**Pathology in Practice**

In collaboration with the American College of Veterinary Pathologists

**History**

A 2-year-old 2.9-kg female domestic turkey (*Meleagris gallopavo*) with a history of weight loss and blindness of unknown duration died and was then submitted for postmortem examination. Other birds from the same backyard flock were not reported to have been sick or to have had any abnormal clinical signs.

**Clinical and Gross Findings**

The turkey was in thin nutritional condition. A raised, immovable cutaneous nodule (2.5 X 2.0 X 2.0 cm) was present above the left orbit, with multiple smaller cutaneous nodules on the neck (Figure 1). On cut surface, the nodules were white to pale tan and contained soft, homogenous, material that dissected into the underlying subcutis, skeletal muscles, and orbital spaces. A raised, ulcerated mass was present on the third digit of the left limb at the base of the nail. The snood and neck were multifocally ulcerated and covered with a dark-red to yellow, dry crusted material that also covered both nares. Necropsy of the bird revealed a raised white nodule (1.5 X 1.5 X 0.5 cm) on the surface of the liver that extended into the parenchyma. A pale-tan nodule (0.5 X 1.0 X 1.5 cm) was present on the cranial pole of the right kidney. No other meaningful gross abnormalities were noted.

Formulate differential diagnoses, then continue reading.

**Histopathologic and Laboratory Findings**

Histologically, the nodules on the head and neck consisted of variably demarcated, expansile, and infiltrative, densely cellular dermal and epidermal neoplasms composed of round cells arranged in solid sheets and supported by fine fibrovascular stroma (Figure 2). The neoplastic cells had distinct cell borders with scant to moderate amounts of homogenous, lightly eosinophilic cytoplasm. The nuclei were round to oval and were located centrally to paracentrally with coarsely clumped to condensed chromatin and inconspicuous nucleoli. Anisokaryosis and anisocytosis were moderate, and mitotic figures were rare (0 or 1 mitotic figure/hpf [400X]). Neoplastic cells infiltrated skeletal muscle and vessel walls. There were multifocal areas of necrosis scattered throughout the masses. The epidermis overlying the masses was often ulcerated, and the exposed dermis was covered with a serocellular crust admixed with degenerate heterophils. Numerous short bacillary bacterial colonies and degenerate heterophils were embedded within the crust. The nasal passages, skull, and major structures of both eyes including the retina, ciliary body, choroid, sclera, conjunctiva, and periorbital connective tissue were also infiltrated by neoplastic cells. Similarly, the heart, great vessels,

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crop, cerebrum, lung, liver, kidney, right abdominal air sac, thyroid glands, thymus, pancreas, peripancreatic mesenteric adipose tissue, spleen, small intestine, and large intestine were variably infiltrated by neoplastic cells. Neoplastic cells revealed immunoreactivity for cluster of differentiation 3 (CD3), a T-cell marker (nuclear and cytoplasmic staining).

Results were negative for PCR assays for lymphoproliferative disease virus (LPDV) and reticuloendotheliosis virus (REV) performed on thymus, spleen, heart, lung, and liver samples; and PCR assays for Marek disease virus (MDV) performed on liver and spleen samples. *Escherichia coli* and *Pseudomonas aeruginosa* were isolated from the air sacs, facial mass, and nose, and *E. coli* was also isolated from the lung. The air sacs had histologic evidence of inflammation, and bilateral crusted material was grossly observed in both nares. There was no histologic evidence of inflammation of the nasal mucosa or the lungs, only the presence of lymphoid neoplastic cells. Coccidial organisms were not observed microscopically in the intestines, but were detected in the contents of the colon through fecal flotation.

**Morphologic Diagnosis and Case Summary**

Morphologic diagnosis: multicentric T-cell lymphoma.

Case summary: spontaneous multicentric T-cell lymphoma in a domestic turkey.

**Comments**

Viral-induced neoplasms are not uncommon in domestic poultry, including turkeys. Clinical signs are nonspecific but can include anorexia and lethargy, as was observed in this case. Microscopically, neoplastic proliferation of lymphoid cells often disrupts and infiltrates the normal architecture in multiple organs. The neoplastic cells can also manifest as nodules that cover featherless skin or that are found within the upper respiratory and digestive tracts. Skin nodules caused by avian pox virus or LPDV are difficult to distinguish grossly, but avian pox can be differentiated histologically by the presence of epidermal hyperplasia, ballooning degeneration, and eosinophilic, intracytoplasmic inclusion bodies (Bollinger bodies).

