Paraneoplastic and Immune-Mediated Skin Diseases in Dogs

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Paraneoplastic Syndromes (PNS)

- Non-cancerous neoplasia-related disorders that occur at a site distant from the primary tumor or metastasis
- Indirect effects of cancer
- May be the initial clinical sign
- Cutaneous
  - 30 disorders reported in humans
- Precede, follow, or coincide with neoplasia
- Other: Endocrine, Blood, GI, Neurological, Renal

Selected paraneoplastic skin diseases/cutaneous manifestations of internal disease

- Nodular Dermatofibrosis
- Feminization Syndrome (Sertoli Cell Tumor)
- Hepatocutaneous Syndrome/Superficial Necrolytic Dermatitis
- Cutaneous xanthomastosus
- Calcinosis Cutis
- Cacinosis Circumscripta

Nodular dermatofibrosis (ND)

Background

- Aka: "Nodular Dermatofibrosis of German Shepherds" (Multiple Cutaneous Fibromas) "Collagenous Nevi" "Renal Cystadenocarcinoma and Nodular Dermatofibrosis" (RCND)
- Multiple, cutaneous nodules (collagen)/collagenous nevi/hamartomas
- Association with renal cystadenocarcinoma or cystadenoma
- German Shepherds are predisposed (autosomal dominated, mutation in tumor suppressor genes- chromosome 5, mutation exon 7 of canine BHD +/- modified folliculin; Birt-Hogg Dube locus), but other breeds are reports, such as the Golden Retriever, Boxer, Rotweiller, and Labrador.
- Suspected that renal tumors secrete collagen-stimulating growth factors or cytokines that accelerate collagen accumulation (TGF-alpha suspected to play a role)

Clinical signs

- Onset is 3-7 years of age on average.
- Skin lesions (around 6 years of age)
  - multiple, firm, well-circumscribed dermal/subcutaneous (freely movable) nodules (2 mm to 5 cm); rarely ulcerated
  - non painful, non pruritic nodules
- anatomical locations: primarily extremities, but also the pinnae, trunk, neck or diffuse
- Renal involvement (around 8 years of age)- may have hematuria, abdominal distension, discomfort (e.g., renal cyst rupture) +/- systemic sign (lethargy, fever, loss appetite), end-stage = renal failure; renal changes are slowly progressive
- The skin lesions are almost always noted before the renal disease is noted/problematic
- The kidneys (gross)- enlarged, irregular, multiple solid or cystic tumors

Diagnosis

- Imaging: ultrasound (86% have renal changes), MRI, CT, nephrography (contrast), scintigraphy
- Pathology (Skin):
  - Cutaneous Nodules- bundles of dense, well-differentiated collagen fibers in the dermis/sub-cutis (no sharp demarcation from surrounding connective tissue
- Pathology (Renal):
  - Cystadenocarcinomas or cystadenomas
  - Gradual process (hyperplastic epithelium → adenoma → adenocarcinoma)
- Pathology (Uterus)
  - Leiomyoma

Treatment

- Supportive care, surgery, possible azathioprine +/- corticosteroid
- Prognosis poor (average life expectancy after diagnosis (cutaneous nodules) is 2.5 years); but many dogs seem to liver greater than 5 years with benign renal cysts

Collagenous Nevi (Hamartoma)

- Nevus/hamartoma = circumscribed developmental defect of the skin, characterized by hyperplasia of one or more skin components
- These have been seen in many breeds as solitary or multiple cutaneous lesions (head, neck, proximal extremities)
- Most are firm, well circumscribed (0.5-5 cm), alopecic, hyperpigmented, cobblestone or orange peel surface, foot lesions can ulcerate
- Hamartoma = just skin

Feminization syndrome with testicular neoplasia

(4) Testicular neoplasms

1. Sertoli Cell Tumor (SCT)
   - Average age: 9YO
   - Arise from estrogen-secreting sustentacular cells of
   - Increased risk with cryptorchidism seminiferous tubules
   - Usually increased estradiol-17B (testicular & peripheral venous blood) vs. normal dogs +/- decreased testosterone ("feminization")
2. Seminoma
   - Arise from germinal epithelium
   - Increased risk with cryptorchidism
   - NOT different estradiol-17B level (testicular & peripheral venous blood) vs. normal dogs not endocrinologically active
3. Interstitial Cell Tumor
   - Arise from Leydig cells
   - Usually increased estradiol-17B (testicular & peripheral venous blood) vs. normal dogs (like SCT)
4. Granulosa Cell Tumor (GCT)

