

CASE REPORT OPEN ACCESS

# Chronic Kidney Disease and Kidney Stone in a Wild Chimpanzee (*Pan troglodytes verus*) in Côte d'Ivoire

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## ABSTRACT

An older wild female chimpanzee (*Pan troglodytes*) was found dead with a large calcium oxalate stone in the renal pelvis. Histopathological changes included glomerulosclerosis, interstitial nephritis and fibrosis, focal mineralization, and medial hypertrophy. Urinary albumin-creatinine-ratio showed increased values from 15 months before death. Causes of the kidney disease remain unconfirmed.

## 1 | Introduction

Non-infectious diseases in wild chimpanzees (*Pan troglodytes*) are rarely reported compared to infectious disease [1–4]. In captive chimpanzees, chronic kidney disease is relatively common in older individuals [5–12]. In wild chimpanzees, only two cases of kidney disease have been reported [11], both from Tanzania, with membranous glomerulopathy, glomerulosclerosis, and tubular protein. We report a case amongst the habituated wild chimpanzees of the Taï Chimpanzee Project, Côte d'Ivoire. No previous kidney disease had ever been detected here, based on post-mortem examinations and urinary dipstick parameters [13].

This case is only the third report of kidney disease in a wild chimpanzee, and the first report of a naturally occurring kidney stone in any great ape [11]. Experimentally, calculi or papillary tip calcification have been induced in laboratory primates, including

chimpanzees, by feeding oxamide [14]. Calcium oxalate crystals and stones in kidney and bladder have been reported to occur spontaneously in laboratory macaques [15–19]. Calcium oxalate stones in the bladder have also been observed in a sanctuary housed baboon (H. van Bolhuis, Foundation AAP, personal communication, June 1, 2022) and in two zoo housed langurs [20], and calcium oxalate crystals in sanctuary housed chimpanzee urine [21].

## 2 | Materials and Methods

Fieldwork was conducted with the Taï Chimpanzee Project in Côte D'Ivoire, observing habituated Western chimpanzee (*P. t. verus*) groups. Urine samples were collected from leaves, rocks, or tree trunks by micropipette. Individuals found dead were necropsied following strict biosecurity protocols [22]. Tissue samples were saved in NAP Buffer, plain cryotubes (stored in

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liquid nitrogen or  $-80^{\circ}\text{C}$  freezers, as were the urine samples), and formalin. Histopathology was performed on formalin-fixed tissues. Calculus analysis was performed by an external laboratory (IDEXX, Germany).

Necropsy tissues, the kidney stone and 15 urine samples collected in the 3 years before death were analyzed by 16S metabarcoding, and by shotgun sequencing for the liver and spleen samples, to determine presence of pathogenic bacteria or dysbiosis. Albumin-creatinine-ratio (ACR) was analyzed in the 15 urine samples. See Appendix S1.

