Diagnostic Exercise
From The Davis-Thompson Foundation*

Case :**257**; Month: **March**; Year: **2025**
Answer sheet

Title: Acute Tubular Injury from oleander (*Nerium oleander*) toxicosis in an alpaca.

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Clinical History: A 2-year-old, alpaca macho was presented to the Texas A&M Large Animal Teaching Hospital with bradycardia, arrhythmia, dehydration, severe azotemia (BUN 260 mg/dl, creatinine 14.93 mg/dl), hyperphosphatemia (13.4 mg/dl), hypermagnesemia (3.4 mg/dl), mild hypokalemia (4.0 mg/dl), leukocytosis (32,500/ul) with neutrophilia (28,600/ul), acidemia, and low body condition score. The patient was placed on supportive treatment, but due to poor prognosis, the owner elected for euthanasia.

Gross Findings: Both kidneys were mottled pale tan to red **(Fig 1).** On cut surface, the cortices were pale and contained linear white areas **(Fig 2).**

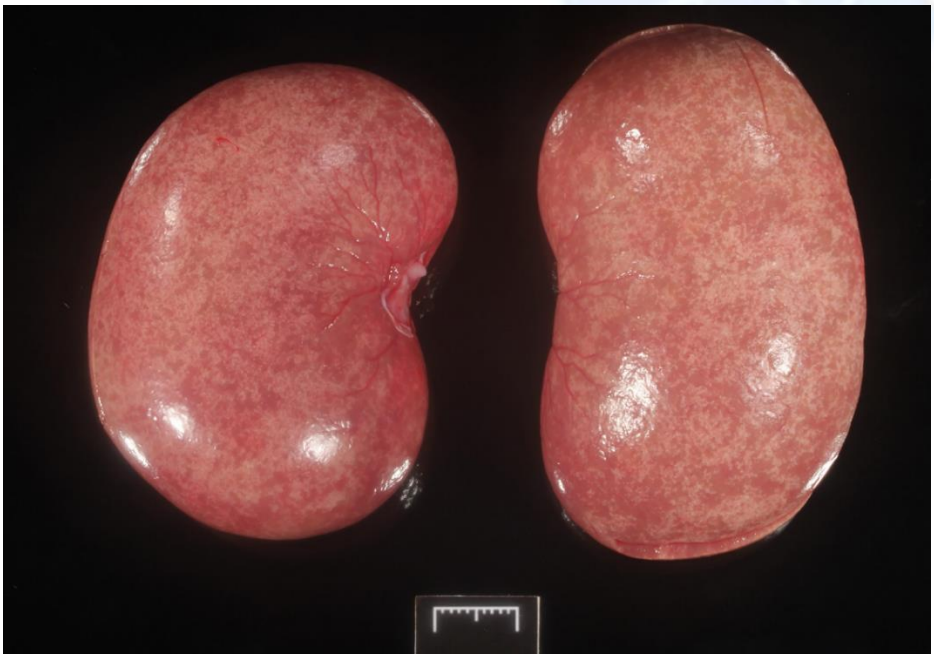

Figure 1. The capsular surface of both kidneys are mottled pale tan to red.

