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CASE I – 10760 (AFIP 2886852)

Signalment: 190 lb, female, large white crossbred, commercial pig.

History: This pig is from a farrow to finishing operation that had experienced dermatitis with pruritis in all ages of pigs for the last 4-5 months.

Gross Pathology: The skin on both ears (pinna and external ear canal), face, and between the claws was thickened and covered with dry yellow-brown crusty exudate (Fig 1-3). Similar exudate was present on the dorsal midline, but the skin was not thickened.

Laboratory Results: Whole mites, dissected from the hyperkeratotic epithelium, were identified as adult *Sarcoptes scabiei* var. *suis* by the clinical parasitology laboratory at Purdue University School of Veterinary Medicine.

Contributor's Morphologic Diagnosis: Skin of ear (pinna); Dermatitis, eosinophilic with marked epidermal hyperplasia, hyperkeratosis, intracorneal abscesses, and numerous intracorneal mites morphologically consistent with *Sarcoptes scabiei*.

Contributor's Comment: Mange was apparently introduced to the farm with a shipment of grower pigs approximately 6 months prior to the submission of this pig. During that time, all areas of production (farrowing, nursery, grower, and finisher) became infested. Two clinical forms of mange are recognized.[1] A large percentage of pigs on this farm had either the hyperkeratotic form of mange as seen in these slides or the immediate hypersensitivity form with reddened skin and papules. Populations of mixed bacteria, mainly coccoid bacteria, within stratum corneum were considered either incidental or minimally contributing to the lesion.

AFIP Diagnosis: Haired skin, pinna: Dermatitis, eosinophilic and proliferative, subacute, diffuse, marked, with parakeratotic hyperkeratosis and intracorneal mites, large white cross, porcine.

Conference Comment: Other diseases in pigs that produce hyperkeratotic lesions include porcine juvenile pustular psoriasiform dermatitis, exudative epidermitis caused by *Staphylococcus hyicus*, and zinc-responsive parakeratosis.

Porcine juvenile pustular psoriasiform dermatitis is also known as pityriasis rosea or pseudoringworm and is a non-contagious, self-limiting disease of weanling pigs. The cause is unknown but a hereditary component has been proposed. Gross lesions are symmetrical, sharply defined, raised red plaques on the ventral abdomen or medial thighs. The lesions heal from the center outward so the skin in the center is normal and is surrounded by a zone of elevated erythematous skin and scales, forming targetoid lesions. These ring lesions often coalesce to form mosaic or serpiginous patterns. Microscopically, there is prominent parakeratotic hyperkeratosis, superficial eosinophilic and neutrophilic perivascular dermatitis, and psoriasiform epidermal hyperplasia.[2]

Exudative epidermitis, also known as greasy pig disease, is caused by *Staphylococcus hyicus* and is an acute, often fatal disease of suckling piglets. Grossly, there are focal cutaneous erosions around the head (eyes, ears, snout, and lips) that spread to the extremities, ventral thorax, and abdomen. A characteristic thick, yellow-brown greasy exudate covers affected erythematous areas and the piglets succumb to severe protein and electrolyte imbalance. Microscopically, there is a thick parakeratotic and orthokeratotic crust, suppurative folliculitis, subcorneal pustules in the epidermis and outer root sheath of hair follicles, and epidermal hyperplasia.[2]

Zinc deficiency causes marked parakeratotic hyperkeratosis, epidermal hyperplasia, and eosinophilic and lymphocytic perivasculitis. Grossly, symmetrical, erythematous macules on the ventral abdomen, medial thighs, face, scrotum, and tail progress to papules covered with a thick, dry crust that forms cracks and fissures.[2]

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CASE II - 03-5830-02 (AFIP 2888625)

Signalment: Seven-week-old female crossbred German Shepherd Dog (*Canis familiaris*).

History: This dog was from an animal shelter; it was one of two that died with respiratory distress. A third dog in the same facility with similar signs and swollen cervical lymph nodes recovered after hospitalization.

Gross Pathology: The liver was yellow and swollen to approximately twice the normal size. Fine yellow strands of tissue (fibrin) were loosely adherent to the capsule. A finely mottled tan and red-brown pattern extended throughout the hepatic parenchyma. The colonic serosa was covered by blotchy red foci of hyperemia and congestion. The colonic lymph nodes were enlarged and swollen with a reddened, wet medullary region.

Laboratory Results: Immunohistochemical staining for canine adenovirus antigen performed on sections of formalin-fixed liver and kidney was positive (Prairie Diagnostic Services, Saskatoon, SK Canada)[1].

