History

A 6-year-old spayed female English Bulldog was evaluated by the referring veterinarian because of crustating and ulcerative cutaneous lesions overlying the dorsal aspect of the cervical and cranial thoracic areas. The owner was instructed to administer enrofloxacin and benzyl penicillin to the dog for 7 days and perform a chlorhexidine scrub (10 minutes' duration) of the affected skin areas weekly. Two weeks later, a follow-up examination was undertaken, and no improvement of the lesions was observed. Treatment with enrofloxacin was again prescribed, and amoxicillin–clavulanic acid was added to the treatment regimen. Excisional biopsy specimens were obtained from multiple dorsal skin lesions at this time for bacterial culture. Culture yielded abundant *Pseudomonas aeruginosa* and *Enterobacter cloacae*, both opportunistic bacteria. Four weeks after initial evaluation, the lesions had still not improved.

Clinical and Gross Findings

The dorsal aspect of the skin in the cervical region and cranial aspect of the skin in the thoracic region had multiple, fairly well-demarcated ulcerative and crustating lesions (Figure 1). The margins of the ulcerated regions were irregular, and adjacent skin was mildly thickened. Adjacent nonulcerated skin had matted hairs and was reddened (erythematous). Biopsy specimens from the lesions were submitted to the University of Illinois Veterinary Diagnostic Laboratory for diagnostic examination.

Formulate differential diagnoses from the history, clinical findings, and Figure 1—then turn the page →
Histopathologic Findings

Sections of the biopsy skin specimens underwent histologic examination. The epidermis had moderate to marked acanthosis (increased thickness of the stratum spinosum), multifocal hypergranulosis (increased thickness of the stratum granulosum) with moderate orthokeratotic hyperkeratosis (increased thickness of the stratum corneum), and multifocal ulceration. Overlying the acanthotic epidermis were serocellular crusts, composed of intact and degenerate neutrophils, eosinophilic cellular and basophilic karyorrhectic debris, and lightly eosinophilic proteinaceous material. Multifocally, the superficial and deep dermal collagen bundles ranged from slightly hypereosinophilic to deeply basophilic and fragmented (Figure 2). Von Kossa staining of skin sections revealed deposition of mineral (Figure 3). Aggregates of macrophages, multinucleated giant cells, lymphocytes, and plasma cells surrounded the mineralized collagen. The superficial dermis was edematous with separation of collagen fibers by clear areas, and there were moderate numbers of plump, stellate immature fibroblasts (fibrosis). Adjacent hair follicles are hyperplastic, dilated, and filled with accumulations of keratin.

Morphologic Diagnosis and Case Summary

Morphologic diagnosis: severe, diffuse, chronic, granulomatous dermatitis, with dermal fibrosis and collagen mineralization, epidermal hyperplasia, and orthokeratotic hyperkeratosis.

Case summary: calcinosis cutis in a dog.

Comments

Common sites of calcinosis cutis in dogs include the temporal area of the head, dorsal aspect of the cervical region, dorsal midline, ventral aspect of the abdomen, and the groin and axillary regions. Grossly, calcinosis cutis appears as pink to white, hard and gritty, well-demarcated skin lesions. Lesions may consist of solitary to multifocal painful erythematous papules, plaques, or nodules that become ulcerated and secondarily infected. Ulceration develops as the mineralized material is extruded through the epidermis. Differential diagnoses for these gross lesions include superficial pyoderma (nonulcerated lesions) and deep bacterial or fungal infections (ulcerated lesions).

Histopathologic findings associated with calcinosis cutis are collagen mineralization, transepidermal extrusion of mineral, acanthosis, ulceration, and granulomatous inflammation. In dogs with hypercortisolism, telogen hair follicles, epidermal and sebaceous atrophy, marked follicular keratosis (comedone), thin dermis, and hyperpigmentation may be observed but are usually more evident in adjacent noncalcified dermis. In the case described in the present report, there was no histopathologic evidence of concurrent hypercortisolism within the sections examined.

