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■ A case of canine squamous cell carcinoma secondary to solar keratosis (actinic carcinoma *in situ*)

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■ Περιστατικό ακανθοκυτταρικού καρκινώματος σε σκύλο σε έδαφος ακτινικής κεράτωσης (ακτινικό καρκίνωμα *in situ*)

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ABSTRACT. We present the case of a squamous cell carcinoma developed in a pre-existing solar keratosis of the trunk in a white-haired Dogue Argentino. Deep pyoderma along with exfoliative erythroderma were the initial clinical findings. Several months after the diagnosis of solar keratosis, the dog presented with multiple nodules and ulcers on the flank and abdomen and the diagnosis of malignancy was confirmed microscopically.

Key words: actinic keratosis, squamous cell carcinoma (SCC), dog

ΠΕΡΙΛΗΨΗ. Παρουσιάζεται ένα περιστατικό ακανθοκυτταρικού καρκινώματος που αναπτύχθηκε σε προϋπάρχουσα ακτινική κεράτωση στον κορμό σκύλου φυλής Dogue Argentino. Οι αρχικές δερματικές αλλοιώσεις ήταν αυτές της εν τω βάθει πυώδους δερματίτιδας και της αποφολιδωτικής ερυθροδερμίας. Μερικούς μήνες μετά την αρχική διάγνωση της ακτινικής κεράτωσης, το ζώο προσκομίστηκε με πολλαπλά οζίδια και έλκη στους κενεώνες και την κοιλιακή χώρα, με την ιστοπαθολογική εξέταση των οποίων επιβεβαιώθηκε η διάγνωση του ακανθοκυτταρικού καρκινώματος.

Λέξεις ευρετηρίασης: ακτινική κεράτωση, ακανθοκυτταρικό καρκίνωμα, σκύλος

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INTRODUCTION

Solar keratosis is an actinic damage of epidermal keratinocytes, developing mainly in the fair coloured skin of animals, as the result of repeated exposure to direct or reflected sunlight (Scott et al. 2001). Ultraviolet B (UVB) seems to be the most phototoxic type of solar radiation inducing dimerization of pyrimidine bases and cross-linking in DNA, which overwhelm possible repair mechanisms along with the production of carcinogenic substances and oncogenes (Affolter 1997). Although UVB radiation damage can be extremely heterogeneous at a molecular level, there are specific morphological cutaneous changes related to it: erythema, dyskeratosis of keratinocytes, elastosis and malignant transformation (Dunstan et al. 1998). The lesions of canine solar keratosis develop over the nose and pinnae, with the trunk and extremities being last affected (Scott et al. 2001). Deep pyoderma (bacterial furunculosis) has rarely been reported as a complication of canine solar keratosis of the trunk (Mason 1997). There are only a few reports in the veterinary literature concerning the development of squamous cell carcinoma on solar keratosis lesions.

A case of solar keratosis of the trunk complicated with deep pyoderma is presented in a white coloured Dogue Argentino that progressively transformed into squamous cell carcinoma.

CASE HISTORY

An 8 year old, intact female, Dogue Argentino was referred to a dermatology private practice because of painful, pruritic, crusted and erythematous skin lesions of approximately 8-week duration, that were located mainly on the ventral and lateral thoracic wall and the abdomen. No treatment had been given to the dog. On physical examination, apart from regional lymphadenomegaly (prescapular) noticed, there were multiple, painful, alopecic and crusted erythematous lesions discharging a sanguinopurulent exudate confined to the non-coloured regions of the skin. Some areas with exfoliation and erythema were also present. The affected areas were hard in consistency and thickened. The differential diagnosis included deep bacterial pyoderma, complicated demodicosis, subcutaneous and systemic mycosis, erythema multiforme, autoimmune disease, epitheliotropic lymphoma and leishmaniosis. Skin scrapings, imprints from exudative