Contributor's Morphologic Diagnoses:
1. Liver: Necrosis, hepatocellular, multifocal and coalescent, acute, severe with intranuclear inclusion bodies, etiology consistent with canine adenovirus -1.
2. Kidney: Intranuclear inclusion bodies, glomerular endothelium, few.

Contributor's Comment: Liver sections contain random, multicentric and coalescing foci of coagulative necrosis of hepatocytes involving at least 50% of the parenchyma. Necrotic hepatocytes have pale eosinophilic cytoplasm and pyknotic or karyorrhectic nuclei. There are necrotic Kupffer cells scattered throughout these foci as well. Small to moderate numbers of hepatocytes contain eosinophilic intranuclear inclusions with a bluish tint that fill affected nuclei.

In sections of kidney, intranuclear inclusions are present in endothelial cells of small numbers of glomeruli. Chromatin is clumped against the inner aspects of nuclear membranes in nuclei with inclusions. Some sections of kidney may not have this change.

Infectious canine hepatitis is a ubiquitous disease of canids. Signs may include abdominal pain, high fever, vomiting, melena, ecchymotic hemorrhages and icterus[2]. The cause is canine adenovirus-1, a member of the genus Mastadenoviridae[3]. The virus's tropism for endothelium, mesothelium, and hepatic parenchyma is grossly evident as edematous and hemorrhagic tonsillar and cervical lymph nodes, blotchy serosal hemorrhages, edematous gallbladder, and enlarged yellow liver with capsular fibrin[2]. A later sequela routinely seen is corneal edema thought to be associated with hypersensitivity to viral antigen[4]. Gross lesions of other organs are inconsistent and linked to endothelial damage. After oral exposure, viral replication occurs in the tonsils

and cervical lymph nodes followed by viremia with ensuing hepatic, renal, ocular, and endothelial lesions. Histologically, the yet unexplained periacinar necrosis resembles the zonal necrosis associated with acute hepatotoxicity. Severe lesions and death are rare (it is thought that most dogs are exposed by two years of age with unapparent signs). Usually the viral cytotoxic effect on hepatocytes is self-limiting and limited to periacinar regions with rapid regeneration on the intact reticulin matrix.

AFIP Diagnoses:
1. Liver: Necrosis, centrilobular and midzonal, diffuse, with intranuclear inclusion bodies, German Shepherd Dog, canine.
2. Kidney, glomeruli: Intranuclear inclusion bodies.

Conference Comment: There is wide variation among slides in the number of intranuclear inclusion bodies present within the glomeruli.

In addition to canine adenovirus type 1, important adenoviruses of animals include canine adenovirus type 2, equine adenovirus type 1, avian adenovirus type 1, and avian adenovirus type 2 in pheasants and in turkeys.[5]

Canine adenovirus type 2 is one of the etiologic agents of canine infectious tracheobronchitis. It causes necrotizing bronchiolitis with intranuclear inclusion bodies in bronchiolar epithelium. Most cases of canine adenovirus type 2 are secondary to immunosuppression, most often caused by canine distemper virus.[5]

Equine adenovirus type 1 causes disease in Arabian foals with severe combined immunodeficiency. Histologic lesions include a severe necrotizing (early) to proliferative (late) bronchiolitis with intranuclear inclusion bodies in bronchiolar epithelium and widespread atelectasis.[5]

Avian adenovirus type 1 causes inclusion body hepatitis in birds and is associated with hydropericardium syndrome of chickens. Co-infection with other viruses or immunosuppression may play a role in severity of adenovirus-induced lesions. Infection with avian adenovirus type 1 causes hepatocellular degeneration and necrosis and intranuclear inclusion bodies within hepatocytes.[6]

Avian adenovirus type 2 causes marble spleen disease in pheasants and hemorrhagic enteritis in turkeys. Lesions of marble spleen disease and hemorrhagic enteritis include splenic hyperplasia of white pulp, lymphoid necrosis, and intranuclear inclusion bodies within lymphoreticular cells. In addition, hemorrhagic enteritis is characterized by intestinal mucosal congestion, sloughing of mucosal epithelial cells, and hemorrhage in the villous tips.[7]

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CASE III – 78105-N (AFIP 2889974)

Signalment: 4-month-old, male, Aberdeen-Angus, *Bos taurus*, bovine.

History: The calf presented to the Large Animal Clinic with neurologic signs. On physical exam, the calf demonstrated a staggering gait and nystagmus. The body temperature was 104^{O}F, with normal respirations and pulse.

Possible diagnoses of polioencephalomalacia, trauma, infection with *Haemophilus somnus*, rabies virus, or *Listeria monocytogenes,* or lead intoxication were considered, and therapy with thiamine HCl was initiated. The body temperature returned to 101.1^{O}F. Neurologic signs progressed over the next day to include head pressing and depression, followed by sternal recumbency. The animal did not respond to the therapy (which had been expanded to include dexamethasone and florfenicol) and was euthanized.

