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Case report

Pathological Findings in a Captive Senile Western Lowland Gorilla (*Gorilla gorilla gorilla*) With Chronic Renal Failure and Septic Polyarthritis

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Abstract

A case of chronic renal failure associated with septic polyarthritis affecting a 39-year-old male Western lowland gorilla (*Gorilla gorilla gorilla*) is described. The gorilla developed a chronic interstitial nephritis associated with severe diffuse renal fibrosis, which was associated with several extra-renal uremic lesions, including uremic pneumopathy and gastropathy. Several joints presented gross and microscopic changes compatible with chronic active arthritis and athrosis, which were associated with inflammation of adjacent soft tissues. *Staphylococcus aureus* was cultured from sites of phlegmon and cellulitis, whereas *Enterobacter* sp. and *Proteus mirabilis* were cultured from osteoarticular lesions. Additional conditions, including testicular atrophy and leydigocytoma, a large cell lung carcinoma, calcinosis circunscripta, among others, have also been diagnosed in this senile gorilla.
Key Words: Western lowland gorilla, *Gorilla gorilla gorilla*, chronic renal failure, nephritis, arthritis.

Introduction

The Western lowland gorilla (*Gorilla gorilla gorilla*) belongs to the family Hominidae, which is divided into two subfamilies, namely Homininae that includes humans, gorillas, chimpanzees, and bonobos; and Ponginae that includes the orangutans. Free ranging Western lowland gorillas live in tropical rain forests in the equatorial Africa. Due to continuous habitat destruction it has become an endangered species, with an estimated population of less than 100,000 individuals (7). Therefore, maintenance of gorillas in captivity is currently an important approach for conservation. Importantly, the amount of information regarding diseases that affect this species is extremely scarce in the scientific literature.

Considering the scarcity of published clinical and pathological information on great apes, particularly in gorillas, the aim of this report is to describe the clinical history and pathological findings in a case of chronic renal failure and bacterial polyarthritis in a senile captive Western lowland gorilla (*Gorilla gorilla gorilla*).

Case Report

This report describes the pathological findings in a male Western lowland gorilla (*Gorilla gorilla gorilla*) with an estimated age of 39 years. The animal was kept in captivity at the Belo Horizonte Zoo in Brazil for 37 years, and has been diagnosed as having chronic renal failure since November 2007, and chronic osteoarthritis since 2010. The gorilla also had periodontal disease, which was under treatment since 1994. In December 2011, the gorilla developed an extensive superficial infection in his left arm, with fistulous tracts and abundant purulent exudate. This cutaneous infection was treated with antibiotics and topical medication. However, on February 2012, the

clinical status of the animal deteriorated due to signs associated with chronic renal failure and chronic osteoarthritis, which were associated with anemia and dehydration. Due to lack of response to intensive therapy, the animal was subjected to chemical restraint for a detailed clinical examination and parenteral hydration. After 60 minutes under anesthesia, performed using a protocol of 8 mg/kg of ketamine intramuscularly followed by maintenance with 3% isoflurane by inhalation, which has been previously employed for the same animal, the gorilla developed respiratory failure and ventricular fibrillation. Resuscitation procedures were immediately performed without success. A complete necropsy was performed within 3 hours after death.

Grossly, the conjunctiva and oral mucosa were markedly pale. There was a gingival pedunculated nodule of approximately 0.5 cm in diameter consistent with the morphological diagnosis of papilloma. Guns were markedly receding, with loss of the medial upper right incisor, one premolar, two left mandibular molars, one premolar, three mandibular right molars, and a left maxillary premolar, and prominent wear of the teeth. There were multiple extensive ulcerative lesions in the skin, including a deep circular ulceration with 8 cm in diameter at the caudal face of the left forelimb, adjacent to the humeral-radio-ulnar joint, exposing the extremity of the olecranon; another deep extend ulceration, with an evident reepithelialization process at the medial side of the left forelimb; multiple superficial cutaneous ulcerations on the right and left hind limbs; ulcerations on the plantar surface of the left foot; and ulcerations at the distal extremities of the third and fifth fingers. The distal phalanges of the second and third fingers of the left hand, and the second and third toes of the right foot were absent.

