lymphocytes, histiocytes, neutrophils and mast cells; bar=100µm)



### CASE 3

A 2-year-old, male Peruvian hairless dog was presented with a nonpruritic, erythematous linear plaque on the thorax. The dog had been treated with itraconazole (10 mg/kg for 3 weeks; Itraconazol, Zoovet) without response and received fluralaner (40 mg/kg every 3 months; Bravecto, MSD). Dermatological examination revealed bilateral asymmetric, polycyclic erythematous plaques with raised and scaly borders on the thorax (Figure 4). Differential diagnoses included dermatophytosis, superficial bacterial pyoderma, and EAC. Fungal culture and cytological evaluation (performed by impression smear at the lesion edge) were negative for bacteria and dermatophytes, and EAC was considered the most likely diagnosis. Histological investigation was not performed. The lesions resolved with prednisolone (1 mg/kg once daily for 5 days then tapered for a total of 15 days; Prednovet, Zoovet). The dog was lost to follow-up.

### DISCUSSION

In humans, EAC belongs to the figurate erythemas<sup>5</sup> and is considered a type IV hypersensitivity reaction to an external or internal antigenic stimulus.<sup>6</sup> It is considered to be a clinical reaction pattern rather than a specific clinicopathologic entity.<sup>7</sup> In humans, EAC has been associated with many infectious entities (particularly dermatophytes), including viruses (e.g. Epstein–Barr virus, poxvirus, human immunodeficiency virus) and bacteria (*Pseudomonas* spp.), ectoparasites (*Phthirus pubis*), drugs (e.g. cimetidine, rituximab, diuretics), Crohn's disease, pregnancy and malignancy, among others.<sup>1</sup> In most cases, no causative agent is found and EAC is considered idiopathic. In the cases described here, limited by the retrospective nature of the work, a full diagnostic work-up of the dogs was not performed. One of

the dogs (Case 2) suffered from AD, raising the question of whether this condition could predispose the skin to EAC-like hypersensitivity reaction. It also could be hypothesised that this skin reaction might be secondary to ectoparasite bites. These dogs were otherwise clinically healthy, were treated with routine ectoparasite preventives, and two of them were followed for 12–24 months after diagnosis with no signs of relapse.

The dogs described here belong to two breeds that suffer from ectodermal dysplasia linked to mutations in the forkhead box transcription factor family (FOXI3) on chromosome 17.<sup>8</sup> A link between the FOXI3 mutation and EAC is difficult to imagine. Interestingly, a variant of figurate erythema is described in Sphynx cats from eastern Europe.<sup>9</sup> This breed has a mutation on the keratin 71 gene that is not linked to ectodermal dysplasia, yet is linked to major hair follicle abnormalities.<sup>10</sup> It is possible that EAC is more common in hairless breeds because of the greater exposure of their skin surface to external antigenic stimuli that can trigger type IV hypersensitivity reactions. Another possibility is that, because of the absence of hair, lesions are easily observed by both owners and clinicians, while in other breeds they may remain undiscovered because of the fur.

In humans, EAC occurs in two clinical forms: superficial and deep. In both forms, the initial lesion spreads centrifugally with central healing.<sup>3</sup> The cases described here are more consistent with the superficial form, because histological examination revealed nonspecific epidermal and superficial dermal changes. We propose that the diagnosis of this entity in dogs, as in people, should be based on its distinctive clinical presentation and ancillary tests that rule out other differential diagnoses, such as superficial bacterial pyoderma, dermatophytosis or cutaneous discoid lupus. The histological findings are not specific to this condition and could be observed in other superficial skin conditions.

In humans, treatment of EAC is aetiological.<sup>5</sup> In practice, in most people, the aetiology is unknown, so symptomatic and empirical treatment, with topical or systemic glucocorticoids, remains an option.<sup>2,3</sup> The cases described were managed with systemic or topical steroids leading to rapid resolution of the lesions in each case. In the follow-up period of cases 1 and 2, the lesions did not relapse. Unfortunately, Case 3 did not have histological evaluation of skin biopsies and was lost to follow-up, which is one of the limitations of this work.

The lesions described here are clinically suggestive of superficial bacterial pyoderma. Cytological evaluation, the recommended test for diagnosis,<sup>11</sup> yielded negative results. The use of antibiotics was not justified in these cases. Unfortunately, bacterial cultures were not performed; though, even if positive, this would not have confirmed the diagnosis of bacterial pyoderma. Furthermore, Gram staining failed to detect microorganisms in any of the histological sections in two cases. Nevertheless, a hypersensitivity reaction to bacterial antigens present on the skin surface cannot be ruled out.



**FIGURE 4** Macroscopic pictures of Case 3. Photograph of linear polycyclic lesions on lateral thorax with raised erythematous and scaly borders.



In conclusion, we describe three hairless dogs with putative EAC. We propose that diagnosis of this condition should be based on its distinctive clinical presentation and the exclusion of other differential diagnoses through cytological evaluation, fungal culture and histological analysis. Future prospective studies are warranted to determine whether these animals suffer from an underlying condition that predisposes them to a unique type-IV hypersensitivity reaction.

## AUTHOR CONTRIBUTIONS

**Renzo Ventura:** Conceptualization; investigation; writing – original draft. **Lluís Ferrer:** Supervision; writing – review and editing. **Pauline Bernard:** Conceptualization; writing – review and editing. **Emmanuella Guenova:** Conceptualization; writing – review and editing. **Maxence Delverdier:** Investigation; resources; writing – review and editing. **Marie-Christine Cadiergues:** Conceptualization; supervision; writing – review and editing. **Daniel Combarros:** Conceptualization; investigation; supervision; writing – original draft; writing – review and editing.

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## CONFLICT OF INTEREST STATEMENT

The authors declare they have no potential conflict of interest with respect to the research, authorship and/or publication of this article.

## DATA AVAILABILITY STATEMENT

The data that supports the findings of this study are available in the supplementary material (Figures S1–S3) of this article.

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## Résumé

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## Resumen

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## Zusammenfassung

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## SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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