

2017 Northeastern Veterinary Pathology Conference

NEVPC CASE 15

IDENTIFICATION NUMBER ON SOURCE MATERIAL: 4042413-02

SIGNALMENT: 6-year-old male German shepherd military working dog

HISTORY: This dog presented for acute onset of depression and lethargy. Generalized severe lymphadenopathy was diagnosed clinically and radiographically. A fine needle aspirate of an unspecified lymph node revealed a monomorphic population of small to medium lymphocytes with occasional mitoses. Clinical pathology results included leukocytosis with neutrophilia, high numbers of circulating abnormal lymphocytes, thrombocytopenia, elevated alkaline phosphatase, hyperbilirubinemia, hyperphosphatemia, hypoglycemia and mild azotemia. Despite corticosteroid and antibiotic therapy, the dog presented the next day weak and unable to stand and humane euthanasia was elected.

GROSS FINDINGS: Generalized lymphadenopathy; 0.5 liters of serosanguineous fluid in an unspecified body cavity; widespread serosal petechiation.

HISTOPATHOLOGIC FINDINGS:

Liver: Diffusely throughout the section, effacing portal areas, filling sinusoids (especially subcapsular), and compressing hepatic cords there is an unencapsulated, densely cellular, infiltrative neoplasm composed of sheets of round cells on a pre-existent stroma. Neoplastic lymphocytes have distinct cell borders, a scant amount of eosinophilic cytoplasm, prominent irregularly round nuclei with coarse chromatin and variably distinct nucleoli. Anisocytosis and anisokaryosis are moderate. Mitoses average 2-3 per high power field. There is frequent apoptosis of neoplastic lymphocytes with low numbers of tingible body macrophages present throughout the neoplasm. Remaining hepatocytes are often compressed and atrophic. Sinusoids are diffusely congested, there are multifocal small aggregates of hemosiderin laden macrophages, and there is moderate to severe edema.

Lung: Multifocally throughout the section, alveolar capillaries and pulmonary venules contain neoplastic lymphocytes which are often necrotic (lymphocytolysis) and admixed with cellular debris, variably-sized globules of basophilic aggregated protein (DNA emboli), hemorrhage, fibrin and edema.

Immunohistochemistry: Non-contributory

A bone marrow aspirate (not submitted) was hypercellular with effacement and replacement of normal myeloid, erythroid and thrombocytic precursors by a population of similar neoplastic lymphocytes, admixed with numerous apoptotic bodies.

MORPHOLOGIC/ETIOLOGIC DIAGNOSIS:

1. Lung: Lymphoma, with acute necrosis (acute tumor lysis syndrome).
2. Liver: Lymphoma.

DISCUSSION: Malignant lymphoma is the most common hemolymphatic neoplasm in dogs and is the most common canine malignancy treated by chemotherapy.¹² In this case, most of the neoplastic lymphocytes in the lung are lysed, and there are multifocal intravascular accumulations of nuclear material and cellular debris. These microscopic features in combination with laboratory abnormalities (hyperphosphatemia and mild azotemia) are consistent with a condition known as acute tumor lysis syndrome (ATLS).³

In human medicine, ATLS is typically associated with rapidly proliferating neoplasms such as high-grade lymphomas and acute leukemias; it may occur spontaneously or it may be associated with chemotherapy, radiotherapy, or steroid treatment.^{4,10} ATLS is characterized by widespread lysis of neoplastic cells which leads to release of intracellular components, such as nucleic acids, potassium, and phosphorous. These are subsequently metabolized into hypoxanthine, xanthine, and eventually uric acid.⁴ When these breakdown products overwhelm normal homeostatic mechanisms they can produce an acute metabolic crisis; ATLS has been associated with acute renal failure, cardiac arrhythmias, neurologic perturbations, metabolic acidosis and DIC.¹⁰ Specific metabolic derangements include hyperuricemia, hyperkalemia, hyperphosphatemia, hypocalcemia and azotemia.^{1,10} Predisposing conditions include chronic renal insufficiency, oliguria, dehydration, hypotension, and acidic urine.⁴ The microscopic lesions associated with ATLS in humans are largely unknown because of the relatively few clinical cases and low rate of mortality.³

Clinically significant ATLS is rarely reported in animals. This may be related to the fact that in most mammals (other than primates) uricase enzymes rapidly degrade excess uric acids to allantoin, which prevents the development of hyperuricemia; however, the other metabolic derangements occur as reported above. When ATLS does occur, it tends to be associated with lymphoid malignancies, as in this case. Malignant lymphocytes contain approximately 4 times the phosphorus of normal lymphocytes due to increased nucleic acid and ATP requirements.¹² Microscopically, most case reports describe microthromboemboli of chromatin, cellular debris, fibrin, and entrapped erythrocytes and malignant cells within blood vessels of multiple organs (especially the lungs and kidneys).^{3,6,9,10} ATLS is most commonly reported in mice with disseminated lymphoma (typically with a large tumor burden and leukemic component) and has been associated with a spontaneous death due to multiple thromboemboli.^{6,10,13} There is one case report in a cat with FeLV-associated lymphoma,² and another report in a Lipizzaner mare with mesothelioma.⁵ To date, all of the confirmed cases in dogs have been associated with lymphoma, often following chemotherapy.⁸ There is also a report of allantoin crystalluria in a dog with acute monocytic or myelomonocytic leukemia, which the authors speculate may have been related to tumor lysis syndrome.⁷

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