*****Sertoli cell tumor (SCT)**

- 24-57% have "feminization syndrome"
- "hyperestrogenism" not always = "feminization"; its really the shift between testosterone & estradiol; not all have elevated estradiol-17B (feminization w/ normal estradiol-17B levels may be b/c increased estriol or estrone--not usually measured)

Cause

- endocrine alopecia and feminization in 1/3 of dogs with SCT (esp. cryptorchid)

Clinical signs

- slowly progressive bilaterally symmetrical alopecia starts in neck, lumbar, perineal and genital regions (+/- thin epidermis)
- +/- linear preputial dermatosis **linear erythematous or hyperpigmentated color change along ventrum of prepuce (preputial orafice to scrotum (mild VD & congestion)**
- coat color change
- macular melanosis (inguinal, perianal, genital)
- enlarged testicle & other soft & atrophic
- +/- seborrhea sicca or oleosa, macular hyperpigmentation

Clinical signs of feminization

- Gynecomastia
- Pendulous prepuce
- Attraction of male dogs
- Prostatitis (squamous
- Metaplasia)
- Estrogen induced BM
- Suppression (aplastic anemia)
- Perianal gland hyperplasia
- Tail gland hyperplasia

Differential diagnosis: Hypogonadism, adrenal sex hormone imbalance, low T4, Cushing

Diagnosis

- Signalment, history, physical examination
- Bloodwork: sex hormone measured (pancytopenia = poor prognosis)
- Histopathology= orthokeratotic hyperkeratosis (OKH), follicular dilatation, atrophy, follicular keratosis, telogenization of hair follicle and sebaceous gland atrophy

Treatment

- Castration (response to this)

Prognosis

- Poor if aplastic anemia, septicemia, thromboembolism
- Good if castration is curative

Superficial Necrolytic Dermatitis (aka: Hepatocutaneous Syndrome) (SND/HCS)

Background

- SND/HCS (dog), MEN, NME (human), diabetic dermatopathy, glucagonoma syndrome (superficial necrolytic dermatitis, hepatocutaneous syndrome, necrolytic migratory eryethema, metabolic epidermal necrosis)
- Tumor-induced depletion of certain physiological substances; necrotizing skin disease that occurs in association with internal disease—well known syndrome in the dog (hepatopathy) and **glucagon-secreting tumors (rare) reported in dogs, rarely described in cats with pancreatic tumors
- Unknown mechanism- disrupts normal nutritional elements getting to the skin; may have sudden necrosis; proposed mechanism: **increased glucagon → increased gluconeogenesis and catabolism of amino acids (decreased amino acids) → epidermal protein depletion and keratinocyte necrolysis
- Almost all cases in the dog have been associated with chronic hepatic disease (e.g. cirrhosis, drug-induced hepatitis (phenobarbital) and chronic active hepatitis and rarely, this condition is linked to a pancreatic, glucagon-secreting tumor (glucagonoma)
- May develop diabetes

Clinical signs

- Weeks to months after onset, patient will present (OFTEN for lameness)
- Erosions/ulcerations; alopecia (acral); erythema; adherent crust (feet, pressure points-elbow, hocks; oral, perineal, muzzle, MCJ) +/- paraneoplastic alopecia
- Elbows, anogenital area, and **footpads** (sometimes only)
- Footpads: hyperkeratosis, deeper effect- ulceration and erosions, deep fissures, cracking, lame when walking/pain, pruritic