crusted lesions, skin biopsies and blood sample for leishmania serology were obtained from the dog. The results were negative for *Demodex canis* (skin scrapings) and IFA antibodies for leishmania (blood), while cytology revealed numerous degenerated neutrophils with phagocytosed cocci along with lower number of macrophages and lymphocytes. Cephalexin was prescribed at the dose of 20 mg/Kg/BID, *per os* for at least 4 weeks along with chlorhexidine shampooing twice weekly, pending the histopathology results. The later consisted of an irregular hyperplasia, dysplasia and parakeratosis of the epidermis, with focal but severe keratinocyte vacuolation of stratum spinosum. The slightly eosinophilic dyskeratotic cells were observed throughout the epidermis. Overall, the dyskeratosis resulted in mild to moderate architectural distortion of the epidermis. The basement membrane appeared intact with no invasion of the dermis by atypical squamous epithelial cells (Figures 1, 2). A mild pyogranulomatous infiltrate was present in the superficial dermis. In the mid dermis there were neutrophilic nodules with variable numbers of macrophages and other mononuclear cells and free hair shafts at their centre (Figure 3). Subsequently, the diagnosis of solar keratosis complicated by the deep pyoderma was made. On follow up examination, there was a significant improvement of deep pyoderma lesions at 3 weeks after the initiation of the treatment.

The precancerous nature of the disease was pointed out to the owner with the notion to avoid the sunbathing of his animal and to give cephalexin for 3-4 more weeks (pyoderma) and acitretin for the actinic keratosis itself. Despite the progressive improvement of deep pyoderma, the owner sought a second opinion, where the diagnosis of atopic dermatitis was subsequently made and prednisolone was prescribed at the dose of 0.5mg/Kg, BID, *per os*. The dog was readmitted to our practice for re-evaluation, 8 months since the initial presentation. At this time, an enlargement of the popliteal lymph nodes along with multiple ulcerative plaque like to nodular lesions with erythema, erosions and crusting were noticed. The lesions were confined to lightly pigmented areas of the skin over the flank, abdomen and the extremities, the pigmented areas were found to be unaffected (Figure 4). Differential diagnosis would include squamous cell carcinoma (SCC) or other cutaneous neoplasms, as well as infectious and sterile granulomas. Microscopic

Figure 1. Epidermal hyperplasia, dysplasia and parakeratosis along with a mild pyogranulomatous infiltrate in the superficial dermis are observed suggestive of solar keratosis in the skin biopsies of a white-haired Dogue Argentino (H-E, x 400).

Εικόνα 1. Παρατηρείται υπερπλασία, δυσπλασία και παρακεράτωση της επιδερμίδας με ήπια πυοκοκκιοματώδη διήθηση του επιπολής χορίου, στοιχεία ενδεικτικά ακτινικής κεράτωσης, σε βιοψία δέρματος λευκού χρώματος Dogue Argentino (H-E, x 400).