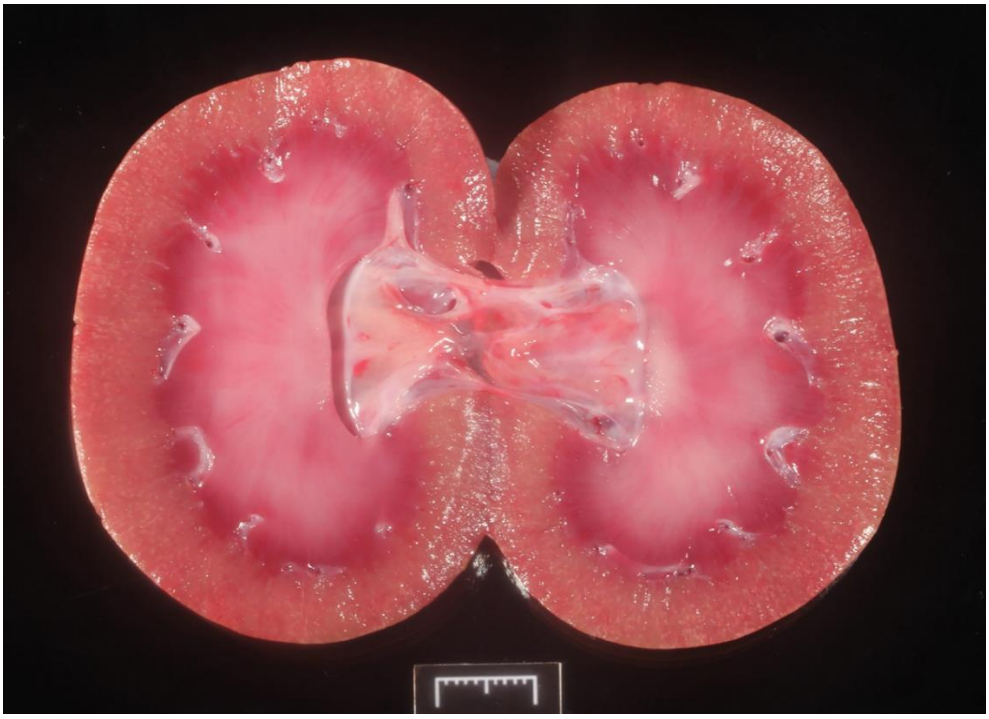

Figure 2. On cut surface, the cortices are pale tan with white foci throughout.

Microscopic description:

Kidney: Approximately 75% of the renal tubules exhibit marked tubular degeneration with attenuated epithelium and a dilated lumen (simplification) (**Fig 3**) that often contain cellular debris (granular cast) (**Fig 4**), and less commonly homogeneous, eosinophilic material (proteinosis), or basophilic, granular material (mineral). Multifocally, tubular epithelial cells often exhibit one of the following: swollen with excessive, hypereosinophilic cytoplasm (degeneration), shrunken with pyknotic nuclei (necrosis), and increased cytoplasmic basophilia and nuclear hypertrophy with occasional mitotic figures (regeneration).

Immunohistochemistry for pancytokeratin indicates positive labeling of intact distal tubular epithelial cells.The intact and affected proximal tubules with a few remaining tubuloepithelial cells are pancytokeratin negative.

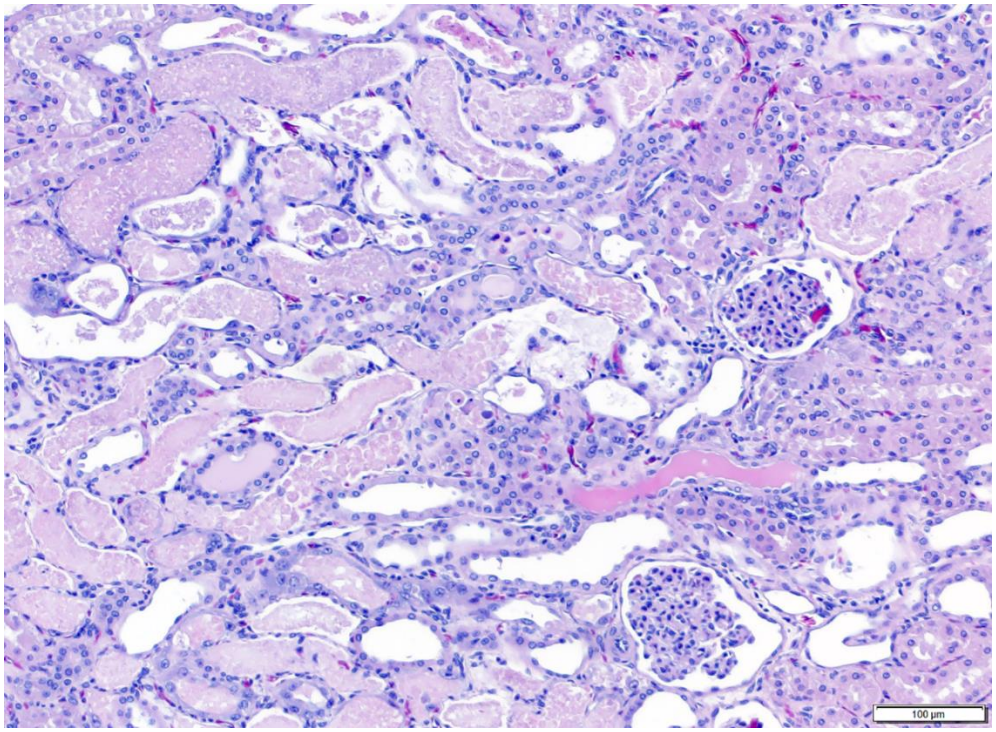

Figure 3. Tubular simplification with degeneration and necrosis of the tubuloepithelial cells with intraluminal granular casts. Occasionally, tubular proteinosis is observed. H&E stain.

