Comparative Medicine
Copyright 2016
by the American Association for Laboratory Animal Science

Vol 66, No 3
June 2016
Pages 254–258

*Case Report*

# Uterine Rupture in a Common Marmoset (*Callithrix jacchus*)

**Louis DiVincenti, Jr,[1,*] Andrew D Miller,[2] Dina J Knoedl,[3] and Jude F Mitchell[3]**

**A 5-y-old multiparous female common marmoset (*Callithrix jacchus*) presented with acute weight loss of approximately 25% over a 1-wk period. An abdominal mass was apparent on physical examination, and radiographs suggested peritoneal effusion. Exploratory laparotomy revealed hemoperitoneum and an enlarged, gray, hemorrhaging uterus; ovariohysterectomy was performed, and the marmoset recovered. Histologic evaluation of the ovaries and uterus revealed uterine rupture, with invasion of placental villi lined by trophoblasts through the myometrium to the serosal layer. Primary uterine rupture is a rare but serious obstetric event in humans and has been reported only rarely in NHP. This report is the first description of primary uterine rupture during early pregnancy in a common marmoset.**

In humans, uterine rupture is an uncommon event but is a significant cause of maternal and fetal mortality and morbidity.[24] Historically, ruptures occurred secondary to obstetric manipulative procedures, but currently, most uterine ruptures are associated with a previous cesarean section or uterine scarring secondary to uterine trauma, uterine curettage, or retained placenta.[12] Consequently, improved obstetric care will not eliminate all cases, and uterine rupture remains a potentially life-threatening condition when complete rupture occurs. In contrast, incomplete ruptures are typically asymptomatic and occur as the dehiscence of a previous uterine scar. Uterine scarring is the most significant risk factor,[19] but although exceedingly rare by comparison, rupture of the unscarred uterus has been reported and is usually traumatic in origin.[26] Because of this low incidence, clinical information concerning primary uterine rupture in the absence of uterine scarring or previous cesarean section is mostly limited to case reports.[8] A leading hypothesis suggests that these patients have a weakened uterus due to multiparity, especially in the presence of a healed lateral cervical laceration, which is common during delivery even in normal childbirth.[22] Further description of this important clinical phenomenon with identification of risk factors could improve maternal and fetal outcomes in patients with uterine rupture.

Common marmosets (*Callithrix jacchus*) are an increasingly common laboratory animal model. The marmoset's size, physiologic and hormonal similarity to humans, relative ease in handling compared with other NHP species, high reproductive efficiency, and availability of transgenic lines allow its potential use in diverse paradigms from neuroscience and cognitive research to infectious disease investigations.[14,17] However, the marmoset's unique reproductive biology within the fundamental similarities shared among all primate species makes it an interesting comparative model for reproduction and fetal development.[21] After a gestation period of 143 to 144 d, the birth of chimeric twins and triplets is most common in marmosets,[4] and, on average, marmosets produce more offspring per delivery than does any other anthropoid primate.[23] In contrast to other primates, marmosets have a postpartum ovulation approximately 10 to 20 d after parturition that often results in a successful delivery in as few as 154 d after the previous birth.[23] Here we describe the clinical course of a spontaneous uterine rupture in a common marmoset in early pregnancy. Whereas pregnancy losses are commonly reported in captive marmoset colonies,[4,23] to our knowledge, this report is the first description of primary uterine rupture in a common marmoset.

## Case Report

A 5-y-old multiparous female common marmoset presented with acute weight loss of approximately 25% over a 1-wk period. The animal was housed in an AAALAC-accredited institution on a breeding protocol approved by the University of Rochester IACUC, and management was consistent with all applicable regulations as prescribed by the Animal Welfare Act and the *Guide for the Care and Use of Laboratory Animals*.[11] The marmoset was used exclusively for breeding, with no experimental manipulations. At approximately 20 mo of age, she received a subcutaneous melengestrol acetate implant for contraception; this implant was removed 4 mo later, after her transfer to a breeding pair. The marmoset then had 2 normal full-term deliveries, which yielded one set of quadruplets and one set of triplets, followed by the premature delivery of twins, which died shortly after birth, and a full-term delivery of twins approximately 8 wk prior to presentation. The interbirth interval (mean ± 1 SD) was 184 ± 62 d.