There were multiple firm well circumscribed sessile subcutaneous nodules, which were whitish on the cut surface, located adjacent to bone prominences, including bilaterally located adjacent to the zygomatic bones, adjacent to the medium-third of the body of the left mandible in the right wall of the chest, adjacent to the proximal and distal ends of the right scapula, and adjacent to the iliac crest. Microscopically, these nodules were all composed of fibrous connective tissue with mild multifocal granulomatous infiltrate and severe fibrosis surrounding multifocal areas of mineralization, which supports the morphological diagnosis of calcinosis circumscripta (Fig 1A).

There were multiple fistulous tracts in the subcutaneous tissue containing purulent exudates, characterizing cellulitis and phlegmon, which were located adjacent to the acromial end of the left clavicle; adjacent to the medial portion of the proximal end of the right humerus, and on the medial portion of the distal right tibia. These lesions were associated with a moderate enlargement of the axillary lymph nodes and marked enlargement of inguinal lymph nodes, respectively.

Several joints had macroscopic changes. Both scapular-humeral and radio-ulnar joints had marked thickening of the joint capsule, and moderately increased amounts of synovial fluid with fibrin clots (Fig. 2A). Histologically, the articular capsule had an intense and diffuse papilliferous hyperplasia of the synovial membrane associated with severe and diffuse mineralization, and mild multifocal histiocytic infiltrate associated with severe fibroplasia, characterizing a mild chronic and diffuse synovitis (Fig. 1B). The joint capsule of the left femoro-tibial-patellar joint was markedly thick, with multifocal hemorrhages and accumulation of large amounts of purulent greenish material with putrid odor within the articular space (purulent arthritis), and there was also moderate edema in the subcutaneous tissue adjacent to this joint. Histologically, the articular capsule of the left femoro-tibial-patellar joint had a diffuse and severe neutrophilic infiltrate associated with accumulation of fibrin and a myriad of bacteria, and a neutrophilic infiltrate in the wall of arterioles (vasculitis), supporting the morphologic diagnosis of severe suppurative synovitis associated with vasculitis and intralesional bacterial colonies, which are findings consistent with a septic arthritis. There were extensive areas of erosion on the articular cartilage of the medial and lateral condyles of the proximal epiphysis of the right tibia, with moderate medial deviation of the patella, and a mild increase in the volume of synovial fluid, characterizing arthrosis. The tibio-tarsal and tarso-metatarsal joints of the right pelvic limb were enlarged with adjacent moderate subcutaneous edema, and the capsule and surrounding connective tissue were markedly thickened and firm with evident fibrosis, with large amounts of pus and fibrin within the articular space. Histologically, in the tissue adjacent to the right tarso-metatarsal joint there was marked accumulation of fibrin and neutrophilic infiltrate associated with diffuse severe fibroplasia, characterizing a chronic cellulitis. There was also hemorrhage and necrosis of the articular cartilage of the distal tibial epiphysis, characterizing a cellulitis and fibrinopurulent chronic active arthritis associated with chondromalacia.

There was mild hydrothorax and hydropericardium. An exophytic, friable, red, and adhered nodule with 0.5 cm in diameter was observed on the endocardial surface of the aortic semilunar valve, which histologically was diagnosed as fibrino-necrotizing valvular endocarditis. In addition, there was multifocal mineralization, and two focally extensive areas with severe loss of muscle fibers associated with hyalinization, fragmentation and accumulation of yellowish pigment into the fibers in miocardium. Thickening of the intima with multifocal histiocytic inflammatory infiltrate associated with mild moderate fibroplasia, and multifocal mineralization of the tunica media was observed in the aorta.

Moderate anthracosis was observed in lungs and mediastinal lymph nodes. There were multifocal petechial

hemorrhages on the visceral pleura and multifocal fibrous adherence between pleurae. Two solid, expansive, gray, and firm nodules, with 0.4 cm and with 0.2 cm in diameter were observed in the dorsal region of the left diaphragmatic lobe, and left apical lobe respectively. Both these nodules had histological features compatible with large cell lung carcinoma. Histologically there was severe multifocal to diffuse mineralization of bronchiolar and alveolar walls; multifocal to diffuse thickening of the alveolar wall associated with mild and diffuse histiocytic infiltrate, and mild multifocal fibroplasia, which support the morphologic diagnosis of a pulmonary uremic syndrome or uremic pneumopathy secondary to the chronic renal failure (Fig. 1C).