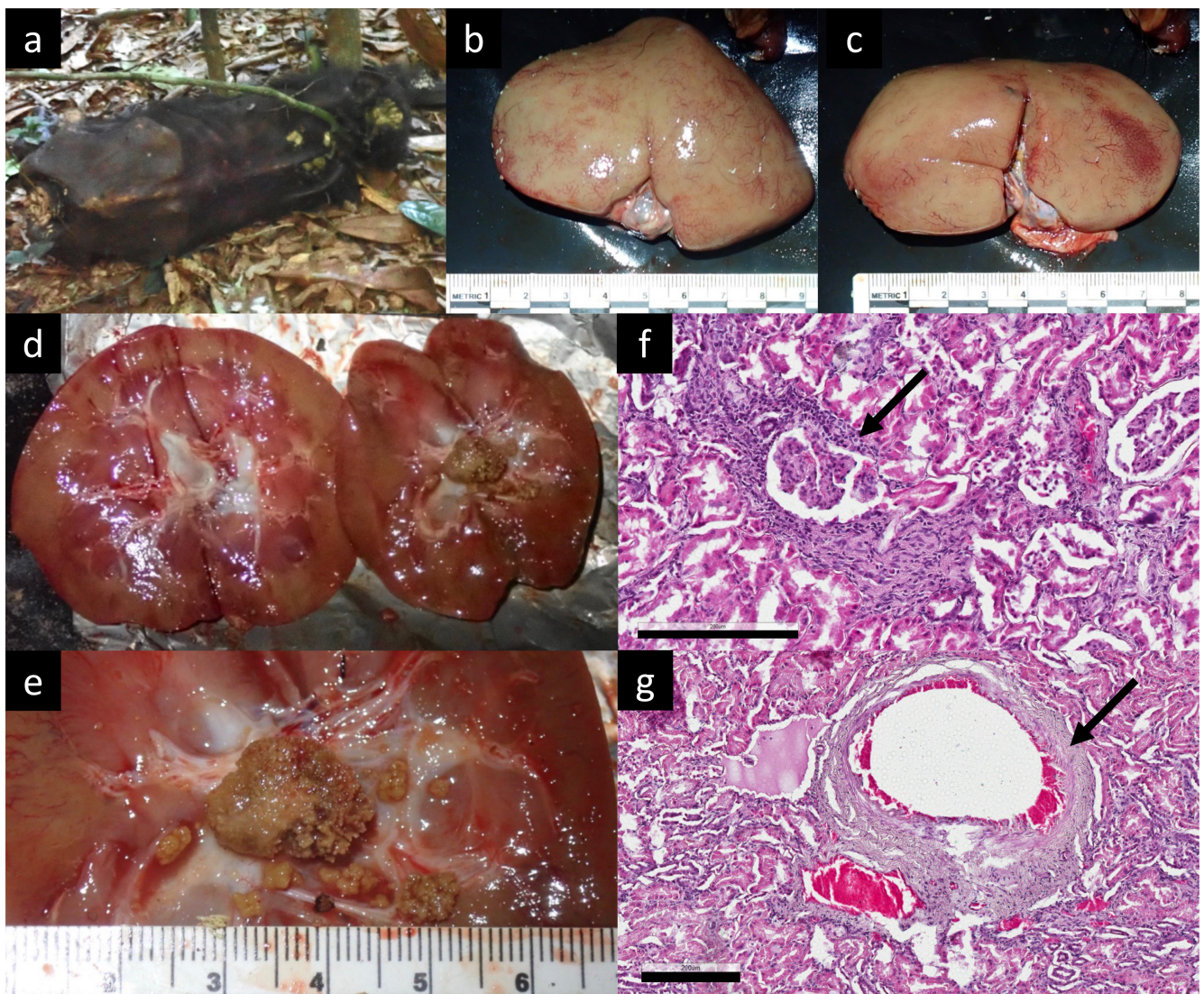
### 3 | Results

“Rwenzori,” a female chimpanzee of approximately 42 years old, was found dead on January 8, 2020, in very poor body

