4-month-old female Irish Terrier dog with well demarcated plaque at the entrance of the ear canal

Which of the following is the most likely diagnosis?

1. Pemphigus vulgaris
2. Erythema multiforme
3. Pemphigus foliaceus
4. Darier-like disease CORRECT
5. Pustular dermatophytosis

Signalment: 4-month-old female Irish Terrier dog.

History: The dog was presented because of a well demarcated, erythematous, hyperkeratotic, alopecic and partially eroded and ulcerated plaque at the entrance of the ear canal, covered by crusts (Fig. 1). Cytological examination revealed the presence of numerous acantholytic cells, with fewer neutrophils and coccoid bacteria.

Histopathologic Description: The epidermis is diffusely, moderately to severely and irregularly hyperplastic (Fig. 2 and 3) and shows a multifocal transepidermal loss of keratinocytes’ attachments (Fig. 2). This loss is prominent above the basal cell layer but is evident also in more superficial layers (Fig. 4 and 5). The superficially located acantholytic cells are often hypereosinophilic with normally appearing or shrunken and hyperchromatic nuclei (dyskeratosis and apoptosis) (Fig. 5). The epidermis is covered by a thick layer of lamellar to compact orthokeratotic hyperkeratosis with intralesional acantholytic cells (Fig. 4). Many of these cells are also recognizable in the crusts (Fig. 6). The acantholysis is multifocal affecting the infundibular walls of the hair follicles. In one of the biopsies a subepidermal band of fibrosis is also present (Fig. 4).

Morphologic diagnosis: Panepidermal acantholytic dermatitis

Name of the disease: Canine Darier-like disease

Comment: In human beings, Darier disease is a rare autosomal dominant genodermatosis, characterized by the loss of epithelial cohesion between keratinocytes. The disease was initially described in three related English Setters as the canine counterpart of the human Hailey-Hailey disease (benign familial chronic pemphigus). Subsequent studies have demonstrated that the disease could more correctly be associated to human Darier disease, which is due to a different genetic mutation in Ca2+ pumps (Ca2+ dependent ATPase). In Hailey Hailey disease the defect involves the SPCA1 (secretory pathway calcium⁄manganese ATPase isoform 1) pump encoded by the ATP2C1 gene and located in the Golgi apparatus, while in Darier disease the defect involves the SERCA2 (sarcoplasmonic reticulum Ca2+-transport ATPase isoform 2) pump encoded by the ATP2A2 gene and located in the endoplasmic reticulum. Using a selective inhibitor of the SERCA2 pump, Suter et al. have demonstrated that the endoplasmic reticulum pump and not the Golgi pump is affected in dogs with the disease. No mutations have been found when sequencing the ATP2A2 gene in the affected dogs; therefore it is thought that the phenotype of the disease in the affected dogs is caused by mutations in genes other than ATP2A2, affecting proteins regulating the calcium function in a similar way to SERCA2. The detailed molecular mechanisms leading to the massive acantholysis are also still under debate. The two main accepted hypotheses involve the roles that the impaired calcium homeostasis can have on the structure and function of the calcium-dependent desmosomal proteins and on the regulation of the keratinocyte cell cycle, respectively. Clinically the disease is characterized by alopecic, erythematous and scaling lesions that become plaques with time and show commonly crusting. Lesions are often located at pressure points on the limbs, ventral thorax, head and pinnae and develop in young animals (approximately 6 months of age). The disease is histologically characterized by loss of
adhesion of the suprabasal keratinocytes associated with abnormal keratinization leading to dyskeratosis and epidermal hyperplasia. In many biopsies there is a transepidermal loss of keratinocyte adhesion involving both the epidermis and hair follicles, conferring the so called “crumbling brick wall” aspect. Acantholytic cells are rounded and hypereosinophilic (dyskeratotic keratinocytes or “corps ronds”). There is often a severe ortho- and parakeratotic hyperkeratosis. Dermal inflammation is rare except in areas of secondary bacterial infection. Immunofluorescence testing for autoantibodies is negative. Lesions in dogs are normally not treated, due to the fact that they are often asymptomatic and localized.

References:


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Figures legend:

**Figure 1.** 4-month-old female Irish Terrier dog. A well demarcated, erythematous, hyperkeratotic, alopecic and partially eroded and ulcerated plaque is present at the entrance of the ear canal, covered by crusts.

**Figure 2.** 4-month-old female Irish Terrier dog. The epidermis is irregularly hyperplastic with severe orthokeratotic hyperkeratosis. A transepidermal acantholysis is visible.
Figure 3. 4-month-old female Irish Terrier dog. The epidermis is irregularly hyperplastic with severe orthokeratotic hyperkeratosis and crusting.

Figure 4. 4-month-old female Irish Terrier dog. The keratinocytes’ adhesion loss is prominent above the basal cell layer (left side) but is evident also in more superficial layers where rafts of acantholytic cells coalesce (right side). A laminar subepidermal band of fibrosis is also visible. In the superficial dermis there is a minimal perivascular infiltration with lymphocytes and fewer neutrophils.
Figure 5. 4-month-old female Irish Terrier dog. There is a suprabasilar cell detachment. In the superficial layers, the acantholytic cells are often hypereosinophilic with normally appearing or shrunken and hyperchromatic nuclei (dyskeratosis and apotosis)

Figure 6. 4-month-old female Irish Terrier dog. The acantholytic cells are also recognizable in the crusts, intermixed with bacterial colonies.