Gross Pathology: The fourth ventricle is filled and the cerebellar vermis is compressed and partially replaced by an approximately 6 cm x 5 cm x 4 cm mass that appears to arise from the anterior aspect of the cerebellum (Fig 1). The mass also causes compression of the brainstem and occipital lobe of the cerebrum. The mass is very soft and gray-tan, with red mottling. The lateral ventricles are moderately dilated (internal hydrocephalus).

Laboratory Results: Cerebrospinal fluid obtained soon after presentation to the clinic was examined and the results include:

Red blood cell count	250/ml
White blood cell count	6/ml
Color/transparency	Colorless and clear
Protein	31.6 mg/dL
Cytology:	
2% segs	
40% lymphocytes	
48% monocytes	
No evidence of abnormal cells	

The serum lead level was within normal limits.

Contributor's Morphologic Diagnosis: Cerebellum and brainstem: Medulloblastoma, with cerebellar and brainstem compression.

Contributor's Comment: In the presented case, the cerebellum and brainstem are compressed by an expansile, soft to gelatinous, gray-tan mass, consistent with origination of the tumor in the cerebellum. Examination of a Diff-Qwik-stained touch impression of the cut surface of the mass is densely cellular and reveals a single population of pleomorphic cells with indistinct cell borders, scant, pale eosinophilic cytoplasm, and a large round to ovoid nucleus with an occasional nucleolus. Fibrillary processes occasionally extend from cells. Anisocytosis and anisokaryosis are present.

Histologically, sections of cerebellum or brainstem contain a non-encapsulated mass composed of sheets of a single, monomorphic population of variably densely packed, round to polygonal cells that infiltrate into and replace a portion of the cerebellum, and extend into the fourth ventricle, with extension to the leptomeninges of the brainstem. In areas of low cellularity, abundant fibrillar, eosinophilic cell processes separate cell groups, forming rhythmic palisades of neoplastic cells and fibrillar material. Cells often palisade around small blood vessels (pseudorosettes) and occasionally form vague, fibrillar (Homer Wright) rosettes. Individual cells have indistinct cell borders, a scant to moderately abundant amount of pale, eosinophilic, homogeneous cytoplasm, and an oval, darkly basophilic nucleus (abundant heterochromatin), sometimes with 1-2 basophilic nucleoli. Anisocytosis and anisokaryosis are moderate. Mitotic figures are 3-5 per 400X field. Areas of necrosis are present. Immunohistochemical staining reveals that the neoplastic cells are strongly positive for S-100 and faintly positive for synaptophysin, especially in the fibrillar areas of the tumor. Neoplastic cells are negative for neuron-specific enolase and glial acid fibrillary protein. Scattered endothelial cell (Factor VIII-positive) proliferation is present, resulting in multifocal thickening of capillary walls within the mass. The adjacent cerebellar folia and subjacent brainstem are compressed, with loss of Purkinje and granular layer cells in the cerebellum, and axonal and mild neuronal degeneration in the brainstem.

The clinical presentation and the gross, cytologic, and histologic lesions described here are typical of a medulloblastoma. Medulloblastomas are a type of malignant, primitive neuroectodermal tumor (PNET) that originate in the cerebellum, usually in young animals and, more commonly, in children.[1,2,3,4] Other PNETs are not histologically distinguishable from medulloblastomas, and are found in locations other than the cerebellum.

Embryonal nervous system tumors described as PNETs are believed to arise from progenitor cells that can differentiate along various cell lineages, including neuronal, glial, ependymal, and perhaps mesenchymal.[1,3] Medulloblastomas are thought to be derived from pluripotent cells of the external germinal cell layer or perhaps are derived from more than one cell type.[3,4] A number of genetic alterations have been identified in human medulloblastomas, including alterations in *hedgehog*, neurotrophin, ErbB receptor, and *Wnt* signal transduction pathways.

The macroscopic and microscopic features typical of medulloblastomas reflect features observed in this case. In addition to the pseudorosettes and Homer Wright rosettes observed in the presented case, Flexner-Wintersteiner-like rosettes have been reported in medulloblastomas of domestic animals.[1] Homer Wright rosettes are sometimes absent or poorly formed in medulloblastomas of humans.[5] The presence of carrot-shaped nuclei is a commonly described feature in medulloblastomas of humans, but poor tissue handling may cause compression of the nuclei of neoplastic lymphocytes, mimicking the nuclei of medulloblastomas.[5] The rhythmic palisading of nuclei and fibrils is observed not only in some human medulloblastomas, but also in several types of gliomas.[5]

Immunohistochemical staining of medulloblastomas in humans reveals consistent expression of synaptophysin.[5] Other reagents useful for the identification of medulloblastomas in humans include antibodies directed to GFAP, neurofilaments, protein gene product 9.5, and S-100.[5]

Ultrastructural examination of medulloblastomas should reveal features of embryonal neuronal cells: microtubules, scant intermediate filaments, and dense core granules.[1] Examination by electron microscopy of the presented case was not performed.