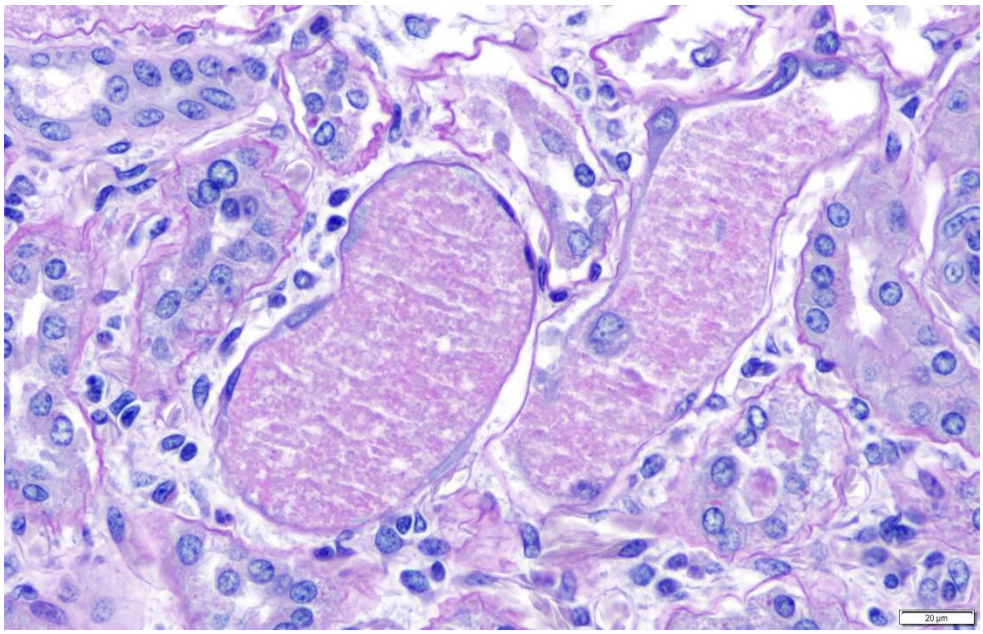

Figure 4. Most of the proximal renal tubules in the cortex are degenerated and necrotic with intraluminal granular casts and intact tubular basement membranes. PAS stain.