Diagnosis

- Physical examination, history, clinical signs
- Biopsy-Pathology: "red, white, blue"
    - Red:
        - parakeratotic hyper-keratosis (vesicular nuclei with eosinophilic cytoplasm)
    - White:
        - severe superficial epidermal edema (spongiosis) + necrosisof keratinocytes in stratum spinosum
    - Blue:
        - acanthosis (deep epidermal layer)
- Complete blood cell count and Chemistry (liver enzymes)
    - anemia, ^glucose, ^liver enzymes, v ALB (carries EFA & Zn), ^ BAs, abnormal US/Rad findings, hypoaminoacidemia (also look for DM), v glucagon
    - Ultrasound (reticulated, honey comb) and radiographs +/- other imaging (MRI, CT)
- Amino acid levels (UC Davis, California)
    - mean values of all amino acids are about 60% or less and total amino acid concentration was 30% compared to normal dogs (exception: glutamic acid, phenylalanine, tryptophan and ornithine)
- Differential diagnosis
    - DDX/R/O-Liver- cirrhosis, neoplasia, Cush, lipidosis, rx, hepatitis etc)-nodular regeneration w/bands of vacuolated hepatocytes & bile duct hyperplasia
    - DDX/R/O-Skin: Distemper, ZRD (arctic breeds- uniform pad hyperkeratosis face/pad w/o pain & rawness), EM, Rx Eruption, PF,SLE, Contact-irritant, Focal Metatarsal Fistulation of GSD, Familial Cutaneous Vasculopathy of GSD (carpal/tarsal pads- drains clear serous material/sterile- 1-2 pads not painful-drain heal on own & cytology shows histiocytic, plasmacytic cells, may try Synotic), "collagen" disorder of GSD, Feline Lymphoplasmocytic Pododermatitis (central distal pad enlarged/balloon & scaly (not PF)-TX= doxy +/- steroids
    - ALSO: demodex, dermatophyte, bacterial folliculitis

Treatment

- Address underlying liver disease (if possible)
    - Stop phenobarbital
    - Mycotoxin removal
- Manage the discomfort (e.g., tramadol)
- Manage infection (antibiotics, antifungal)
- Nutrition- high protein (egg yolks/eggs = 1/10kg BW/day); ProMod®; ProCel®; diet change
- Amino acid IV infusions (Aminosyn II®) – initially every 3-7 days, then monthly (25ml/kg over 6-8 hours, use jugular vein) (side-effects: thrombophlebitis and depression)
- Corticosteroids (palliative)- not an initial treatment usually (long-term may predispose to diabetes)

- Elemental Zinc (2-3mg/kg/day) + omega 3 fatty acids
- Octreotide Acetate (Sandostatin®)
- Colchicine 0.03mg/kg/day- anti-fibrotic (cirrhosis)
- SAMe + milk thistle
- Surgery (if glucagonoma)- rare

Prognosis

- Poor (average 6 months from time of diagnosis)
- Skin manifestations may improve temporarily with resection of the tumor in the pancreas (surgery)- very rare

Cutaneous Xanthomatosis/Xanthoma

Background

- SEE Feline notes for more detail.
- Yellowish, cutaneous or subcutaneous lesions associated with an accumulation of lipid in dermal connective tissue
- Very rare in dogs, but when reported, associated with:
    - diabetes mellitus (hyperlipidemia)
    - acute pancreatitis (NO hyperlipidemia unless pancreatitis secondary from diabetes mellitus)

Clinical signs

- non painful nor pruritic papules, plaques and cutaneous and subcutaneous nodules

Diagnosis

- Clinical signs skin biopsies, abnormal lipid metabolism
- Pathology: histiocytes, multinucleate giant cells and Touton
- Lipid metabolism checked- cholesterolaemia, triglyceridaemia, lipoprotein electrophoresis, chylomicron test, pancreatic lipase

Treatment

- Prognosis and treatment (depends on cause)

Calcinosis Cutis

Background

- calcinosis cutis- pathological calcification in the skin
- dystrophic calcification: phospho-calcium metabolism is unaffected; due to hyperadrenocorticism (Cushing's) or diabetes mellitus
- metastatic calcification: phospho-calcium metabolism is disordered; due to renal insufficiency (e.g., chronic renal failure, persistent urachus, renal dysplasia) and secondary hyperparathyroidism (e.g., reduced active vitamin D production → hypercalcemia) (+/- increased serum calcium and/or phosphate)
- iatrogenic calcinosis: local hypercalcaemia (e.g., topical application of a calcium chloride or carbonate product; calcium gluconate injection, or progesterone injection
- idiopathic (e.g. idiopathic calcinosis universalis and calcinosis circumscripta- bony prominences and digits)

Clinical signs

- Skin: erythematous-salmon colored (sometimes white) papules and firm, gritty, cutaneous or subcutaneous nodules +/- erosive-ulcerated +/- discomfort; footpads mau be an overrepresented location for the metastatic calcification (especially Shi Tzu and Pekinese with renal disease/dysplasia)

Diagnosis

- Clinical signs (skin and kidney), skin biopsies (basophilic, granular material in dermis/hypodermis, focal areas of mineralization surrounded by macrophages, giant cells, and epithelioid cells), blood work (increased BUN, CR, CA, Phosphate; increase in phospho-calcium balance), urinalysis, ultrasound

