

## Case Report

# Obstructive Uropathy Secondary to Uterine Leiomyoma in a Chimpanzee (*Pan troglodytes*)

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Complications due to uterine leiomyomata in chimpanzees have rarely been documented. Here we describe a female chimpanzee that developed severe hydronephrosis in the right kidney due to leiomyoma. Because hysterectomy did not alleviate the hydronephrosis, nephrectomy was elected. After these procedures, the chimpanzee is doing well. Leiomyomata screening programs with treatment algorithms are a useful component of a comprehensive chimpanzee program.

The prevalence rates for the occurrence of uterine leiomyomata, or fibroids, in female captive chimpanzees are reported to be similar to those for humans.<sup>16</sup> However, in contrast to humans, complications secondary to uterine leiomyomata in chimpanzees have been documented infrequently. Here we present a case of obstructive uropathy due to uterine leiomyoma that resulted in severe hydronephrosis and surgical removal of a kidney in a female chimpanzee.

### Case Report

A 28-y-old, 55-kg multiparous female chimpanzee was transferred to the AAALAC-accredited Michale E Keeling Center for Comparative Medicine and Research from another facility in Spring 2007. This chimpanzee is on an IACUC-approved protocol and is managed in accordance with the US Department of Agriculture Animal Welfare Regulations<sup>2</sup> and the *Guide for the Care and Use of Laboratory Animals*.<sup>11</sup> Currently, this animal is on a protocol that involves applied research to improve captive management and maintenance of chimpanzees. She has not been involved in any known experimental protocols. Previous medical records and physical examinations performed during the initial quarantine period alerted the veterinary staff to a large uterine mass (13 cm × 9.58 cm × 16 cm by transabdominal ultrasonography) and bilateral hydronephrosis, with the right kidney being the more affected. The right kidney measured 8.3 cm × 4.22 cm and had a large (6.03 cm × 4.03 cm) fluid-filled mass in the area of the medulla. The left kidney measured 9.68 cm × 5.48 cm and had a fluid-filled mass (1.91 cm × 1.53 cm) in the area of the medulla. The uterine mass and bilateral hydronephrosis were identified in 2000 and 2002, respectively, at the previous facility. Treatment strategies at the previous facility included intramuscular administration of leu-

prolide acetate (11.25 mg, every 3 mo), which reduced the size of the mass slightly.

Serum biochemistry at the current facility revealed a mildly elevated creatinine (1.4 mg/dL, normal range 0.7 to 1.1 mg/dL). The chimpanzee appeared clinically normal, but because of the size of the leiomyoma and the presence of hypercreatinemia and bilateral hydronephrosis, we elected to surgically excise the uterine mass to prevent further deterioration in renal function. Histopathology after total abdominal hysterectomy and bilateral salpingo-oophorectomy confirmed the mass to be a leiomyoma. We initially intended to preserve the ovaries in situ, but because of their close attachment to the mass, it was surgically necessary to remove them. The chimpanzee recovered uneventfully.

During the subsequent year, the chimpanzee received multiple physical examinations, which included CBC, serum biochemistry analyses, and ultrasonography of the kidneys. The severe hydronephrosis of the right kidney did not improve; the mild hydronephrosis of the left kidney improved slightly, in that the fluid-filled mass decreased to 1.61 cm × 0.89 cm. In addition, intravenous pyelography prior to surgery indicated that the right kidney had extremely poor function, whereas the left kidney had normal function. In light of concerns regarding possible rupture of the hydronephrotic right kidney and its overall lack of functionality, the right kidney was removed. The chimpanzee was sedated with tiletamine-zolazepam (4 mg/kg IM) and maintained on isoflurane. We considered a routine flank approach, but because of the close proximity of the costal border and iliac crest in this chimpanzee, we opted for a midline approach, to obtain increased exposure and visualization.