At the time of presentation, the marmoset was housed with her family group, which consisted of an unrelated male partner, 2 approximately 1-y-old juvenile offspring, and 2 approximately 8-wk-old neonatal offspring. The group was housed in an en-

*Received: 13 Aug 2015. Revision requested: 10 Sep 2015. Accepted: 13 Oct 2015.*
*[1]Department of Comparative Medicine, University of Rochester, Rochester, New York; [2]Department of Biomedical Sciences, Section of Anatomic Pathology, Cornell University College of Veterinary Medicine, Ithaca, New York; and [3]Brain and Cognitive Sciences, University of Rochester, Rochester, New York*
**Corresponding author. Email:louis_divincenti@urmc.rochester.edu*

riched stainless steel cage (30 in. × 36 in. × 72 in. high) in a housing room maintained at 80 °F (26.7 °C) with a relative humidity of 30% to 70% and a 12:12-h light:dark cycle. Food (Mazuri Callitrichid Gel 5M15, PMI Nutrition, St Louis, MO) and water were provided free choice. Semiannual physical exams including tuberculosis testing were performed, and her weight was monitored weekly to assess for any health problems.

Prior to the observation of acute weight loss, caretakers observed a nonspecific slight change in the marmoset's behavior over the previous 2 d but no noteworthy changes in appetite or attitude. No other clinical signs were reported. A routine weekly weighing revealed a 25% weight loss since the previous week. The marmoset was anesthetized by using isoflurane in an induction chamber, and then anesthesia was maintained with isoflurane at 2% by face mask. She was noted to be underweight (body condition score, 2 of 5) and approximately 6% to 8% dehydrated based on increased skin turgor and a slight increase in capillary refill time (approximately 3 s). A marble-sized, firm, moveable mass was palpated in the caudal abdomen. The urinary bladder could not be palpated. No bleeding or discharge from the vaginal tract was detected, and a limited cervical and rectal exam revealed no abnormalities. A blood sample was taken from the femoral vein and submitted for a serum chemistry panel. In addition, 10 mL of lactated Ringers solution was administered subcutaneously. Recovery from anesthesia was uneventful, and the marmoset was returned to her home cage with her partner only, to facilitate observation. Serum chemistry analysis revealed hypokalemia (2.6 mmol/L) and hypoalbuminemia (2.3 g/dL) with suspected hypoproteinemic hypocalcemia (7.5 mg/dL). All other values were within published reference intervals.[20] In addition to her normal chow, nutritional support (Ensure, Abbott, Abbott Park, IL; Nutri-Cal, Tomlyn, Lodi, CA) was offered overnight.

The following day, the marmoset again was anesthetized for physical examination. While in the induction chamber, she defecated a pea-sized, very firm, dry fecal pellet, and the abdominal mass appeared to be slightly more caudal in the abdomen, leading to suspicion of constipation. A warm-water enema resulted in the passage of an additional small, hard, dry fecal pellet. Subcutaneous fluids were administered, and lactulose (0.25 mL/kg PO BID) and ranitidine (2 mg/kg PO BID) were initiated. This treatment plan proceeded for 2 d, during which time the marmoset gained weight, became more active, and appeared more comfortable. However, on the third day (5 d after initial presentation), the animal appeared weaker and hunched. In addition, no change in the abdominal mass was appreciated.

The animal was anesthetized with ketamine hydrochloride (10 mg/kg IM) and dexmedetomidine (0.1 mg/kg IM) and transported to the central vivarium for further evaluation and treatment. Right lateral and ventrodorsal abdominal radiographs were obtained (Figure 1) but were nondiagnostic due to a lack of serosal detail attributed to insufficient intraabdominal fat or the presence of peritoneal effusion. At that time, an exploratory laparotomy was elected. The animal was intubated, and anesthesia maintained by using 1% to 2% isoflurane in oxygen. The ventral midline was shaved and aseptically prepared and a routine laparotomy performed. Upon exposure of the abdomen, approximately 2 to 3 mL blood was apparent in the peritoneal cavity. The uterus was enlarged, rounded, and had an overall gray color. Active bleeding was noted from a uterine rupture on the posterior uterine wall, prompting ovariohysterectomy. The