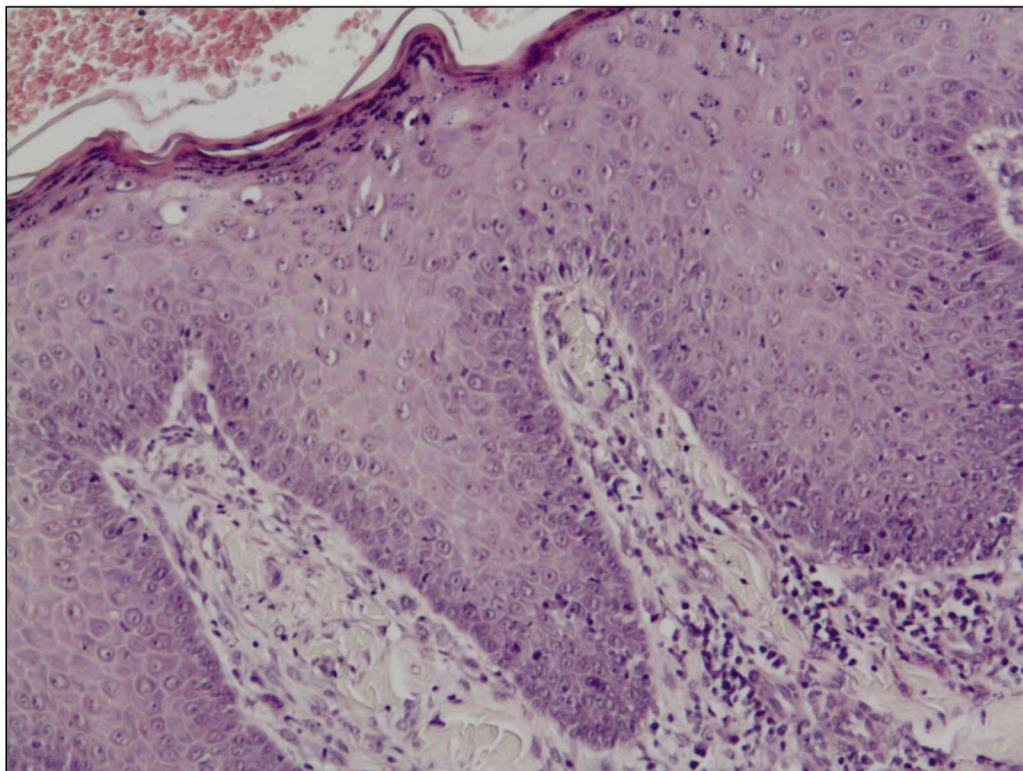


Figure 2. Epidermal hyperplasia, vacuolar degeneration of spinous layer keratinocytes and mixed cell perivascular and lichenoid infiltrate of the upper dermis. The granular layer seems to be lost, while it is obvious that the basement membrane is intact and there is no infiltration of the dermis with atypical squamous epithelial cells (H-E, x 400).

Εικόνα 2. Υπερπλασία της επιδερμίδας, κενοτοποιώδης εκφύλιση των κερατινοκυττάρων της ακανθωτής στοιβάδας και περιαγγειακή και λειχηνοειδής κυτταρική διήθηση μικτού τύπου στο επιπολής χόριο. Η κοκκιώδης στοιβάδα φαίνεται να έχει απολεστεί, ενώ είναι προφανές ότι η βασική μεμβράνη είναι ανέπαφη και δεν υπάρχει διήθηση του χορίου από άτυπα κερατινοκύτταρα (H-E, x 400).

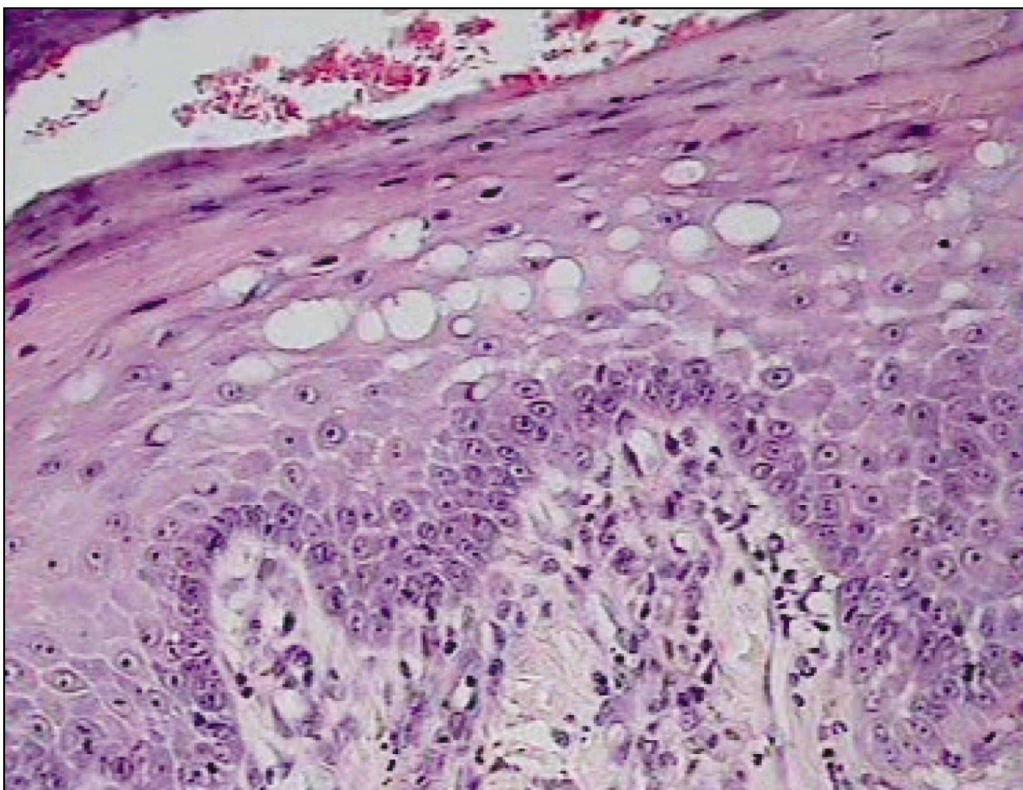


Figure 3. In the mid dermis there were neutrophilic nodules with variable numbers of macrophages and other mononuclear cells and free hair shafts at their centre in an area of a ruptured hair follicle (H-E, x 400).