On exposure, the right kidney was fluid-filled and grossly distended, with a very thin presumed cortex. The right renal artery and vein were identified and ligated. The right ureter was visualized and ligated at its insertion to the bladder. The right kidney was removed and sent to histopathology for evaluation. The left kidney was identified and appeared grossly normal on surgical exploration. Exploration of the remainder of the abdomen was unremarkable. Closure and recovery were uneventful. The

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**Figure 1.** Gross characteristics of the right kidney. The renal pelvis is greatly distended and fluid-filled. The parenchyma surrounding the pelvis is thin, measuring as little as 2.5 mm in some areas.

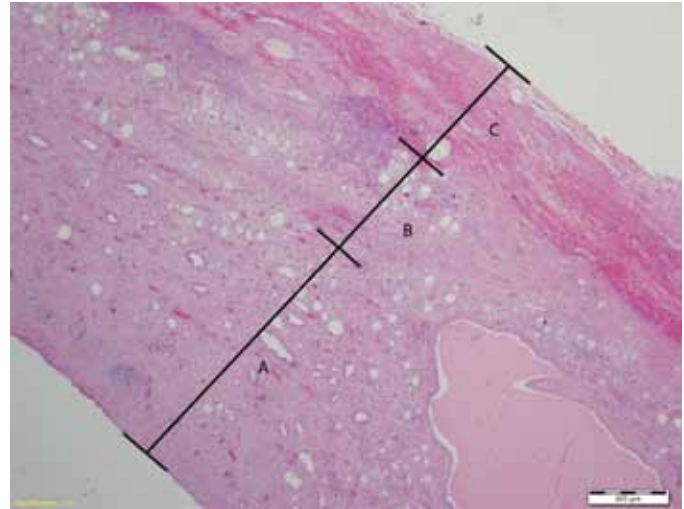
chimpanzee received buprenorphine (0.05 mg/kg IM) for post-procedural analgesia. At 2 y after nephrectomy, the chimpanzee is doing well, and the mild hypercreatinemia (1.2 to 1.3 mg/dL) remains stable.

On gross examination, the pelvis of the resected right kidney was greatly dilated and sac-like in appearance. The parenchyma was thin, measuring as little as 2.5 mm in some areas (Figure 1). An attached short segment of ureter was mildly dilated. Microscopically, the renal parenchyma was atrophic, with marked alteration of the normal structures. The cortex had prominent areas of interstitial fibrosis, with multifocal infiltrates comprising numerous lymphocytes and moderate neutrophils, amyloid deposits, and rare large dilated tubules. In one area, the cortex was less than 1 mm thick, with capsular fibrosis and hemorrhage. Glomeruli were reduced in number and had membranous degenerative changes. The renal medulla was diffusely fibrotic, with occasional dilated tubules, small areas of hemorrhage, and sporadic infiltrates of low numbers of lymphocytes and neutrophils (Figure 2). The morphologic diagnoses were hydronephrosis, hydroureter, capsular fibrosis, capsular hemorrhage, and renal parenchymal atrophy.

## Discussion

Obstructive uropathy is a well-documented complication of uterine masses in humans.<sup>3</sup> The typically reported pathophysiology is direct compression of the ureter(s) at the pelvic brim, indirect obstruction of the ureter by displacement of the bladder anteriorly to cause a severe urethrovesical angle, or a combination of both.<sup>1,10</sup> Studies have demonstrated that the size of the mass is less important than is the position of the mass in causing obstructive uropathy. The cervical location is noted as the most causative, compared with a fundal or central location.<sup>3</sup> The uropathy typically begins as a hydroureter but can progress over time to either unilateral or bilateral hydronephrosis. In unilateral obstructions, the right kidney is affected more often, because the sigmoid colon may protect the left side.<sup>1</sup>

In humans, the primary treatment for obstructive uropathy secondary to a uterine mass is to remove the mass either by a complete hysterectomy or a uterine-sparing surgery (for example, uterine artery embolization, myomectomy).<sup>3,6,10</sup> After removal of the mass, the hydronephrosis may spontaneously resolve.<sup>1</sup> One study of hydronephrosis after uterine artery embolization showed resolution in 87% of affected kidneys.<sup>1</sup> When the hydronephrosis does not resolve, techniques such as ureteral stenting