**Figure 1.** (A) Ventrodorsal and (B) right lateral radiographs of the abdomen. There is an overall lack of serosal detail suggestive of peritoneal effusion or a lack of body fat.

remainder of the abdominal viscera was examined, but no other pathology was observed. The peritoneum and skin were closed routinely. Meloxicam (0.2 mg/kg IM), buprenorphine (0.02 mg/kg IM), cefazolin (22 mg/kg IV), and lactated Ringers solution (15 mL SC) were administered. The marmoset had an uneventful recovery, with supplemental heat provided until she was perching. The following day, the animal was returned to her family group, and antimicrobials and analgesics were administered as clinically indicated. By 1 wk after surgery, her appetite was near normal, and her weight had begun to increase. She remained the socially

dominant female in her group, despite having a daughter near breeding age within the group.

The intact uterus and ovaries were submitted in 10% neutral buffered formalin for histopathology. Grossly, the uterus had a 1-mm area of red–brown discoloration, which extended from the serosal surface of the body of the uterus into the muscular wall and which corresponded to the clinically observed region of hemorrhage. Both ovaries contained large corpora lutea and several smaller follicles in various stages of development. Within the uterus, there was complete rupture of the muscular wall; the endometrium extended through the rupture and wrapped along the serosal surface (Figure 2). Small amounts of fibrin were adherent to the serosal surface at the site. This section and the nonruptured regions of the uterus had normal placental tissue, which was characterized by arborizing, trophoblast-lined tissue that interdigitated with hyperplastic, papilliferous endometrial tissue that extended along the endometrium through the ruptured uterus (Figure 3). The uterine lumen contained moderate numbers of multinucleated trophoblasts admixed with eosinophilic cellular debris and hemorrhage. A trichrome stain did not reveal any fibrosis at the site of rupture, indicating the lack of a previous lesion at the site of the rupture. Smooth-muscle actin staining confirmed the presence of endometrium extending through the defect and along the uterine surface but failed to reveal any smooth-muscle abnormalities (Figure 4).

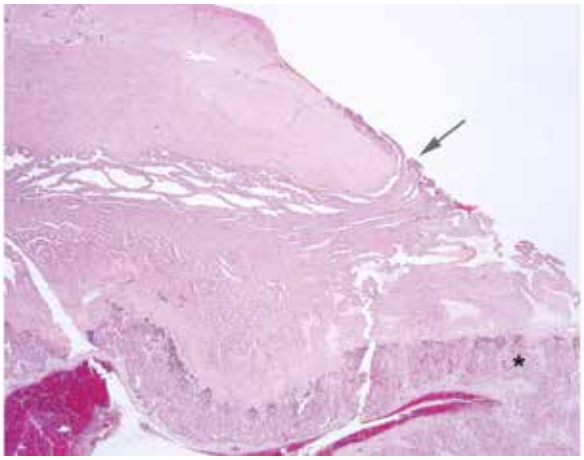

**Figure 2.** Section of uterine rupture, with the endometrium extending through the defect and wrapping along the serosal surface (arrow). Normal placenta is present (asterisk) adherent to the endometrium and extends through the ruptured uterus. Hemorrhage is present in the lemon of the uterus. Hematoxylin and eosin stain; magnification, 20×.

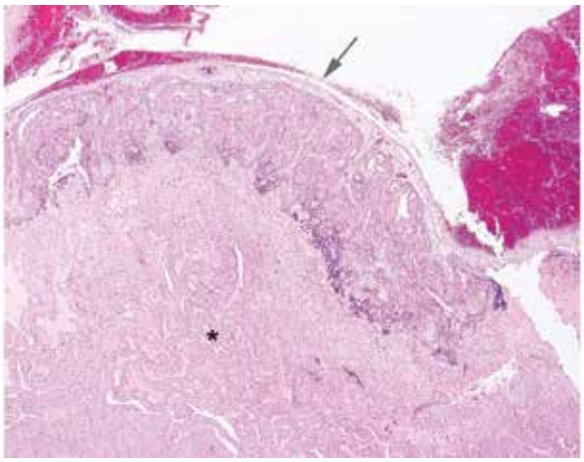

**Figure 3.** At the site of rupture, the endometrium is proliferative (asterisk) and interdigitates with the overlying placenta (arrow). Hematoxylin and eosin stain; magnification, 40×.