Calcinosis cutis is characterized by an inappropriate deposition of mineral within the epidermis, dermis, or subcutis. Mineral deposition usually occurs on the elastin or collagen matrix of the dermis. There are 4 main categories...
(subtypes) of calcinosis cutis in dogs: dystrophic calcification, metastatic calcification, idiopathic calcification, and iatrogenic calcification. The idiopathic type is considered to be the most common. In human medicine, calcinosis cutis is divided into 5 subtypes: dystrophic calcification, metastatic calcification, idiopathic calcification, iatrogenic calcification, and calciphylaxis. Calciphylaxis is a term referring to small vessel calcification, in which blood vessels of the dermis or subcutaneous fat are mainly affected.

It is theorized that dystrophic calcification develops secondary to tissue damage, and serum calcium and phosphorus concentrations are within reference ranges in affected dogs. In dogs, dystrophic calcification most commonly occurs with hypercortisolism. It is speculated that excess circulating cortisol alters collagen and elastic fibers, predisposing them to calcification. Metastatic calcification is attributable to aberrant serum calcium and phosphate homeostasis and has been reported as a result of chronic renal failure, primary hyperparathyroidism, or hypervitaminosis D in dogs. More specifically, metastatic calcification develops when the calcium-phosphorus product (ie, serum calcium concentration multiplied by the serum phosphorus concentration) exceeds 70 mg²/dL. However, some authors dispute the role of calcium-phosphorus product on ectopic calcification as having no experimental basis. Instead, O’Neill contends that microenvironment factors are more important in determining ectopic calcification. Iatrogenic calcification is often due to medical intervention, specifically resulting from percutaneous absorption of calcium chloride and calcium gluconate during treatment of hypocalcemia. English Bulldogs are reportedly prone to iatrogenic calcinosis cutis.

Idiopathic calcification develops in the absence of underlying tissue damage and aberrations in serum calcium and phosphorus concentrations. The diagnosis of idiopathic calcification is made after all other forms of calcification have been excluded. A condition called idiopathic calcinosis universalis develops in otherwise healthy dogs < 1 year old and is characterized by widespread lesions that spontaneously regress within 1 year. The lesions are grossly and histologically similar to dystrophic calcification secondary to hypervitaminosis D. Idiopathic calcinosis cutis has been associated with severe systemic disease, amphotericin B treatment for blastomycosis, leptospirosis, and pachyonychia. In those reports, the calves had features of multiple classifications of calcification (ie, dystrophic and metastatic), but a true underlying pathomechanism could not be identified. Speculative explanations have included adverse drug reaction to amphotericin B and increased calcium concentration secondary to conversion of 25-hydroxycholecalciferol to 1,25-dihydroxycholecalciferol by monocytes and macrophages within areas of chronic granulomatous inflammation. In contrast, other authors speculate that osteoclast-like cells actually prevent mineralization by producing native calcification inhibitors fetuin A and pyrophosphate.

Treatment for calcinosis cutis depends on the cause, which highlights the importance of categorizing calcinosis cutis by etiologic classification. Treatment of the underlying disease usually results in gradual and complete resolution of the calcinosis cutis over several months. Dogs in which cutaneous ossification has occurred will require surgical removal of the lesions because the lesions will not regress spontaneously. Treatment of mild to moderate calcinosis cutis with probenecid or low-calcium diets, oral administration of phosphate binders (eg, aluminum hydroxide), or oral or parenteral administration of osteoclast inhibitors (eg, bisphosphonate) may aid in the resolution of metastatic calcinosis cutis via correction of the abnormal calcium-phosphorus product. Additionally, once-daily topical application of dimethyl sulfoxide applied to dogs with severe calcinosis cutis will hasten resolution of the lesions because dimethyl sulfoxide is able to breakdown calcium deposits and to prevent further crystallization of calcium and phosphorus. It is recommended that serum calcium concentrations be monitored periodically if dimethyl sulfoxide is being applied to extensive lesions because the breakdown of calcium deposits can lead to hypercalcemia. Treatment of any secondary infections is also important for resolution of lesions. Additional treatments used in human medicine include topical administration of sodium thiosulfate; systemic administration of warfarin, minocycline, ceftriaxone, diltiazem, or probenecid; IV administration of immunoglobulin; shock wave lithotripsy; surgical removal of lesions; and carbon dioxide laser therapy for vaporization or ablation of the lesion. Unfortunately, owing to financial constraints, further diagnostic testing was not performed and the dog was euthanized. This dog did not have a history of glucocorticoid administration; thus, iatrogenic hypercortisolism as a cause of the calcinosis cutis was less likely.

References