Εικόνα 3. Στο μέσο χόριο, παρατηρήθηκαν οζώδεις διηθήσεις από ουδετερόφιλα, μακροφάγα και άλλα μονοπύρρηνα κύτταρα καθώς και ελεύθερα στελέχη των τριχών στο κέντρο τους σε περιοχή με ρήξη του θυλάκου των τριχών (H-E, x 400).

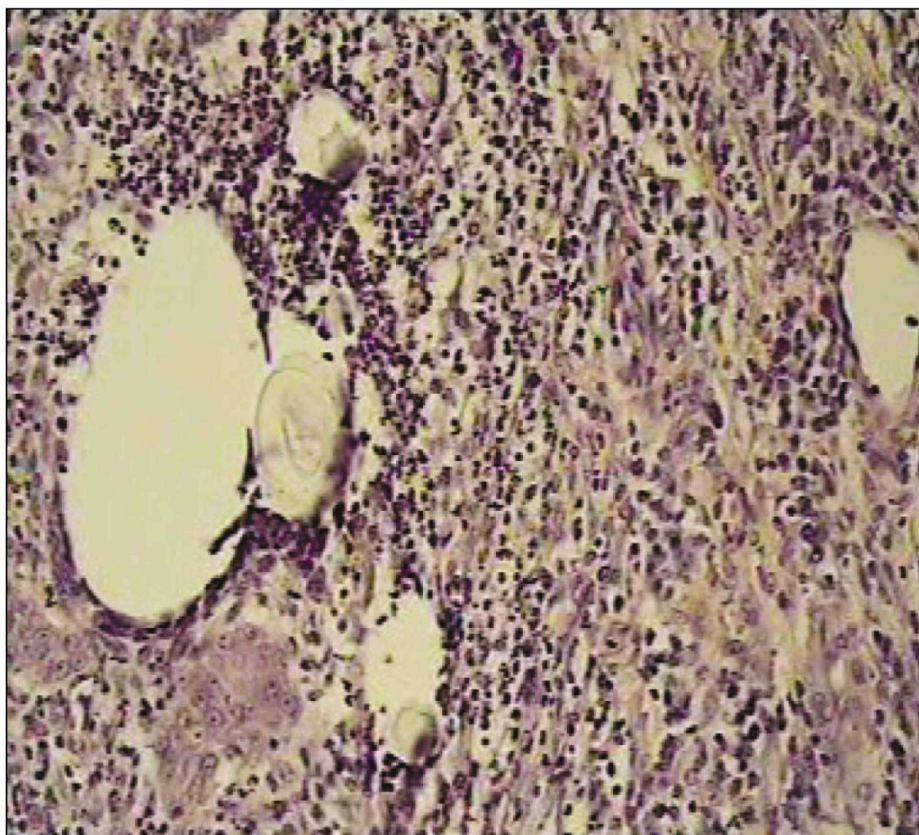


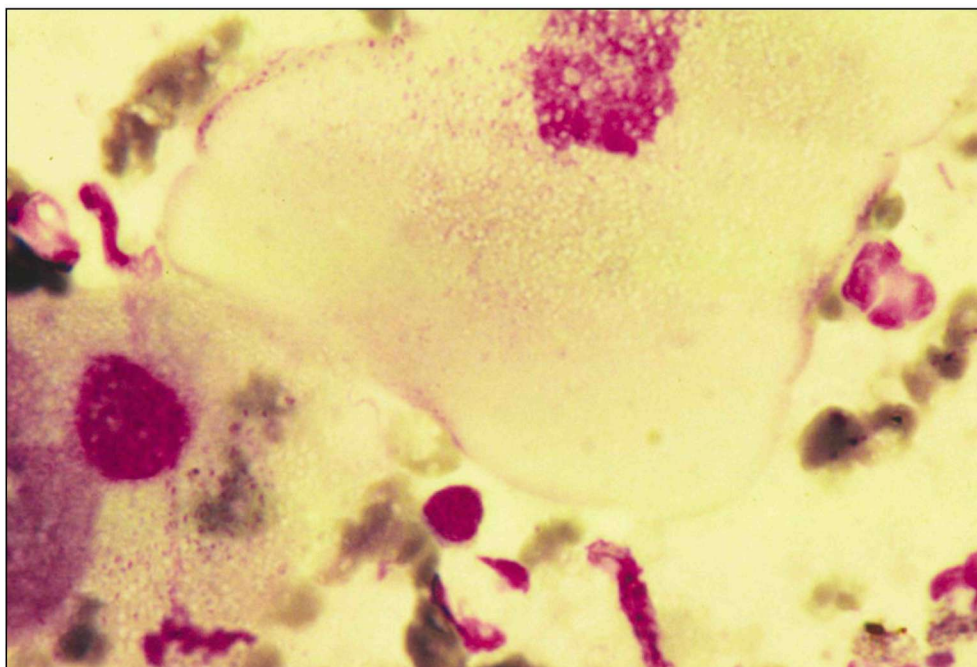
Figure 4. Mild erythema, with ulcerated plaque-like lesions and shallow ulcerations with or without crusting, which were mostly confined to white and lightly pigmented areas of the inguinal skin in an adult Dogue Argentino with SCC secondary to solar keratosis.