Prognosis and treatment

- Metastatic calcification associated with kidney disease has a poor prognosis and goal of treatment is to reduce the phospho-calcium balance (e.g. aluminium and magnesium hydroxide) and activated charcoal.
- Other causes of calcification (see above)- have a better prognosis if the underlying cause is addressed

Calcinosis Circumscripta (variant of calcinosis cutis)

Background

- SEE above- calcinosis cutis
- unknown etiology-idiopathic (ectopic) is most likely +/- other (dystrophic, metastatic (usual) or iatrogenic mineralization)
- subtle tissue trauma is a likely prerequisite for calcium deposition, based on the usual localization of idiopathic calcinosis circumscripta to sites of 'trauma' (e.g., footpads – daily trauma from ambulation or tongue form moving tongue)
- Associated with a high calcium x phosphorous product and a 'sensitizing' agent, such as parathormone or vitamin D12

Clinical signs

- usually occurs as a solitary, firm lesion (usually dystrophic calcification):
- over pressure points
- other areas of putative trauma (tongue or even spine)

- other trauma such as ear cropping, bite wounds, etc.
- renal disease → multiple footpads +/- parathyroid hyperplasia, and visceral calcification (metastatic form)

General/typical renal pathology findings

- chronic interstitial nephritis
- bilateral renal hypoplasia
- nephrosclerosis

Treatment

- Identify/manage the underlying problem
    - e.g., renal failure and phosphate binders (magnesium or aluminum antacids; caution to avoid magnesium or aluminum toxicity)
- Manage secondary infections (subcutaneous- calcium deposits may erode the skin and predispose these areas to secondary infection)
- DMSO (dimethyl sulfoxide) (Beal and Morris, 1995)
- Colchicine (suppress local inflammation)
- Intralesional corticosteroids (anti-inflammatory and inhibitory effects on fibroblast activity → solitary lesions); e.g., calcinosis circumscripta
- Sodium etidronate/diphosphonates (reduce bone turnover and inhibit the growth of ectopic hydroxyapatite crystals); risk paradoxical hyperphosphatemia
- Myo-inositol hexaphosphonate (dietary substance → inhibit the crystallization ofcalcium salts); topical (studies) and oral
- Surgical Management
- Warfarin
- Calcium-channel blockers (diltiazem)- antagonism of the calcium-sodium ion pump
- Probenecid: uricosuric (increase uric acid excretion in urine (gout and hyperuricemia)
- Sodium thiosulfate
- Surgery – remove affected area

Selected immune-mediated disease

- Pemphigus foliaceus
- Discoid Lupus Erythematosus
- Erythema Multiforme

Pemphigus foliaceous

Background

"cell adhesion" autoimmune disease—circulating auto-antibodies targetd against **desmosomal proteins** on keratinocyte surface → separation of epidermal cells→ spaces created

Pustular-crusting dermatitis

Auto-Abs to dsg1 (150-160kd glycoprotein; cadherin group of adhesion molecules; (skin below stratum corneum)

Only the epidermal desmosomes are affected (NO mucosal lesions! - would need to affect dsg-3)

Signalment

- Dogs- mean is 4.2 years old, 65% < 5 years old, history of allergy, demodicosis, may be drug induced (NSAID and antibiotics)
- Breed Predispositions/Overrepresented: Chow, Akita, Bearded Collies, Doberman Pinchers, Daschshunds, Finnish Spitz and Schipperkes
- Any gender
- Usually adults, can occur in dogs less than 1 year old

History

- Wave-like lesions across the face and body, ACUTE flare-ups overnight are reported, may have intrinsic cyclicity, crusting (ear, eye, nose- and generalized→ back etc.); may wax/wane
- Transient vesicles and pustules evolve rapidly into erosions & crusts
- Pustules have polycyclic borders (large) +/- follicles coming out
- Season/UV light/Photoexacerbated (suggested)
- Lack ABX and Anti-fungal response
- Precipitating Factors: genetics, UV light, drugs, infection, allergy
- Systemic Illness: lethargy, fever, decreased appetite, lymphadenopathy, etc.

