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DERMAL-EPIDERMAL JUNCTION DISEASES

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Introduction

The dermal-epidermal junction is very thin, but when it malfunctions, the animal (or person) may have grave problems. The DEJ is made up primarily of proteins whose function may be summarized as keeping the epidermis attached to the dermis. A simplified schematic is shown below:

Diseases of the DEJ may either be 1) congenital, with a defect in some structure, caused by mutations of encoding genes leading to protein absence or dysfunction, or 2) autoimmune, with
autoantibodies that attack the structures. It is important to remember that these diseases are rare, and that the terminology, particularly in regards to the structures themselves, is often changing.

CONGENITAL DISEASES

EPIDERMOLYSIS BULLOSSA (EB)

This term includes a number of diseases typified in human beings by the common finding of blister formation after minor trauma. Most forms are congenital and apparent soon after birth. In animals and in human beings, subsets of EB are classified by the histologic location of the blister or cleft. These subsets (and respective cleft location) are termed EB simplex (basal cell layer of the epidermis), junctional EB (intralamina lucida or basal cell layer), and dystrophic EB (sublamina densa).

While more commonly described in horses, this disease has been described in dogs\textsuperscript{1,4} and two cats.\textsuperscript{5,5a} There may be a genetic predilection in German Shorthair Pointers\textsuperscript{3,4} and Golden Retrievers.\textsuperscript{4a} The lesions described include cutaneous and mucosal (oral) ulcers, scaling of the foot pads, atrophic skin, hyperpigmentation, alopecia and dystrophic nails. Initial occurrence of the lesions varied from soon after birth to 1 year of age. Histology and/or electron microscopy showed both the junctional or dystrophic variants were found in both dogs and cats.

In general, treatment is not successful in the congenital diseases, beyond palliative efforts. A previous study showed \textit{in vitro} correction, mediated by retroviral vectors, of canine (Golden Retriever) dystrophic epidermolysis bullosa.\textsuperscript{5b} In a recent article, epidermal cells from two affected dogs (German Shorthair Pointers) with dystrophic EB were genetically modified to produce normal epithelial cells, which were then successfully transplanted as autografts on to the dogs.\textsuperscript{6} This interesting study could lead to further successful treatment in both canine and human EB.

AUTOIMMUNE DISEASES

These diseases are best differentiated based on immunohistology.

BULLOUS PEMPHIGOID (BP)

This is a rare disease in dogs\textsuperscript{7,8} and very rare in cats.\textsuperscript{9} There may be a predilection in Collies. Clinical signs are ulcers found in the oral, peri-orificial, axilla, and/or inguinal areas. Secondary infections may be present. The etiology is the production of antibodies (usually IgG) to the transmembrane portion of bullous pemphigoid antigen II (collagen XVII).\textsuperscript{8,9} Collagen XVII binds the basal layer keratinocytes to the basement membrane zone, thus its destruction results in a sub-basal cell cleft. Histopathology shows this cleft, usually accompanied by a dermal infiltrate of eosinophils. Immunohistology shows immunoglobulin deposition on the epidermal side of the
Some of these dogs have antibodies to laminin-332 (laminin-5), a basement membrane protein. Treatment is similar to pemphigus foliacues, involving the use of prednisolone and azathioprine in dogs, and prednisolone and chlorambucil in the cat. Cyclosporine may be an alternative treatment in cats.

MUCOUS MEMBRANE PEMPHIGOID (MMP)

This disease may be the most common of the autoimmune diseases of the epidermal-dermal junction. German Shepherd dogs have been noted to be predisposed. Clinical signs are ulcers noted in the oral cavity, lips, peri-ocular, nasal planum, concave pinnae, genitalia, and anus. Etiology is caused by anti-bodies to bullous pemphigoid antigen II (collagen XVII), or to laminin-332 (laminin-5). Treatment is as for bullous pemphigoid, but this disease may be easier to control.

EPIDERMOLYSIS BULLOSA AQUISITA (EBA)

This is a very rare disease seen in young dogs with a possible predilection in Great Danes. Clinical signs are urticaria, oral ulcers, and epidermal sloughing. Etiology is the production of antibodies (usually IgG) to collagen VII. Again, some of these dogs have antibodies to laminin-332 (laminin-5).

Collagen VII binds the lamina densa of the BMZ to the dermis. Histopathology shows an dermal-epidermal separation and a neutrophilic infiltrate in the dermis. Immunohistology reveals immunoglobulin deposition on the dermal side of the BMZ. Treatment is similar to the pemphigoid diseases, but recently a Great Dane was successfully treated with the addition of colchicine and intravenous human immunoglobulin to the treatment regimen. Twelve months later, the dog was still in remission and all drugs were discontinued without recurrence.

BULLOUS SYSTEMIC LUPUS ERYTHEMATOSUS (BSLE)

This condition was reported in a dog that had both confirmed SLE as well as an acquired, vesicular, erosive and ulcerative eruption. Histology showed subepidermal vesicles with neutrophil-predominant inflammation at the dermal-epidermal junction. Immunohistology showed deposition of IgG at the BMZ. The dog also had circulating IgG autoantibodies against type VII collagen (similar to EBA).

Too few cases have been reported to recommend treatment.

BULLOUS LINEAR IgA DERMATOSIS (LAD).

Another rare disease, LAD is associated with skin-fixed and circulating antibodies that target LAD-1, the processed extracellular form of type XVII collagen. The two dogs diagnosed with this disease had erosive, ulcerative, and crusted lesions seen on the face, in the oral cavity, and on the extremities. Histopathology showed dermoepidermal clefting present in the basement membrane lamina lucida. Immunoochemistry showed basement membrane-fixed IgG and/or IgA.
antibodies as well as circulating IgA and IgG autoantibodies that target the 120-kd soluble protein LAD-1\textsuperscript{17}. Too few cases have been reported to recommend treatment.

References