Εικόνα 4. Ήπιο ερύθημα με εξελκωμένες πλάκες και ρηχά έλκη με ή χωρίς εφελκίδες, κατά κύριο λόγο στις λευκές ή ελαφρά χρωματισμένες περιοχές του δέρματος της βουβωνικής χώρας σε ενήλικο Dogue Argentino με SCC σε έδαφος ακτινικής κεράτωσης.



Figure 5. Touching preparation smear from an ulcerated plaque: Abnormal keratinocytes with marked vacuolated and pyknotic nuclei as well as vacuolated and pale blue to gray cytoplasm are observed thus presenting cytological characteristics of malignancy (Haemacolor stain, x 1000).

Εικόνα 5. Χρωσμένο εντύπωμα από εξελκωμένη πλάκα: Ατυπα κερατινοκύτταρα με κενοδοποίηση και πύκνωση του πυρήνα, καθώς και κενοδοποίηση και ανοικτό μπλε προς γκρι χρωματισμό του κυτταροπλάσματος, χαρακτηριστικά συμβατά με κακοήθεια (χρώση Haemacolor, x 1000).



examination of stained touching preparation smears from ulcers and ulcerated plaques was suggestive of malignancy due to the presence of abnormal keratinocytes with marked vacuolated and pyknotic nuclei as well as vacuolated and pale blue to gray cytoplasm (Figure 5). Furthermore, fine needle aspiration cytology of the popliteal lymph nodes, revealed numerous atypical epithelial squamous cells among the lymphocytes. Wedge biopsies from the affected areas were obtained, processed routinely and stained with hematoxylin-eosin. A poorly differentiated malignant squamous cell carcinoma was subsequently diagnosed. It consisted of solid nests of cords of severely atypical squamous cells with basophilic cytoplasm, hyperchromatic nuclei, high mitotic rate and frequent atypical mitoses. Individual dyskeratotic keratinocytes were also present (Figures 6a, 6b).

The final diagnosis of squamous cell carcinoma secondary to actinic keratosis with regional metastasis was made. The owner refused any further treatment and elected the euthanasia solution for his animal.

DISCUSSION

Deep pyoderma is an unusual complication of solar keratosis, which is the result of chronic actinic damage to keratinocytes of the follicular infundibulum thus predisposing to furunculosis (Mason 1997, Ihrke 2004). In the sunny areas of the planet, pyoderma

secondary to solar damage is usually underdiagnosed (Ihrke 2004). In our case the diagnosis was made at the initial admittance of the animal, but therapy was delayed because of the misdiagnosis made by local practitioner to whom the case had been referred. Exfoliative erythroderma lesions confined to white areas of the skin were the characteristic clinical sign favoring the diagnosis of photodermatitis, although autoimmune skin disease, erythema multiforme, leishmaniasis and epitheliotropic lymphoma could not be outright ruled-out. In the subsequent skin biopsies the histopathological picture confirmed the clinical impression of solar radiation damage and actinic keratosis (Gross et al. 1992, Scott et al. 2001). Corticosteroid administration has been proposed as a systemic treatment for solar keratosis (Rosenkrantz 1993), but it was non-effective in our case, though given to control the supposed atopic dermatitis. The suggested treatment with acitretin has been shown to be quite effective for the treatment of canine solar-induced preneoplastic lesions, at the dose of 1mg/Kg, twice daily, for 2 to 3 months (Marks et al. 1992).

