Lung Lobe Torsion in an Adult Male Common Marmoset (Callithrix jacchus)

Case Report: Lung Lobe Torsion in an Adult Male Common Marmoset (*Callithrix jacchus*)

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Abstract

A 6-y-old, intact, pair-housed male common marmoset (*Callithrix jacchus*) presented with acute onset dyspnea and tachypnea immediately after sedation with alfaxalone, although a history of gradual weight loss initiated the sedation. Thoracic radiographs revealed significant right lung consolidation with a vesicular gas pattern in the right caudodorsal lung field, pleural effusion, and dorsal displacement of the heart. Due to the animal's unstable condition and poor prognosis, euthanasia was elected. At necropsy, the cranial and middle lobes of the right lung were homogenously dark red-brown, enlarged, edematous, and twisted around its longitudinal axis at the hilus. The left lung lobes were pale pink and slightly edematous. Based on clinical and gross necropsy findings, acute torsion of the right cranial and middle lung lobes with lobar infarction was diagnosed. Predisposing conditions for lung lobe torsion include trauma, neoplasia, pulmonary disease, previous thoracic surgery, or diaphragmatic hernia, none of which were apparent in this case. Initial therapy for lung lobe torsion (or LLT) should stabilize and treat for underlying conditions, with prompt surgical resection as the treatment of choice. To our knowledge, this is the first report of lung lobe torsion in an experimentally unmanipulated New World monkey.

Abbreviations and Acronyms:
Lung lobe torsion (LLT)

Introduction

Lung lobe torsion (LLT) is a rare and life-threatening condition in mammals, including humans, that occurs when a lung lobe rotates on its longitudinal axis, usually at the level of the hilus. This torsion causes occlusion of the bronchus and pulmonary veins, however arterial circulation is maintained, and may lead to congestion, edema and necrosis if the torsion remains unresolved.[20] LLT can occur spontaneously, though underlying conditions such as respiratory disease, history of thoracic surgery, pneumothorax, and trauma, that may change the spatial relationship among lung lobes, are associated with increased risk of developing LLT.[8,13] While there have been multiple case reports of LLT in companion dogs and cats, the occurrence of LLT in an experimentally unmanipulated laboratory animal has not yet been reported.[12,14,19] Here we describe the clinical progression of a spontaneous LLT in a laboratory-reared adult male common marmoset; to our knowledge, this is the first report of LLT in a New World primate. Because small nonhuman primates like marmosets are increasingly used in pulmonary disease research due to their homologous parenchymal and bronchial architecture to humans[4], knowledge of their respiratory pathology is exceptionally important.

Case Report

A 6-y-old, 331-g, pair-housed male common marmoset with a history of declining body weight (approximately 10% over a 3-mo period) presented for sedated physical examination, weight measurement, and blood collection. The animal was part of a breeding colony (*n* =12 breeding pairs) housed in an AAALAC-accredited institution on an animal use protocol approved by the MIT Committee on Animal Care, and was housed and maintained according to the standards in the Animal Welfare Act & Regulations and the *Guide for the Care and Use of Laboratory Animals*.[1,2,9] This marmoset was used exclusively for breeding, without experimental manipulation, and was housed in an 57.875 in x 30.5 in x 30.5 in enriched stainless steel and polycarbonate cage in a housing room maintained at 74.0 +/- 2.0°F, with a relative humidity of 30% to 70% and a 12:12-h light:dark cycle. Diet consisted of extruded biscuits (Teklad New World Primate Diet 8794, Envigo, Madison, WI, USA) soaked lightly in water, supplemented with washed fruits and vegetables, yogurt, eggs, beans, cottage cheese, ZuPreem canned diet (Premium Nutritional Products, Inc., Shawnee, KS), and mealworms. Reverse osmosis dechlorinated water was provided *ad libitum*. Health monitoring for marmosets in the colony consists of a complete annual physical, hematologic, and biochemical evaluation. In addition, the colony is monitored semi-annually for the presence of pathogenic bacteria and parasites. Animals were seronegative for squirrel monkey CMV, *Saimiriine herpesvirus 1*, *Saimiriine herpesvirus 2*, and measles virus upon arrival to the facility (C panel, VRL Laboratories, San Antonio, TX). At least twice daily, veterinary staff examine marmosets for injuries and for changes in behavior and fecal output. Daily health records are maintained for each animal with clinical signs necessitating veterinary attention.