**Figure 2.** The renal parenchyma was atrophic, with marked alteration of the normal structures. The medulla (region A) was diffusely fibrotic, with occasional dilated tubules, small areas of hemorrhage, and sporadic infiltrates of low numbers of lymphocytes and neutrophils. The cortex (region B) had prominent areas of interstitial fibrosis, with multifocal infiltrates of numerous lymphocytes and moderate neutrophils, amyloid deposits, and rare large dilated tubules. The cortex (region C) was less than 1 mm thick, with capsular fibrosis and hemorrhage. Glomeruli were reduced in number and had membranous degenerative changes. Hematoxylin and eosin stain; magnification, 2 $\times$ ; bar, 500  $\mu$ m.

or placement of a nephrostomy tube can be attempted. In severe cases, nephrectomy may be required.<sup>13,14</sup> In the present case, nephrectomy was performed, because the natural aggression of group-housed chimpanzees increased the risk of intraperitoneal rupture of the hydronephrotic kidney.<sup>4,9</sup>

Medical management of fibroids in humans has primarily been limited to gonadotropin-releasing hormone agonists (for example, leuprolide acetate) and, more recently, selective progesterone-receptor modulators (for example, ulipristal acetate).<sup>5,8,12</sup> These medications are not curative but are designed to control signs such as excessive menstrual bleeding and to reduce the size of the tumor.<sup>6,15</sup> Leuprolide acetate downregulates gonadotropin-releasing hormone at the pituitary creating a hypoestrogenic state that results in amenorrhea. Leiomyomata are often hormone-responsive, so this suppression has been shown to decrease their size.<sup>15,17</sup> Ulipristal acetate, in comparison, directly targets endometrium to inhibit ovulation and induce amenorrhea without downregulation of estrogen. Furthermore, in vitro, ulipristal has been demonstrated to inhibit proliferation of cultured leiomyoma cells, downregulate vascular epithelial growth factors in leiomyoma cells, and enhance the breakdown of extracellular matrix in leiomyoma cells.<sup>7,15</sup> In our case, leuprolide was administered at the previous facility in an attempt to decrease the size of the uterine mass and alleviate the bilateral hydronephrosis. Although subsequent sonograms revealed improvement in the hydronephrosis of the left kidney and slight reduction in the size of the mass, the hydronephrosis of the right kidney continued to worsen.

Uterine leiomyomata are the most common tumor that affects captive female chimpanzees. The prevalence (approximately 25%) in chimpanzees is similar to that in humans.<sup>5,16</sup> Although complications due to leiomyomata have been suggested to occur in chimpanzees, case reports are sparse. One report<sup>18</sup> describes

anemia that may be associated with heavy menses due to leiomyoma. However, the chimpanzee in that report also had lead intoxication, which may have contributed to the anemia.<sup>18</sup> Obstructive uropathy secondary to a uterine mass has not previously been reported in chimpanzees. During other hysterectomies in chimpanzees at our facility, we have identified ureters that were adhered to the uterus or a uterine mass. Although uropathies had not occurred in these other cases, any additional tumor growth likely would have resulted in obstruction. In addition, treatment of a hydronephrotic kidney in a chimpanzee has not been reported previously.

To our knowledge, the current report is the first to describe removal of a chronically hydronephrotic kidney due to obstruction from uterine leiomyoma in a chimpanzee. Although hydronephrosis due to a uterine mass is a rare complication in humans and although no complications of this severity in chimpanzees have previously been reported, the current case illustrates the importance of evaluating uterine masses. We therefore support a previous recommendation<sup>16</sup> for the institution of aggressive screening programs and appropriate treatment plans for uterine leiomyoma that may include surgical removal of large and potentially obstructive masses to limit potential complications.

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