## Discussion

In humans, the key clinical feature of uterine rupture is acute abdominal pain and signs of intraabdominal hemorrhage. Although the marmoset we present initially demonstrated a mild behavioral change and extreme weight loss, she did not present with signs typically considered to indicate pain, such as hunching and lethargy, until nearly a week after the initial presentation. Although pain was not a predominant sign at any point in this case, the lack of overt signs of pain is likely an indicator of the marmoset's instinct to hide pain rather than the condition not being painful.[10] This observation highlights the need to carefully observe animals for even subtle indicators of pain. Similarly, vaginal bleeding was not observed in this case, but hemorrhage secondary to uterine rupture can be entirely intraabdominal.[24] In fact, no clinical signs or physical examination findings suggested reproductive pathology until the exploratory laparotomy revealed an enlarged, gray uterus. Ultrasonography has become a mainstay of pregnancy monitoring in humans and animals, and had this imaging modality been available to evaluate this marmoset, pregnancy assessment or presurgical diagnosis might have been accomplished.

The cause of the uterine rupture in this case remains unclear. Given the scarcity of published information, spontaneous uterine rupture in NHP may be exceedingly rare or may be an unrecognized condition. Pregnancy losses and dystocia are common in marmosets,[9,23] but only a single case report describes uterine rupture in a marmoset.[16] In that case, the animal had 8 previous successful pregnancies and delivered a normal youngster at full-term before the discovery on the following day of an abdominally born twin after abdominal palpation of a nonviable fetus in an otherwise healthy, nursing dam. The rupture apparently occurred during labor, and at the time of exploratory laparotomy after the failure to deliver the fetus, the marmoset displayed no clinical signs.[16] Perhaps uterine rupture in NHP is more common than has been reported, but most cases go unrecognized, given that the presentation is more similar to that of the previous case[16] than the current one.

In contrast to the previous case,[16] the uterine rupture in the current case was discovered approximately 8 wk after the most recent parturition, in the face of a deteriorating clinical status. Although placental expulsion was not observed, placental retention after the parturition 8 wk prior to presentation was considered unlikely. In that previous pregnancy, birth occurred overnight; the following morning, the progeny were observed nursing on the dam, and no placenta was evident in the cage. The absence of the placenta was not a cause for concern, given that (in our experience) it is typically consumed by cage mates. The animal was maintained in her family group after an apparently normal parturition, and research staff observed breeding in the intervening period between parturition and clinical presentation. Histopathologically, there was no necrosis or

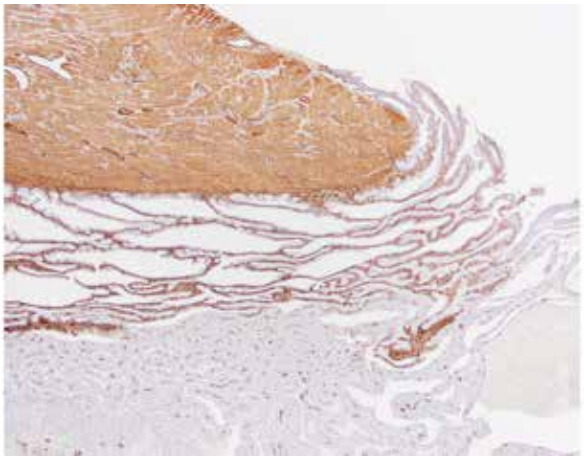

**Figure 4.** At the rupture site, smooth-muscle actin is arranged normally, and the endometrium emerges through the defect. Immunohistochemistry; magnification, 40×.

tissue devitalization suggestive of a retained placenta. Instead, other than the placental tissue that exited the uterine defect, the placenta appeared to be developing normally after a new pregnancy. All of these findings suggest that, as is common for the species and for this particular animal in light of her previous interbirth intervals, postpartum ovulation resulted in conception and pregnancy.