To further evaluate the animal for the chronic weight loss, a sedated examination was scheduled. However, lethargy and increased respiratory effort were noted upon removing the animal from the cage weight for sedation. Immediately after sedation (6 mg/kg IM alfaxalone, Alfaxan, Jurox, Inc., Kansas City, MO), the animal's dyspnea worsened, and flow-by oxygen with facemask (at 2 L/min) was initiated. On physical exam, the animal had pale mucous membranes, reduced body condition (body condition score, 2 of 5), as well as an increased respiratory effort and rate (60-80 bpm). Decreased bronchovesicular sounds and muffled heart sounds were ausculted over the right thorax. No external lesions or evidence of trauma were observed.

Thoracic radiographs, performed in right and left lateral and ventrodorsal views (Toshiba Rotanode™ at 40kVp and 3.75 mAs), revealed significant right lung consolidation with a vesicular emphysema pattern in the right caudodorsal lung field (Figure 1). The costophrenic angle also appeared blunted, suggesting a mild amount of pleural effusion within the pleural space. The heart was dorsally displaced. The animal received furosemide (4mg/kg IM, Lasix, Merck Animal Health, Madison, NJ) and Dexamethasone-SP (2mg/kg IM, MWI, Boise ID), was intubated with a 1.5 mm endotracheal tube and was administered 100% O_2 (at 300 ml/min). The animal's heart rate, pulse rate, temperature, and oxygen saturation were continuously monitored (SystemVET® Vet Trends® Series 6400 monitor configured with Covidien Nellcor SpO_2 monitor, Ivy Biomedical Systems, Inc, Branford, CT). Persistent hypoxemia was noted (SpO_2 75-77%). Ultrasound (Sonoscape S9, Universal Solutions, Inc., Bedford Hills, NY) using a 4-16 MHz 52mm Linear "T" probe showed consolidated lung fields with fibrin tags and pleural fluid. Differential diagnoses included pneumonia with severe consolidation, neoplasia, pulmonary hemorrhage from trauma or coagulopathy, pyothorax, and foreign body. Due to poor prognosis,

euthanasia was elected. Prior to euthanasia, blood was collected via the femoral vein (approximately 1ml) for an in-house complete blood count in an EDTA tube and serum separator tube for chemistry submitted to IDEXX Bioresearch (North Grafton, MA); full chemistry findings are listed in Table 1. Pertinent serum chemistry findings included an elevated creatinine kinase (1036 U/L), hypoalbuminemia (2.8 g/dL) and hypoglobulinemia (1.4 g/dL). BUN and creatinine were mildly elevated (31 mg/dL and 0.4 mg/dL, respectively). The animal was hyperglycemic (660 mg/dL) and hyperphosphatemic (12.2 mg/dL) with an elevated anion gap (26 mEq/L). All other values were within published reference intervals.[16] Complete blood count revealed a mild microcytic normochromic anemia (RBC 3.71 M/μL; Hgb 8.5 g/dL; MCV 65.1 fl; MCHC 35.1 g/dL; RDW 14.4%) and thrombocytosis (458 K/μL) (HemaVet 950FS®, Drew Scientific, Inc., Oxford, CT).

Thoracocentesis in the left 7th intercostal space obtained approximately 0.2ml of dark red-brown serous fluid. The fluid was moderately proteinaceous (4.2 g/dL), with few (0-3) RBCs/hpf, 1,800 WBCs/μL (40% neutrophils, 38.5% lymphocytes), consistent with a modified transudate. Bacterial aerobic and anaerobic cultures of the fluid were negative. Directly after intubation, the animal was kept anesthetized on sevoflurane (up to 2%), extubated, and then given ketamine hydrochloride (7mg/kg IM, Putney, Inc., Portland, ME) and midazolam (0.2mg/kg IM, Fresenius Kaba USA, LLC, Lake Zurich, IL). The animal was euthanized approximately 2 hours after presentation via terminal perfusion with 4% paraformaldehyde, followed by immediate necropsy.