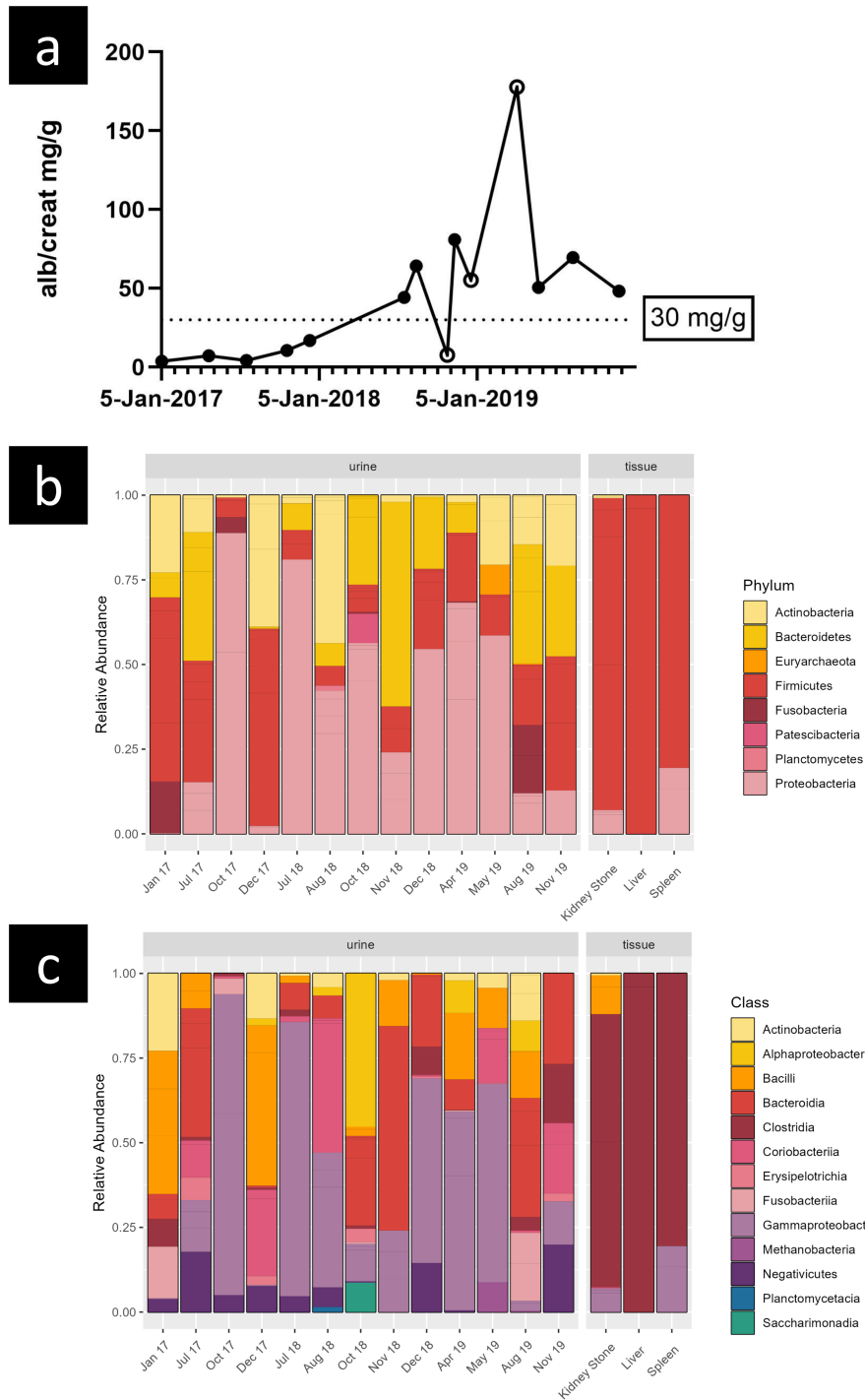
condition (Figure 1a). Her body condition had been moderate to poor for several years, deteriorating in the months before death, with muscle wasting and progressively more prominent bony protuberances. Otherwise, no abnormalities had been noted. She was still carrying a 2-year-old suckling infant in the days before death.

#### 3.1 | Gross Pathology

Bilaterally the kidneys were diffusely pale beige to light brown, with prominent blood vessels evident on removal of surface capsule (Figure 1b,c). Longitudinal sections revealed a diffuse red brown parenchyma (Figure 1d). The left renal pelvis contained an irregularly shaped, pale brown, friable calculus (18×12 mm) with a rough surface (Figure 1e). No abnormalities were seen in the bladder.



**FIGURE 1** | Post-mortem findings RWE. (a) RWE as found dead, in very poor body condition; (b) bilaterally pale beige kidneys with prominent blood vessels, right kidney; (c) left kidney; (d) diffuse red brown parenchyma on longitudinal sections; (e) close up of calculus in left renal pelvis; (f) mild interstitial nephritis and glomerulosclerosis; (g) medial hypertrophy kidney vessel. Black scale bar = 200  $\mu\text{m}$  (f and g).



**FIGURE 2** | Urine, kidney stone and tissue analysis. (a) Urinary albumin-creatinine-ratio (ACR) in mg/g in the 3 years before death; open circles indicate low creatinine values ( $\leq 0.5$  mg/mL) which may have affected the ACR; dotted line indicates clinical threshold for chronic kidney disease in humans (30 mg/g) [23]. (b and c) 16S bacterial metabarcoding analysis of urine samples, kidney stone, liver and spleen on phylum level (b) and class level (c).