In the abdominal cavity, there was a mild increase in the volume of the abdominal fluid, and multiple fibrous adhesions of the omentum to the gastric and intestinal serosa, and between the large intestine and the adjacent parietal peritoneum. The gastric mucosa was diffusely and severely hyperemic, with petechial hemorrhages, and diffuse mucosal mineralization that was confirmed histologically, suggesting a diagnosis of uremic gastropathy, consistent with chronic renal failure (Fig. 2B). There was also a scar of approximately 3 cm in diameter in the gastric mucosa of the pyloric region, which was interpreted as a result of a previous perforated gastric ulcer. The liver and spleen were moderately congested. The internal iliac lymph nodes had moderate lymphoid hyperplasia.

Both kidneys were intensely pale with whitish coalescing to diffuse spots, and the renal cortex had an irregular surface with multiple cysts ranging from 0.2 to 3 cm in diameter (Fig. 2C and 2D). Histologically, there was an interstitial multifocal moderate linfo-histio-plasmocytic infiltrate, associated with diffuse and severe interstitial fibroplasias and fibrosis, multifocal interstitial mineralization, thickening and mineralization of the basal membrane of tubules, and multifocal glomerular sclerosis, associated with multiple cysts in the renal cortex, supporting a morphologic diagnosis of chronic interstitial nephritis associated with severe diffuse renal fibrosis (Fig. 1D).

