Case #20
Slide #: 15-1943-5

Institution: North Carolina State University

Signalment: 7-year-old, castrated male Border Collie mix

History:
This dog was referred for progressive azotemia, fever, and right forelimb lameness. He had a 1.5 year history of chronic renal disease. On initial physical examination, he had distal limb edema and a painful, swollen right carpus. Serum chemistry was notable for azotemia (BUN 108mg/dL, Crt 11.0mg/dL), marked hyperamylasemia (21,260 IU/L), marked hyperlipasemia (36,980 IU/L), and mild panhypoproteinemia (Alb 2.2g/dL, Glob 1.6g/dL). In addition, he had a moderate normocytic normochromic nonregenerative anemia (PCV 25%), mature neutrophilia (11,564/UL) with regenerative left shift (503/UL bands), and thrombocytopenia (103,000/UL). Abdominal ultrasound showed bilateral severe chronic degenerative renal changes, scant peritoneal effusion, and hyperechoic mesentery. The patient received one hemodialysis treatment and promptly began to show signs of distributive shock characterized by tachycardia, refractory hypotension, hyperlactatemia (8.4 mmol/L), worsening peripheral edema, and acute pulmonary edema. In addition, he became febrile (104.1F) and neutropenic (1,486/UL) with a degenerative left shift (1,715/UL). A focused echocardiogram showed no evidence of valvular endocarditis. The patient was euthanized due to progressive respiratory dysfunction.

Gross findings:
There was marked peripheral edema, especially of the distal limbs. The carpal and tarsal synovial membranes were congested with a small amount of loosely adherent fibrin. Bilaterally, there were discrete areas of yellow-grey discoloration within the patellar fat. The pancreas was diffusely pale and slightly firm. Distributed throughout the omental adipose and mesoduodenum, there were multifocal flat, round, white, 4-8mm foci with a peripheral rim of hemorrhage. Similar foci were present within the epicardial adipose tissue along coronary grooves. The kidneys were bilaterally small and firm with an irregularly undulating cortex secondary to large areas of cortical atrophy. All lung lobes were diffusely dark pink to purple, failed to collapse, and oozed serosanguinous fluid on cut surface.

Histopathology:
Heart (slide 5): Within the epidcardial adipose tissue, there are multifocal large areas of coagulative necrosis characterized by loss of differential staining and retention of tissue architecture. Necrotic adipocytes are variably filled by amphophilic to basophilic finely granular material (calcification/saponification). Areas of adipocyte necrosis often track along coronary vessels and are sometimes bordered by mild hemorrhage and mild neutrophilic inflammation. Within the myocardium, there is rare individual myocyte mineralization.

*Similar areas of adipocyte necrosis with variable saponification and neutrophilic inflammation were observed within the omentum, mesoduodenum, patellar fat pad, synovium (right tarsus), and periarticular skin (right carpus).

Relevant Morphologic Diagnoses:
Heart, omentum, mesoduodenum, patellar fat pad, synovium, haired skin: multifocal acute adipocyte necrosis with saponification and mild to marked suppurative inflammation

Pancreas: multifocal, mild, chronic fibrosis

Kidney: bilateral, severe, diffuse, chronic, lymphoplasmacytic interstitial nephritis with marked fibrosis and cortical atrophy

Discussion:
In this patient, the combination of severe pancreatic enzyme elevation and widespread adipocyte necrosis is consistent with Pancreatitis, Panniculitis, and Polyarthritis (PPP) syndrome, a rare condition described in both humans and animals. In humans, the primary causes of PPP are acute or chronic pancreatitis, pancreatic duct obstruction, and less commonly pancreatic acinar cell neoplasia. Suspected PPP has been reported in several dogs with pancreatitis or pancreatic neoplasia and one cat with pancreatic neoplasia. While the pathogenesis is not entirely understood, widespread adipocyte necrosis is thought to be triggered by systemic release of pancreatic enzymes (especially lipase) by the injured pancreatic tissue or pancreatic neoplasm. The most common sites of adipocyte necrosis include the panniculus, periarticular tissues, and bone marrow. Skin lesions are often papular to nodular and erythematous with variable draining tracts that ooze thick yellow oily material. Polyarthritis is thought to be the consequence of periarticular adipocyte necrosis, which releases high concentrations of free fatty acids into the synovial fluid. Radiographically, bone marrow lesions may appear as moth-eaten osteolysis. Panniculitis and polyarthritis often precede clinical signs of pancreatic disease, which complicates diagnosis. In humans, treatment is primarily supportive and dependent on the underlying cause of pancreatic disease. Variable success is reported with somatostatin analog therapy and plasmapheresis. The majority of veterinary cases are diagnosed on post mortem examination.

Given the absence of pancreatic neoplasia or active pancreatitis in this patient, we postulate that severe pancreatic enzyme elevation is the consequence of both chronic pancreatitis and reduced renal clearance of pancreatic enzymes due to end stage renal disease. To our knowledge, this is the first case of PPP with involvement of the epicardial adipose tissue. This case highlights the importance of PPP as a differential diagnosis for polyarthritis and panniculitis in the context of severe pancreatic enzyme elevation.

References
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