As mentioned earlier, the single most important risk factor for uterine rupture in humans is the presence of a uterine scar, typically associated with a previous cesarean section, manual placental extraction, or other uterine surgery. However, in one survey, 11.5% of patients with uterine rupture had no known uterine scar.[26] The marmoset in the current case had no previous caesarean section, uterine surgery, or history of trauma, and the lack of fibrosis on trichrome staining substantiates the absence of a uterine scar at the site of the rupture. In cases without a known uterine scar, grand parity[8] and the age of the mother[25] have been implicated as contributing factors. Accordingly, this was the fifth pregnancy for the marmoset in this case, and at 5 y of age, she was approaching the maximal average breeding lifespan for captive marmosets.[23] In contrast to human pregnancies, most marmoset pregnancies result in multiple births,[4,23] such that multiparity seems an unlikely contributing factor to uterine rupture in marmosets. Although rupture usually occurs at or near full-term in a scarred uterus, primary uterine rupture can occur early in pregnancy.[8] Several published human reports describe early uterine rupture during the first or second trimester.[3,6,13,18] These cases resulted from placenta accreta, a general term used to describe a range of conditions in which an abnormal, firmly adherent placenta implants with some degree of invasion or penetration into the uterus.[5] In the most severe cases, termed placenta percreta, the placenta invades through the serosal layer of the uterus, potentially invading other organs, such as the urinary bladder. We considered this diagnosis in the current case, but the placental tissue was regular and followed the endometrial tissue through the uterine rupture. Although the placenta did emerge through the uterine defect, it did not invade the myometrium, a prerequisite for a diagnosis of placenta accreta.[2] The fact that the endometrium did indeed wrap along the serosal surface indicates a process that took some time to develop, thus accounting for the worsening clinical signs between presentation and surgical intervention.

Subtotal hysterectomy is often the treatment of choice in human patients with uterine rupture and significant hemorrhage,[24] but suture repair of the uterus is also possible and preserves the woman's reproductive future.[1] Considering that a definitive diagnosis had not been reached and that neoplasia remained a possible differential at the time of surgery in the current case, we elected total ovariohysterectomy without considering or evaluating alternatives, in an effort to save the life of the nursing dam. Had a presurgical diagnosis been made, a more conservative approach might have been possible to preserve the reproductive ability of this marmoset. These approaches may be useful to consider in the future. However, vessel occlusion and resection of the uterine rupture would be technically challenging in light of the small size of marmosets. Furthermore, the mortality rate after conservative treatment reportedly is 4 times higher than that after immediate hysterectomy.[7] In cases of excessive bleeding secondary to uterine rupture, hysterectomy is likely to remain the treatment of choice to preserve the life of the dam.[2,15]

In conclusion, we describe uterine rupture in a common marmoset in early pregnancy. The primary clinical signs were weight loss and an abdominal mass, and ovariohysterectomy was curative. The cause of the uterine rupture could not be identified, but the animal's age and previous pregnancies might be contributing factors. Uterine rupture, although rare, should be considered in any breeding female marmoset with the acute onset of significant weight loss.