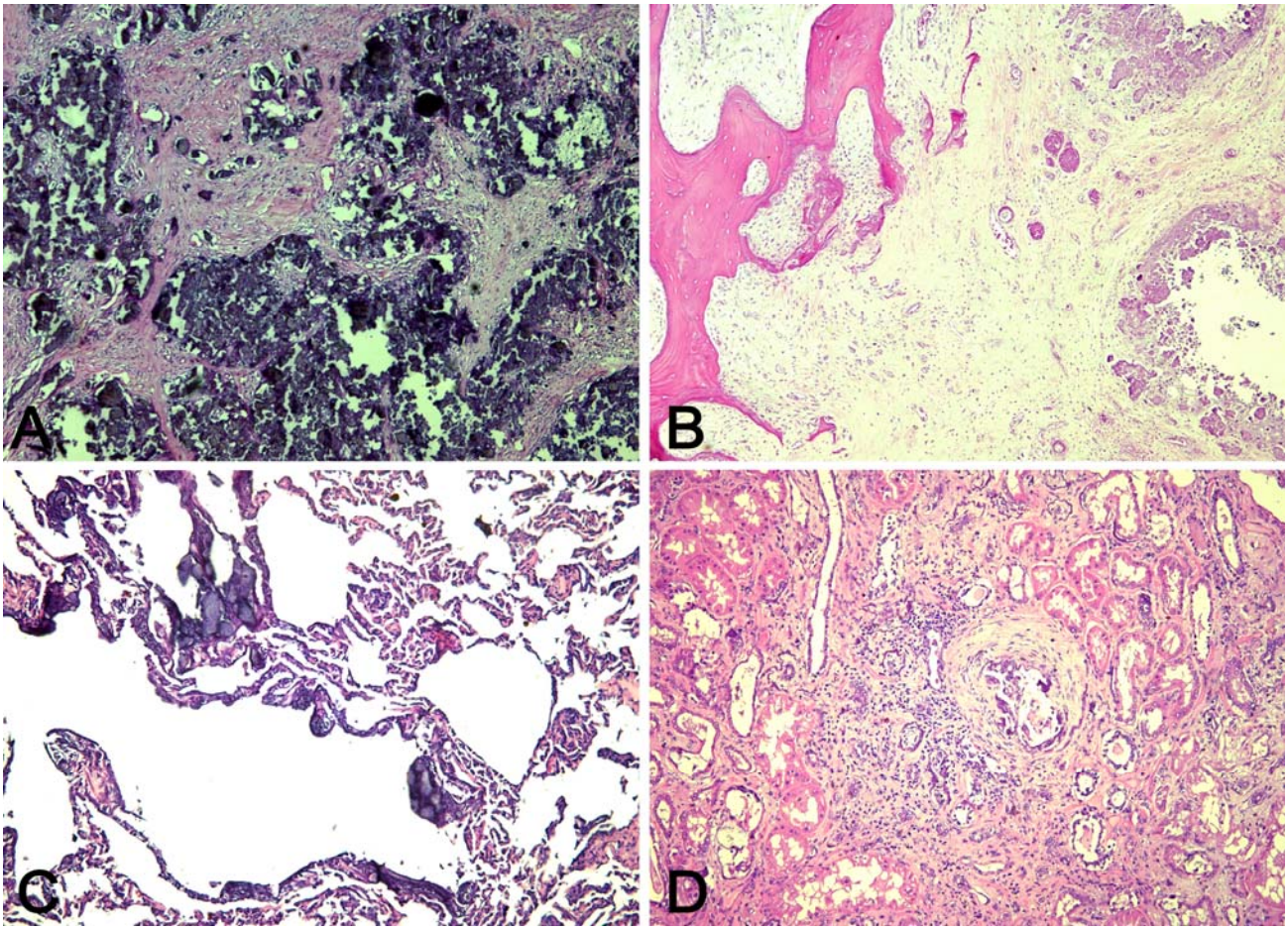

Figure 1. Western lowland gorilla (*Gorilla gorilla gorilla*) with chronic renal failure associated with septic polyarthritis. (A) Subcutis; calcinosis circumscripta characterized by extensive multifocal areas of mineralization surrounded by fibrous connective tissue and a mild histio-lymphocytic infiltrate with abundant epithelioid macrophages. HE, 5x objective. (B) Bone and synovial capsule; synovial surface with inflammatory infiltrate and fibroplasia, and mild multifocal mineralization. HE, 5x objective. (C) Lung; uremic pneumopathy characterized by multifocal mineralization of alveolar and bronchiolar walls. HE, 10x objective. (D) Kidney; marked glomerular atrophy and glomerulosclerosis, moderate interstitial lymphocytic infiltrate with interstitial fibrosis, and mild dilation of tubules. HE, 10x objective.

The testes were markedly reduced in volume, with a nodule of 1 cm in diameter, gray, solid, and firm in the testicular parenchyma. Histologically, both testes had absence of spermatogenesis, and marked loss of seminiferous tubules associated with severe interstitial fibrosis and diffuse multifocal interstitial cell hyperplasia, characterizing a severe and diffuse testicular hypotrophy or hypoplasia. The testicular nodule was expansive, solid, composed of well differentiated interstitial cells, supporting the morphologic diagnosis of leydgocytoma. In the prostate, some of the acini had a luminal proliferation and projection of glandular epithelium, and some acini were moderately dilated associated with dense connective tissue, and rare concretions, which was compatible with a moderate multifocal cystic prostatic hyperplasia.

Staphylococcus aureus was cultured from different sites of phlegmon and cellulitis, whereas *Enterobacter* sp. and *Proteus mirabilis* were cultured from osteo-articular lesions, located in the right tarsal metatarsal joint and the left femoral-tibial-patellar joint, respectively.

Considering all gross, microscopic and bacteriological findings described above, the most important diagnoses in this case were chronic renal failure secondary to a diffuse chronic interstitial nephritis and bacterial chronic polyarthritis with extensive cellulitis and phlegmon. In addition, we were able to detect other significant lesions including arthrosis, a large cell lung carcinoma, a leydogocytoma, an oral papilloma, a fibrino-necrotizing valvular endocarditis, and multiple areas with calcinosis circumscripta.