On gross necropsy, the cranial and middle lobes of the right lung were homogeneously dark red-brown, enlarged, edematous, and twisted around its longitudinal axis at the hilus (Figure 2). The left lung lobes were pale pink and slightly edematous. There was an associated left lateral displacement of the heart. The liver was enlarged and compressed against the diaphragm, but no diaphragmatic herniation was noticed. Tissues were fixed in 10% neutral buffered formalin, embedded in paraffin, sectioned at 5μm, and stained with hematoxylin and eosin. On histopathological examination, the right cranial and medial lung lobes were compressed and coiled around the bronchial bifurcation with clear separation between unaffected parenchyma and severely affected pulmonary parenchyma (Figure 3A). Moderate pleural thickening with reactive mesothelial proliferation was also noted (Figure 3B). The affected infarcted parenchyma was characterized by severe effacement of normal architecture by massive hemorrhage, alveolar septal necrosis, proteinaceous fibrinous material, and scattered degenerate cellular debris (Figure 3C). Comparatively, the left lung lobes were atelectatic but otherwise normal in appearance (Figure 3D). Additional histologic findings included a mild bilateral progressive glomerulonephropathy with associated minimal multifocal tubular degeneration, regeneration and hyperplasia of tubular epithelia, and occasional proteinaceous casts in the tubules. Based on clinical presentation, gross necropsy, and histopathological findings, acute torsion of the right cranial and middle lung lobes with lobar infarction was diagnosed.

Discussion

This is the first report detailing LLT in an adult male common marmoset. This animal developed a right cranial and middle LLT with no known history of chest disease and was experimentally unmanipulated. Aside from the acute onset of tachypnea and dyspnea, the animal had no relevant medical history other than chronic weight loss. Routine preventative health testing performed prior to the event, including fecal examination, rectal culture, and bloodwork, revealed no significant findings. In humans and animals, LLT presents similarly, with the

predominant clinical signs being lethargy, progressive dyspnea, coughing, anorexia, and vomiting.[8,15] Physical examination frequently reveals pale mucous membranes, dull cardiopulmonary sounds on auscultation, pain on abdominal palpation, pyrexia, and cyanosis.[8] Complete blood count and chemistry findings are often nonspecific, and can include mild anemia, hypoproteinemia, and elevated creatinine, as seen in this case.[8] The physical exam and laboratory test findings of the marmoset affected in this case suggest that this species presents similarly to other mammals, including humans.

Imaging results were consistent with typical findings in other mammals presenting with LLT, including pleural effusion, lung consolidation, and an emphysematous vesicular pattern in the affected lung lobe.[5,7] The modified transudate obtained from thoracocentesis is consistent with some reports in domestic species, though suppurative inflammation and hemorrhage have also been noted, and thus the type of effusion generally does not help identify the cause.[5] While radiographic and ultrasonographic techniques are used to aid diagnosis of LLT, the findings can be non-specific. Though not accessible at our institution in the event, other imaging modalities such as computed tomography (CT) and bronchoscopy can be more confirmative.[17] In particular, CT is a critical diagnostic tool in cases of LLT; an abrupt ending bronchus and enlargement and consolidation of the torsed lobe are the most common diagnostic findings.[3,5,17] Definitive diagnosis of LLT is made by either exploratory thoracotomy or at necropsy.

Initial therapy for LLT is symptomatic and involves relieving respiratory distress by removing pleural fluid, if necessary, and providing supplemental oxygen, immediately followed by treatment of any concurrent respiratory disease, followed up with prompt surgical resection of the affected lobe(s) as the treatment of choice. A thoracotomic approach in canines is recommended to best visualize and remove the affected lobe, though resection via thoracoscopy has been reported.[6,11] Reported post-operative complications include recurrence of LLT, pneumonia, infection, and chylothorax.[8,18] In companion animal patients, prognosis is fair with spontaneous LLT to guarded if the LLT is associated with other intrathoracic pathology and longer time to lung lobe resection.[14]