Etiology/classification

(3) Classes/forms

1. Spontaneous –Akitas and Chows
    - No previous skin disease or drug exposure
2. Drug and Food induced—Labradors and Doberman Pinchers

- TMS/SMZ, Cephalexin (horses) enalapril (people); lime-sulfur or ITZ (cats)
- People:
- Drug Caused PF (TX: remove the drug)
- Drug Triggers PF in Predisposed Person (TX: life-long)
    - (ipodate in cats)

3. Chronic skin disease- history of chronic skin disease (1-2 years of uncharacterised puritic skin disease/allergies)

Clinical signs

- Bridge of nose (planum nasale and philtrum); depigment "premonitory" (later finding in PF vs. PE); also dorsal muzzle
    - muzzle, pinnae, periorbital regions, periocular (often starts: face/ears)
- Footpads- hyperkeratosis (villous hyperkeratosis/"hard-pad"), fissuring, pustules, crusts, +/- ulcers (usually erosive at most) +/- lamness
    - Footpad only reported
    - Claw- onychodystrophy, onychoclasis (breaking), onychorrhexis (brittle/breaking), onchogryphosis (abnormal curvature/hypertrophy)
        - start as erythematous macules or papule → pustule → rupture and ooze → desiccate→ crust/scale → alopecia/erosions bordered by epidermal collarettes (often only lesion seen)
        - secondary bacterial infection
        - often feet & face (+/- photodermatitis- more with PE)
        - become generalized over 3-12 months
        - may have annular, target-shaped or polycyclic pattern +/- alopecia +/- exfoliative erythroderma
        - 50% of dogs are pruritic
        - +/- systemic signs: anorexia, depression, fever & weight loss (when widespread erosive lesions)

Acute vs. Chronic lesions

- Acute
    - Erythematous macules→ papules→ pustules/pustular phase (erosive, not ulcerative) → crust (dry yellow or honey-colored)
- Chronic
    - Alopecia (follicular epithelium), scale, crusts, +/- epidermal collarettes, etc.

Forms/lesions:

(3) Forms: ("Focal form of PF= PE")

1. Localized- genitals, nailbeds, footpads (DDX: mosq-bite-hypers and
    - hepatocutaneous disease/MEN) (almost 30% remain
    - localized for 1-3 years)
2. Generalized- rare (60% have generalized disease within 6 months)
    - Pustular (crusting dermatitis)
    - Exfoliative + Erythroedema (diffuse scale + edema)
3. Systemic-anorexic, febrile, depressed, large LNs, pitting edema

Diagnosis

- History, physical examination, histopathology, Tzanck preparation
- Differential Diagnosis

Bacterial pyoderma, sterile pustular dermatitis, allergies, scabies, dermatophytes, etc.

Treatment

- Glucocorticoid, azathioprine, mycophenolate, leflunamide, chlorambucil, cyclosporine, tetracycline + niacinamide, etc.

Prognosis

- Depends on response to therapy

Discoid Lupus Erythematosus (DLE)

Background

- Discoid lupus erythematosus (DLE) is often difficult to get a firm diagnosis with biopsy, but clinical signs are often suggestive enough. DLE is an auto-immune skin disease that is for the most part benign in that this is not reported to progress to a systemic disease. This condition is photoexacerbated, thus photosensitivity seems to play a role. T-cells (lymphocytes) and plasma cells (other immunologic cells) inflitrate the skin and cause a reaction.

Clinical signs

- There is depigmentation, scaling, loss of cobblestone appearance, and erosion/ulceration on the nose (planum nasale) +/- other areas (e.g., lip folds, vulvar are, perianal). German shepherds, Shetland Sheepdogs, and Collies and their crosses seem to be predisposed to DLE.

Diagnosis

- DLE is a diagnosis based on history, physical examination, and skin biopsy (classic pathology). It is important to rule-out other possibilities for the clinical presentation, including: pyoderma (e.g., superficial bacterial infection and mucocutaneous pyoderma), lip

fold dermatitis (intertrigo), demodicosis (mites), dermatophytosis (ringworm), yeast dermatitis (Malassezia or candidiasis), autoimmune/immune-mediated skin disorders (e.g., mucus membrane pemphigoid, pemphigus foliaceous or erythematosus, etc.), cutaneous adverse drug reaction, vasculitis/ischemic/dermatomyositis, Zn-responsive dermatosis, and cutaneous T-cell (epitheliotropic) lymphoma/cancer).

Treatments

- Several medications have been used including oral and topical steroids, immunomodulatory medications (e.g., cyclosporine, tacrolimus, corticosteroids), vitamin E, chemotherapy medications (azathioprine, chlorambucil), even anti-malarial medications have been tried (in humans). Over the recent years we have used a combination of vitamin B and an antibiotic (doxycycline/tetracycline) together for their synergystic immunomodulatory effects. Topical steroids are used initially (e.g., triamcinolone, betamethasone, fluocinonide, and clobetasole) use, but contraindicated long-term (especially daily) as corticosteroids breakdown collagen and weaken the skin barrier. For topical therapy, 0.1% tacrolimus (Protopic) is the current treatment of choice. Sometimes we start with topical corticosteroids, but this may not be necessary.