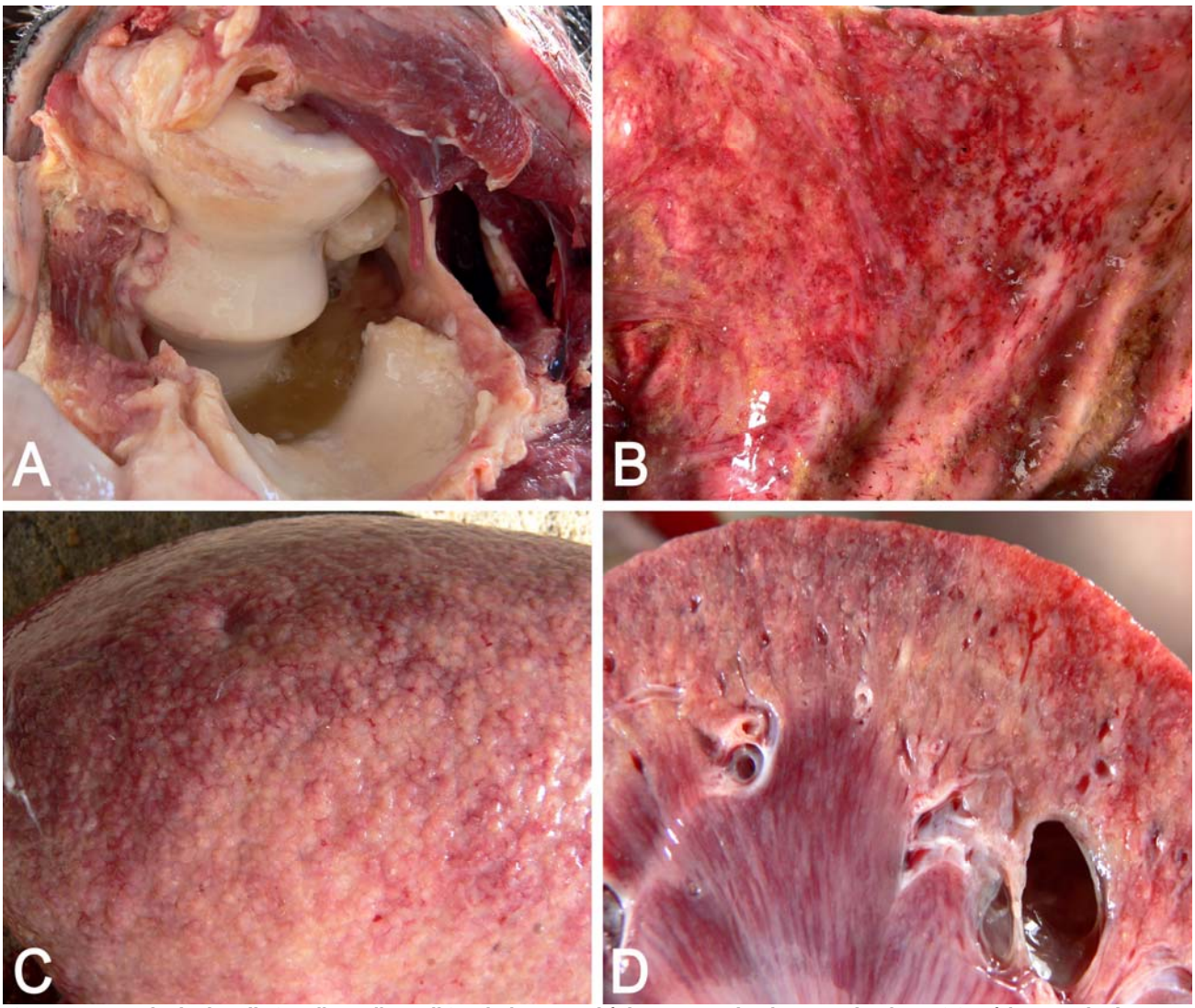

Figure 2. Western lowland gorilla (*Gorilla gorilla gorilla*) with chronic renal failure associated with septic polyarthritis. (A) Left humeroradioulnar joint; thickening of the articular capsule with synovial proliferation, mild erosion of the distal humeral articular cartilage, and accumulation of fibrinous exudate in the articular cavity. (B) Stomach; gastric mucosa with multifocal hemorrhage and whitish discoloration due to mineralization. (C) Kidney, renal cortex with an irregular pale surface with coalescing whitish foci. (D) Kidney; cut surface with a diffuse whitish discoloration due to a chronic interstitial nephritis associated with severe diffuse renal fibrosis.