## References


1. **Al Sakka MA, Hamsho A, Khan L.** 1998. Rupture of the pregnant uterus— a 21-y review. Int J Gynaecol Obstet **63:**105–108.
2. **American College of Obstetricians and Gynecologists.** [Internet]. 2012. Committee opinion 529: placenta accreta. [Cited 3 August 2015]. Available at: http://www.acog.org/Resources-And-Publications/Committee-Opinions/Committee-on-Obstetric-Practice/Placenta-Accreta.
3. **Archer GE, Furlong FA.** 1987. Acute abdomen caused by placenta accreta in the 2nd trimester. Am J Obstet Gynecol **157:**146–147.
4. **Ash H, Buchanan-Smith HM.** 2014. Long-term data on reproductive output and longevity in captive female common marmosets (*Callithrix jacchus*). Am J Primatol **76:**1062–1073.
5. **Benirschke K, Burton GJ, Baergen RN.** 2012. Pathology of the human placenta, 6th ed. New York (NY): Springer.
6. **Esmans A, Gerris J, Corthout E, Verdonk P, Declercq S.** 2004. Placenta percreta causing rupture of an unscarred uterus at the end of the first trimester of pregnancy: case report. Hum Reprod **19:**2401–2403.
7. **Fox H.** 1972. Placenta accreta, 1945–1969. A review. Obstet Gynecol Surv **27:**475–490.
8. **Gibbins KJ, Weber T, Holmgren CM, Porter TF, Varner MW, Manuck TA.** 2015. Maternal and fetal morbidity associated with uterine rupture of the unscarred uterus. Am J Obstet Gynecol **213:** 382.e1–382.e6.
9. **Hobson BM, Hobbs KR.** 1975. Abnormal fetal development in the marmoset (*Callithrix jacchus*). J Reprod Fertil **44:**323–324.
10. **Institute for Laboratory Animal Research.** 1992. Recognition and alleviation of pain and distress in laboratory animals. Washington (DC): National Academies Press.
11. **Institute for Laboratory Animal Research.** 2011. Guide for the care and use of laboratory animals. Washington (DC): National Academies Press.
12. **Kieser KE, Baskett TF**. 2002. A 10-y population-based study of uterine rupture. Obstet Gynecol**100:** 749–753.

13. **Kinoshita T, Ogawa K, Yasumizu T, Kato J.** 1996. Spontaneous rupture of the uterus due to placenta percreta at 25-w gestation: a case report. J Obstet Gynaecol Res **22:**125–128.
14. **Kishi N, Sato K, Sasaki E, Okano H.** 2014. Common marmoset as a new model for neuroscience research and genome-editing technology. Dev Growth Differ **56:**53–62.
15. **LeMaire WJ, Louisy C, Dalessandri K, Muschenheim F.** 2001. Placenta percreta with spontaneous rupture of an unscarred uterus in the 2nd trimester. Obstet Gynecol **98:**927–929.
16. **Lunn SF.** 1985. Uterine rupture during labour in a common marmoset (*Callithrix jacchus*). Vet Rec **116:**266–267.
17. **Mansfield K.** 2003. Marmoset models commonly used in biomedical research. Comp Med **53:**383–392.
18. **Nagy PS.** 1989. Placenta percreta induced uterine rupture and resulted in intraabdominal abortion. Am J Obstet Gynecol **161:**1185–1186.
19. **Ofir K, Sheiner E, Levy A, Katz M, Mazor M.** 2004. Uterine rupture: differences between a scarred and an unscarred uterus. Am J Obstet Gynecol **191:**425–429.
20. **Richter CB, Lehner NDM, Henrickson RV.** 1984. Primates, p 298–393. In: Fox JG, Cohen BJ, Loew FM, editors. Laboratory animal medicine. San Diego (CA): Academic Press.
21. **Rutherford JN.** 2012. Toward a nonhuman primate model of fetal programming: phenotypic plasticity of the common marmoset fetoplacental complex. Placenta **33 Suppl 2:**e35–e39.
22. **Sweeten KM, Graves WK, Athnassiou A.** 1995. Spontaneous rupture of the unscarred uterus. Am J Obstet Gynecol **172:**1851–1855.
23. **Tardif SD, Smucny DA, Abbott DH, Mansfield K, Schultz-Darken N, Yamamoto ME.** 2003. Reproduction in captive common marmosets (*Callithrix jacchus*). Comp Med **53:**364–368.
24. **Turner MJ.** 2002. Uterine rupture. Best Pract Res Clin Obstet Gynaecol **16:**69–79.
25. **Wu S, Kocherginsky M, Hibbard JU.** 2005. Abnormal placentation: 20-y analysis. Am J Obstet Gynecol **192:**1458–1461.
26. **Zwart JJ, Richters JM, Ory F, deVries JI, Bloemenkamp KW, van Roosmalen J.** 2008. Severe maternal morbidity during pregnancy, delivery, and puerperium in the Netherlands: a nationwide population-based study of 371,000 pregnancies. Br J Obstet Gynecol **115:**842–850.