In human patients with cerebellar neoplasia, the differential diagnoses of small cell carcinoma and lymphoma are entertained. The presence of fibrillar cell processes and Homer Wright rosettes are important in the identification of medulloblastomas, and the lack of cytokeratin and CD3 expression aid in refuting carcinoma and lymphoma, respectively.

AFIP Diagnosis: Cerebellum: Medulloblastoma, Aberdeen-Angus, bovine.

Conference Comment: The contributor gives a concise overview of the features of this neoplasm. Some sections contained only brainstem. Without a section of cerebellum, the most specific diagnosis would be primitive neuroectodermal tumor (PNET).

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CASE IV - 1778 (AFIP 2887457)

Signalment: Seven-day-old Standardbred foal.

History: At four days of age, the foal experienced acute onset of progressive respiratory disease, unresponsive to antibiotic treatment. No other horses on the premises exhibited signs of respiratory disease prior to, during, or following the illness. The foal and mare were turned out daily with a mature Quarter Horse, which had recently returned from another farm with an unknown history.

Gross Pathology: The lungs failed to collapse, were edematous with stable tracheal froth and exhibited generalized reddish discolouration with scattered foci of tan mottling. All lung lobes were rubbery with small, firm, randomly situated nodules throughout. The bronchial lymph nodes were enlarged, wet, and mottled tan and red on cut surface. There was moderate mediastinal edema.

Laboratory Results: Serum immunoglobulin G levels measured 1100 mg/100 ml. Routine bacterial culture of the lung was negative. Cultures for equine herpes virus type 1 and adenovirus were negative. Influenza A was identified by egg inoculation and PCR analysis of lung tissue (pooled influenza A antigens). Immunohistochemistry demonstrated positive staining for influenza A antigen in the epithelium of terminal

bronchioles. The influenza virus isolated from the foal showed hemagglutination-inhibition with A2 (1:80) and A1 (1:20) equine flu subtypes using reference antisera for A2/Miami/63 and A1/Prague/56. Genetic analysis by nucleotide sequencing determined that the strain was most closely related phylogenetically to A2/Kentucky/97.

Contributor's Morphologic Diagnosis: Bronchointerstitial pneumonia, acute, necrotizing, with hemorrhage and hyaline membranes. Etiology - Equine Influenza A2.

Contributor's Comment: Influenza virus is a common cause of non-fatal respiratory disease in horses. The disease most often presents as outbreaks in susceptible horses following exposure to individuals that are shedding virus. Death can occur either as a result of secondary bacterial bronchopneumonia or severe viral infection[1].

Bronchointerstitial pneumonia in foals less than one week of age is considered uncommon. The peak occurrence of bronchointerstitial pneumonia at 1.5 to 2.5 months of age coincides with declining maternally-derived immunoglobulins, implying that passive immunity is protective in younger foals[2].

Equine bronchointerstitial pneumonia is considered to be primarily of viral etiology[2]. This condition has been reported as a sporadic cause of death in foals[2] but definitive etiological diagnosis of these cases has proven frustrating. Early clearance of virus with sloughed necrotic bronchiolar epithelium may render identification attempts futile by the time the lung lesion has progressed to regenerative epithelial hyperplasia and secondary bacterial pneumonia[3]. In the early stage of bronchiolar necrosis, influenza A antigen is more readily identified[3]. The presence of active bronchiolar epithelial necrosis in this case likely facilitated viral isolation and identification.

AFIP Diagnosis: Lung: Pneumonia, bronchointerstitial, necrotizing, acute, multifocal to coalescing, moderate, with hemorrhage and hyaline membranes, Standardbred, equine.

Conference Comment: Equine influenza is caused by infection with one of the virus subtypes, influenza A/equine-1 (H7N7) or influenza A/equine-2 (H3N8). The glycoproteins hemagglutinin and neuraminidase are surface antigens on the virus envelope. An antigenic drift occurs when there are point mutations in the gene coding for a surface antigen. Antigenic shift occurs when there is genetic reassortment between the two subtypes, resulting in a new subtype with completely different antigenicity. Antigenic drift of the H3N8 strain, such as that isolated in this case, has created subgroups of the virus that contribute to epizootics in equine populations.[4,5]

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