Prognosis

- The prognosis for DLE is usually good, but usually requires (intermittent) some form of life-long therapy. This condition may overlap with a condition known as mucocutaneous pyoderma (MCP). Mucocutaneous pyoderma (MCP) is a relapsing bacterial infection of mucocutaneous junctions. This is the region just between the skin and the mucus membranes (e.g., oral gums, perivulvar/prepucial, periocular, etc.).

Erythema multiforme (EM)

Background

- Uncommon skin disease that is often sudden in onset
- Can affect skin and mucus membranes or even the junction between the two (mucocutaneous junction)
- Condition can wax and wane and can be self-limiting, or require therapeutic intervention/diagnostic work-up
- Believed that there is a cell-mediated hypersensitivity reaction directed against certain substances (antigens)-- include infectious organisms, medications (griseofulvin, aurothioglucose, cephalosporines, penicillins, sulfonamides, polythiouracil), foods, and other possible causes; also may be associated with neoplasia (paraneoplastic syndrome) or connective tissue disorders
- Underlying cause is idiopathic (meaning the underlying cause is unknown)—these antigenic substances can all alter the keratinocyte so that lymphocytes are attracted (satellite); attraction eventually leads to individual cell death (apoptosis) in the affected area. EM has classically been organized into several different categories (in human medicine); these are based on the severity of the condition and how much of the skin is affected
- These are classified as “major” and “minor.”
    - if one region/mucocutaneous junction were affected, this would be classified as EM “minor” (does not predict the outcome to treatment)
    - The “major” form is often used interchangeably with Stevens Johnson Syndrome (SJS).

Background/Etiology

- Acute for of a cutaneous drug reaction
- Associated with infections (systemic)
- Associated with neoplasia (e.g., thymoma)
- Idiopathic (most common)

Clinical signs

- Various presentations—papular, pustular, erosive/ulcerative, classic “target” lesions, hyperpigmentation, scaling, etc.
- Classic lesions include a target lesion that is raised on the borders with erythema centrally. While this is classic, this is not always seen, especially if only the mucocutaneous regions are affected.
- There may be erythematous areas of hyperpigmented macules or raised erythematous papules or even plaques. There may also be scaling, crusting, or oozing of lesions (sometimes associated with secondary infection).
- Areas of the skin most affected include the ventrum, inguinal and axillary region, oral cavity, pinnae, and footpads.
- Almost 50% of the cases have a mucocutaneous involvement (e.g., around the eyes or mouth).
- Diagnostic work-up often includes bloodwork, imaging, and other possible tests (in addition to a skin biopsy).

Diagnosis

- Clinical signs, history, physical examination
- Histology
- Differential Diagnosis
    - Drug reaction, auto-immune, infection, lymphoma, metabolic, other

Treatment

- Stop current medications (oral & topical), supplements +/- diet (e.g., novel protein diet may be indicated).
- Search for neoplasia or other systemic disease and address this concern (i.e., surgery to remove thymoma)
- Immunomodulatory therapy
    - Pentoxifylline
    - Cyclosporine (oral) or tacrolimus (topical)

    - Tetracycline + Niacinamide
    - Corticosteroids (oral or topical)
    - Prognosis
- Depends on response to treatment and severity of disease

Paraneoplastic pemphigus (PNP)

- Uncommon, but well-characterized, immune-mediated blistering disorder associated with both benign and malignant lymphoproliferative processes (humans)
- Shares some similarities with classic pemphigus (pemphigus vulgaris (PV)) file to the human counterpart
- Rarely reported in dogs (e.g., Boxer and mediastinal lymphoma); Bouvier Dog; mediastinal Lymphoma (oral lesions, anorexia)
- Criteria
    - Mucocutaneous eruption with blisters and/or erosions.
    - Histological features including epidermal acantholysis, keratinocyte necrosis, and vacuolar interface dermatitis.
    - Epidermal and basement membrane-zone deposition of immunoglobulin G and complement (via direct immunofluorescence).
    - Detection of serum autoantibodies reactive to normal epithelia (via indirect immunofluorescence).
    - Immunoprecipitation with serum antibodies of the above characteristic complex of proteins