### 3.2 | Histopathology

The kidneys showed mild medial hypertrophy of the larger renal vessels, tubular protein, glomerulosclerosis of individual glomeruli within areas of mild focal interstitial nephritis and fibrosis, and focal mineralization (Figure 1f). The blood vessels of the kidneys and other organs showed medial hypertrophy (Figure 1g), indicating hypertension; suggesting

“cardiorenal syndrome” [5]. No abnormalities were seen in the bladder.

### 3.3 | Calculus Analysis

Calcium oxalate dihydrate (>90%), minor component tricalcium phosphate (<10%).

### 3.4 | Urinalysis

Albumin-creatinin-ratio (ACR) measurements were relatively low up till July 2018 ( $\leq 30$  mg/g) and higher from October 2018 onwards (30–178 mg/g), see Figure 2a.

### 3.5 | 16S Bacterial Metabarcoding Analysis of Urine Samples, Kidney Stone, and Post-Mortem Tissues

Of the samples (liver, lung, spleen, kidney, kidney stone, and urine), the liver, spleen, kidney stone and 13 of 15 urine samples tested positive by PCR. Amplicons were prepared for high-throughput sequencing and analysis of the sequencing reads showed no evidence of bacterial infection in the tissue samples, but rather the normal necrobiota found post-mortem. The urine samples also showed no predominance of any bacterial class, rather a mixed composition, likely due to sample contamination and post-collection overgrowth (Figure 2b,c). To confirm 16S results hinting towards *Clostridium* sp. in the liver and spleen (with the kidney stone showing similar results), we performed shotgun sequencing, but found no further evidence of any significant bacterial (or viral/fungal) presence. See Appendix S1.

## 4 | Discussion

To our knowledge, this is the first description of a kidney stone in either wild or captive great apes. Nephrocalcinosis (diffuse calcification) has been reported in laboratory primates [16, 19] including chimpanzees [7]. Calcium oxalate stones in humans are generally caused by diet, metabolic, or genetic disorders rather than infection [24], but we used 16S and shotgun sequencing to explore all possible underlying causes of disease. Cardiorenal syndrome in older captive chimpanzees is linked to heart disease and metabolic diseases such as diabetes and obesity [5], which are less likely in wild chimpanzees. In our case, the histological changes in the kidney indicated (chronic) nephritis and glomerulosclerosis. Acute kidney disease in laboratory chimpanzees has been associated with bacterial infection [25–27]. Though our 16S metabarcoding and histopathology results did not indicate active infection in the kidney or other internal organs at the time of death, it is possible that a previous infection causing chronic kidney disease occurred, potentially in 2018, when urinary ACR started increasing. Microbiome analysis of the urine could not pinpoint a specific causative pathogen. However, the chance of catching a bacterial infection with the urine samples available would always be relatively low: the number of urine samples was limited, and with a high probability of bacterial contamination and post-collection overgrowth (with samples collected from the environment and not immediately cooled). No microbiome data from wild primate urine samples is available to compare; however, vaginal swabs from captive and wild baboons (*Papio* sp.) show comparable microbiomes to our urine samples [28].

The exact interplay between possible causes of chronic kidney disease, high blood pressure, and formation of the calcium oxalate stone cannot be determined. Urinary ACR (Figure 2a) suggests kidney disease started at least 15 months before

death. This fits with the chronic changes seen on histopathology and the poor body condition years before death. Energetic costs and hydration burden due to lactation may have exacerbated the clinical course of disease [29, 30]. More post-mortem examinations including histopathology in wild chimpanzees should give a better idea of the prevalence of renal disease; reports up till now indicate it is uncommon. This case report provides a rare illustration of chronic kidney disease progressing over time in a wild chimpanzee, including cardiorenal syndrome, and with a pelvic kidney stone so large, it likely caused considerable pain [31].

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### Ethics Statement

The authors confirm that this study was performed in accordance with the ethical policies of the journal, as noted on the journal's author guideline page.

### Conflicts of Interest

The authors declare no conflicts of interest.

### Data Availability Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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### Supporting Information

Additional supporting information can be found online in the Supporting Information section.