Discussion

The renal changes observed are diffuse and bilateral, and associated with extra-renal lesions such as uremic pneumopathy and uremic gastropathy, which are consistent with chronic renal failure. No detailed reports of chronic renal failure affecting gorillas are available, but there have been communications of captive gorillas that die due to renal failure in zoo parks. Chronic nephritis, especially glomerulonephritis, has been diagnosed quite frequently in nonhuman primates. These renal diseases are important causes of death among new world monkeys (14). Usually chronic nephritis has no specific etiology, but immune complexes have been implicated in the pathogenesis of nefropathy affecting callitrichids (14). Humans and also the great apes, may have high uric acid levels due to mutation in the gene that encodes uricase, thus affecting the ability to regulate uric acid levels in serum. Studies in humans suggest that uric acid is a risk factor for kidney disease. Elevated uric acid may cause glomerular hypertension and cortical vasoconstriction inducing progressive glomerular damage and tubular ischemia (5).

Polyarthritis and bacterial cellulitis should be considered as an important aggravating factor of the clinical condition in this case. Ulcerative lesions of the skin contained fistulous tracts, which extended to foci of joint infection. Possibly, the animal developed bacteremia, which may have predisposed to the vegetative valvular endocarditis. There were no lesions compatible with septicemia. Degenerative and inflammatory arthropathies, including osteoarthritis, chronic poliarthritis or spondyloarthropathy seem to be common in free ranging (9, 20) and captive gorillas (15). Osteoarthritis is a progressive degenerative disease process commonly observed in heavy and senile animals, so it was not a surprising finding in this case. Joint diseases with similar aspects to human disease such as arthritis-positive rheumatoid factor or reactive arthritis accompanying enteric infection, have been more deeply investigated in gorillas (3, 6, 17, 19). Septic arthritis is less frequently reported in gorillas. It can affect several joints and be caused by purulent agent such as *Staphylococcus* and *Streptococus* sp. (2). In this case, *Staphylococcus aureus* and also *Enterobacter* sp. and *Proteus mirabilis* are isolated from subcutaneous and articular lesions.

Cardiac fibrosis associated with congestive heart failure is reported as important cause of death in captive gorillas (22). However, there were no evidences that congestive heart failure played any significant role in this case.

The large cell carcinoma of the lung diagnosed in this case is a malignancy in an early stage of development. There were no signs of invasiveness of the tumor and no metastatic site. Primary tumor of lung is rare in nonhuman primates (2, 8). Large cell carcinoma in nonhuman primates or primary tumor of lung in gorillas have not been previously reported. In humans, the most common type of primary lung tumor is squamous cell carcinoma that is associated with cigarette smoking. Large cell carcinoma, a less common form of lung cancer, is highly invasive and has poor prognosis in human patients (21).

Calcinosis circumscripta is a benign process of soft tissue mineralization characterized by single or multiple cutaneous nodules containing calcium salts. The constant friction of bony prominences regions of the body is the triggering factor of cutaneous dystrophic mineralization in these cases, which affect animals and humans, but this lesion can also have a mineralization of metastatic or idiopathic origin (18, 23). Renal failure is considered a predisposing factor for calcinosis circumscripta in dogs (11). There are reports of calcinosis criscuscripta in non-human primates (13, 18, 24), but no cases of calcinosis circumscripta have been reported in gorillas. Here, the gorilla presented multifocal calcinosis circunscrita, which may have been enhanced by the concurrent chronic renal failure.

Intense and diffuse testicular hypotrophy/hypoplasia is compatible with previous cytological findings included in the medical records of this gorilla, which were compatible with azoospermia. Testicular atrophy has been reported in captive gorillas and it appears to be a frequent cause of infertility in this species (1, 4, 15, 22). However, the causes of testicular dysfunction in captive gorillas are unknown. Leydgocitoma is a usually benign interstitial cell tumor of the testicle that is often observed in senile animals. Prostatic hyperplasia is also a frequent change associated with senility (16). Although there is a previous report of Leydgocitoma in a captive gorilla (10), testicular tumors are considered rare in nonhuman primates (10, 25), while prostatic hyperplasia occurs in nonhuman primates (12).

In conclusion, here we report the pathological and microbiological findings of a case of chronic renal failure associated with septic polyarthritis in a senile Western lowland gorilla.

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