The development of SCC occurs most frequently in a pre-existing solar keratosis in veterinary patients (Hargis et al. 1977, Madewell et al. 1981, Nikula et al. 1992, Rosenkrantz 1993, Scott et al. 2001). Ultraviolet radiation is supposed to alter the immune system, most probably by a 20% to 50% decrease of epidermal

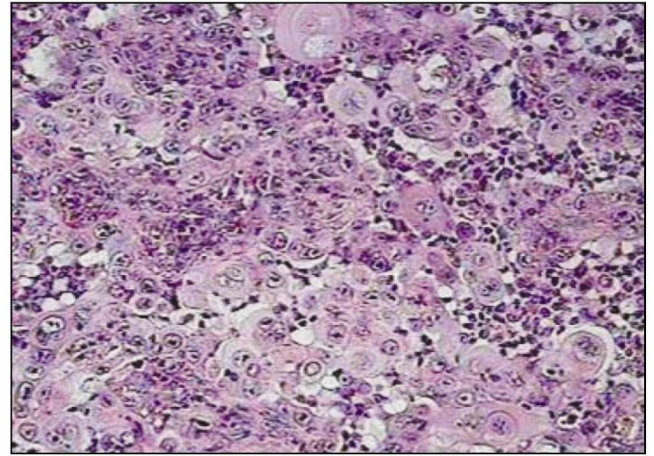
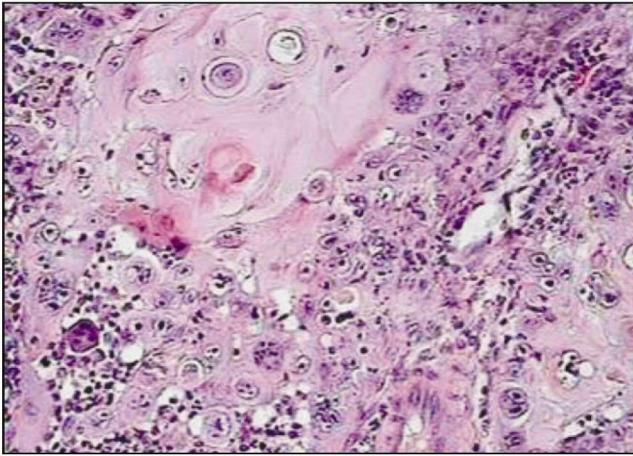


Figure 6a and 6b. Poorly differentiated squamous cell carcinoma with well visualized cellular atypia and foci of keratinization (H-E, x 1000).

Εικόνα 6α και 6β. Αδιαφοροποίητο ακανθοκυτταρικό καρκίνωμα με ευδιάκριτη κυτταρική ατυπία και εστίες κερατινοποίησης (H-E, x 1000).

Langerhans cells (Thiers et al. 1984). Since these cells are potent antigen presenting cells in the epidermis, those changes modify greatly the local immune response and cell kinetics that along with keratinocyte damage could contribute to malignancy. The majority of SCC in dogs are well-differentiated and with low metastatic potential (Gross et al. 1992, DeVico et al. 1994). However, the SCC of our dog fulfilled the cytopathological criteria of poorly-differentiated neoplasm (Garma-Avina 1994). At the time of diagnosis the metastasis to regional lymph nodes had already been established. It is unknown whether malignant transformation of the solar keratosis could be prevented by acitretin administration at the initial stage of the disease. At that state of the disease, cryosurgery, electro surgery, hyperthermia, laser therapy and radiotherapy could be used instead. However, the owner refused any further treatment and asked to have his dog euthanized.

Solar keratosis was diagnosed in 36.6% of 991 beagle dogs in the study of Nikula et al (1992). The combination of solar keratosis with SCC has also been reported in cats, horses and other mammals (Mason 1997, Campbell et al. 1987). Morphologic and histopathological features of canine and human solar keratosis are similar, with two exceptions. Solar elastosis (coarse, fragmented, wavy and basophilic elastic fibers) is not easily produced in dogs. Second, abnormal pigmentary accumulations noted in humans have not been observed in dogs. In both species solar keratosis is considered precancerous and metastasis of SCC is rare (Hargis and Thomassen 1979).

The clinician should always suspect solar keratosis and SCC whenever exfoliative erythroderma, pyoderma, masses, erosions and ulcers are confined to white areas of the skin, especially in animals that live in places with sunny climate. ■

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