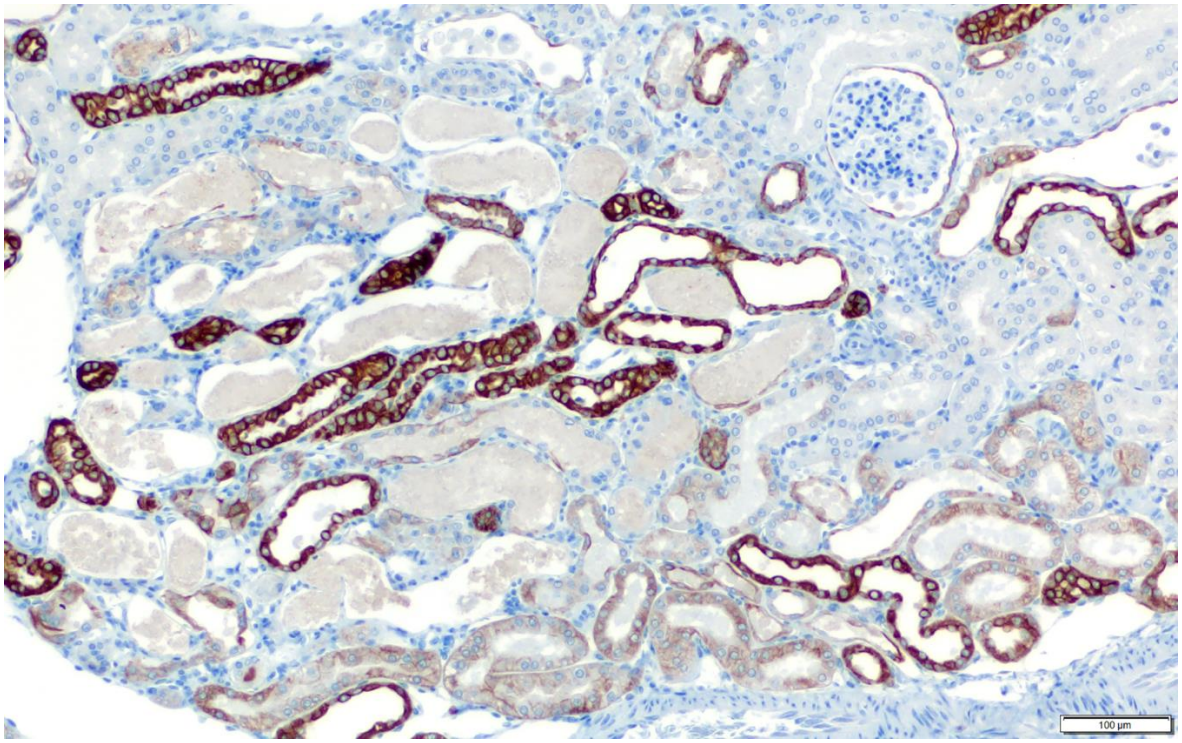

Figure 5. Immunohistochemistry for pancytokeratin in the renal cortex highlights intact strongly positive distal renal tubules.

Morphologic diagnosis:

Kidney: Marked, acute, multifocal, tubular degeneration, simplification, and necrosis with marked granular casts, mild tubular proteinosis and mineralization.

Potential causes: The findings are consistent with acute kidney injury with marked tubular degeneration and necrosis. *Leptospira* spp. rtPCR was negative. A nephrotoxin was therefore suspected.

Toxicology results: Toxicology evaluation of C1 contents revealed microscopic fragments of oleander.

Final diagnosis: Oleander toxicosis.

Discussion:

Oleander (*Nerium oleander*) is a well-known toxic plant of mainly ruminants, camelids, and horses. The most common route of exposure is accidental plant clippings incorporated into bales. As the plant dries, it loses its bitter taste, yet remains toxic. As little as 0.005% of an animal's body weight of dry leaves of oleander may be lethal. Oleander is a drought tolerant, evergreen shrub of the

Apocynaceae family, native to Europe, Africa, and Mediterranean Sea, and globally cultivated as an ornamental plant (1).

Typical signs of oleander toxicosis include a triad of simultaneous gastrointestinal tract, cardiac, and renal injury (1,2,3,4,5). Cardiomyocyte degeneration/necrosis is a reliable diagnostic marker for oleander toxicosis; however, this lesion may be subtle or hindered by autolysis (4). In this case, serous atrophy of fat was present within the coronary and interventricular sulci epicardial adipose tissue with no other significant histological cardiac findings. The definitive diagnosis of oleander exposure is confirmed by finding leaves in the gastrointestinal tract (5) and by testing serum, plasma, urine, liver, or gastrointestinal contents for oleandrin (1,4).

The toxic principles of oleander include cardenolides and triterpenoids. Cardenolides inhibit Na/K-ATPase in plasma membranes of cardiomyocytes. This results in increased intracellular sodium and extracellular potassium concentrations thus inhibiting downstream calcium efflux, altering the resting membrane potential causing hyperexcitability (1,3). Gastrointestinal lesions are associated with the irritant effects of triterpenoids saponins on the mucosa. Cardenolides may directly alter ATPase-dependent transporters in the renal tubules (4).

Acute tubular injury in oleander toxicosis mainly affects the proximal tubules due to their high metabolic rate and as a potential direct effect of oleandrin in the renal tubules (4). Despite 10% of the oleandrin is excreted by the kidney, it is likely the serum concentration of the toxicant plays a role in the development of acute kidney injury (4). The degree of acute tubular necrosis in this case may have exacerbated by dehydration, as the proximal convoluted tubules are most susceptible to renal ischemia.

References

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