In turkeys, LPDV and REV are the most commonly reported oncogenic retroviruses associated with neoplasms, and MDV, which is the oncogenic herpesvirus (Gallid alphaherpesvirus 2) is less likely. The immunoreactivity to CD3 indicated T-cell lymphoma in this case. T-cell lymphomas have been reported in turkeys associated with oncogenic viruses including LPDV, REV, and MDV. In this case, a virus associated with neoplasia was not detected, but because false-negative results can occur with any PCR-based testing, viral involvement cannot be ruled out completely. However, the absence of detection of a virus in this case suggested that a spontaneous, noninfectious neoplastic process must be considered. Immunohistochemistry for virus antigens, such as Meq protein for Marek disease, would further strengthen the diagnosis. Avian leukosis virus is another oncogenic retrovirus that causes lymphoid, erythroid, or myeloid leukemia, alone or in combination, but was not considered in this case as lymphoma has not been reported in turkey populations and is associated with B-cell lymphomas rather than T-cell lymphomas. Turkey herpesvirus coinfection with LPDV was detected from a free-ranging turkey with multicentric neoplasia with morphology consistent with myeloid origin. Turkey herpesvirus was not tested for in this case; it is a nononcogenic virus and its use in vaccination is associated with reduced development of lymphoma in Marek disease in chickens. LPDV is an oncogenic C-type retrovirus that has been found in both wild and domestic turkeys. Historically a disease limited...
to Europe and Israel, LPDV was detected in United States’ wild turkey populations in 2009. Since that first report, LPDV has been isolated in wild turkeys throughout the United States, but clinical disease is thought to be uncommon. The method of transmission of retroviruses associated with neoplasia in wild turkeys is not known, but is suspected potentially to be vector borne. The method of transmission of retroviruses associated with neoplasia in wild turkeys is not known, but is suspected potentially to be vector borne. The method of transmission of retroviruses associated with neoplasia in wild turkeys is not known, but is suspected potentially to be vector borne. LPDV has been demonstrated to infect both turkeys and chickens experimentally, but natural LPDV infection has been reported only in turkeys. Histologically, lymphoproliferative disease is characterized by a pleomorphic infiltration of lymphocytes in different organs. The spleen, thymus, liver, and pancreas are affected most commonly, although other organ systems, including skin, can also be affected. Confirmation of LPDV infection can be determined through PCR assay, which is reported to have high specificity and sensitivity when performed on samples of either whole blood, buffy coat, or bone marrow. REV is another oncogenic C-type retrovirus that can cause acute reticular or chronic lymphoid neoplasia in a variety of avian species, including turkeys. Natural outbreaks are not common, economic losses are minimal, and disease is rarely reported in commercial flocks in the United States. Horizontal or vertical transmission can occur. Mosquitoes from the genus Culex, insects from the genera Musca and Triatoma, and ticks from the genus Ornithodoros potentially play a role in spreading REV; however, further studies are needed to prove their role in transmission of the disease. Chronic lymphoid neoplasms and acute reticuloendothelial neoplasia are the major histopathologic findings. The ability to differentiate REV from other viral-induced neoplasia is difficult, which is why virus detection is the gold standard test. The virus can be detected through serology for antibodies, virus isolation, or PCR assay. The presence of systemic neoplasia in the turkey in this report likely caused immunosuppression, leading to secondary bacterial infections in a similar pathogenesis of Marek disease. Bacteria were isolated from the air sacs, lungs, and nasal passages, and an airsacculitis was confirmed histologically. Evidence of pneumonia or rhinitis was not observed microscopically. The presence of crusted material from the nares was suggestive of rhinitis, and histologic evidence of inflammation may have been masked by the marked presence of infiltrative neoplastic round cells. The lung parenchyma was less affected by the neoplastic round cells than the nasal passages, so the absence of histologic inflammation suggests the E coli isolated was a result of possible contamination during processing. In addition to cachexia from neoplasia and potential behavioral changes in accessing and eating food from the associated blindness and likely also olfactory changes, the bacterial infection likely played a role in the poor body condition in this case. The importance of coccidia identified on fecal flotation was unknown, as intestinal disease resulting from coccidiosis was not observed microscopically, but subclinical coccidial infection has been documented to affect weight gain negatively. Viral-induced neoplastic processes in poultry cause more economic losses than spontaneous, non-infectious causes, which is why identification of a viral agent is important in maintaining flock health in commercial operations. Spontaneous, systemic round cell tumors occur in older turkeys, but are not a common cause of death. If an operation reports an increased number of turkey deaths, further diagnostic procedures are warranted to rule out a viral agent. Cases of viral-induced neoplasia are rarely reported in backyard poultry, but they may be underdiagnosed because full workups, including retroviral testing, are not always pursued. Clinicians should be aware of viral-induced and spontaneous neoplasms as causes of nonspecific clinical signs and skin lesions in domestic backyard turkeys.

References