Histopathologically, the lung lesions were consistent with acute intra- and extrapulmonary hemorrhage and lobar infarction, supporting the right and cranial middle lobar infarction seen grossly. The reactive changes in the pleura and surrounding mediastinal adventitial tissue in the thoracic cavity are consistent with leakage of blood and protein contents from affected lung lobes causing reactive mesenchymal early fibroplasia and *de novo* hematopoiesis. This pathology is consistent with the observed clinical signs of respiratory distress that necessitated immediate action in this case. These findings are consistent with previous histologic analyses of dogs and cats with LLT.[5] Interestingly, both the right cranial and middle lobes were torsed in this case. In dogs and cats, the most common affected lobes are the right middle and left cranial lobes, and torsion of multiple lobes rarely occurs.[5,12,19] There is no characteristic affected lobe reported in humans.[13] It remains unclear what presentation may be most common in the marmoset since this is the first report of this morbidity occurring in a nonhuman primate. The progressive bilateral glomerulonephropathy noted on histopathology was likely spontaneous and commonly reported in marmosets, and thus considered an incidental finding.[10]

The cause of the lung lobe torsion in this case remains unclear, and most likely was spontaneous given the lack of history of chronic respiratory disease, experimental manipulation, or injury, and acute onset of clinical signs. Animal movement during capture for sedation may have been an inciting factor. It is unlikely that a fight between cage-mates instigated pathology,

as there were no injuries or observed behaviors of incompatibility noted between the pair. There is a paucity of published information on this condition, as it is exceptionally rare and has not yet been reported in captive primates.

In conclusion, we report the first case of spontaneous lung lobe torsion in a nonhuman primate. The primary clinical signs were acute onset tachypnea and persistent dyspnea, with similar radiographic and ultrasonographic findings reported in other species. Although this condition is rare in all mammals, it should be included in the differential diagnoses for marmosets with acute dyspnea, despite a lack of history of respiratory disease. We recommend including chest radiographs to screen for underlying causes of respiratory distress and disease as part of preventative health exams. Though subtle, the clinical presentation and radiographic findings can suggest lung lobe torsion and prompt workup, including a CT scan and prompt surgical intervention.

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References

1. **Amended. AWA as**. 2017. Animal Welfare Act as Amended. 7 USC §2131–2156.
2. **Animal Welfare Regulations**. Animal Welfare Regulations. 2008. 9 CFR § 3.129.
3. **Choi M, Lee N, Keh S, Choi H, Yim Y, Kim H, Jung J, Choi M**. 2015. Usefulness of CT imaging for segmental lung lobe torsion without typical radiographic imaging in a Pomeranian. J Vet Med Sci **77**:229–231.
4. **Curths C, Knauf S, Kaup F**. 2014. Respiratory Animal Models in the Common Marmoset (Callithrix jacchus). Vet Sci **1**:63–76.
5. **D'Anjou MA, Tidwell AS, Hecht S**. 2005. Radiographic diagnosis of lung lobe torsion. Vet Radiol Ultrasound **46**:478–484.
6. **Duan L, Chen X, Jiang G**. 2012. Lobar torsion after video-assisted thoracoscopic lobectomy: 2 case Reports. Thorac Cardiovasc Surg **60**:167–169.
7. **Felson B, Hung T-T, Chen T-Y, Liu H-C, Nichols F, Trastek V, Pairolero P**. 1987. Lung torsion: radiographic findings in nine cases. Radiology **162**:631–638.
8. **Gicking J, Aumann M**. 2011. Lung lobe torsion. Compend Contin Educ Vet **33**:E4.
9. **ILAR**. 2011. The Guide for the Care and Use of Laboratory Animals. Eighth. Washington, D.C.: National Academies Press.
10. **Isobe K, Adachi K, Hayashi S, Ito T, Miyoshi A, Kato A, Suzuki M**. 2012. Spontaneous Glomerular and Tubulointerstitial Lesions in Common Marmosets (Callithrix jacchus). Vet Pathol **49**:839–845.
11. **Laksito MA, Chambers BA, Yates GD**. 2010. Thoracoscopic-assisted lung lobectomy in the dog: Report of two cases. Aust Vet J **88**:263–267.
12. **Millard RP, Myers JR, Novo RE**. 2008. Spontaneous Lung Lobe Torsion in a Cat. J Vet Intern Med **22**:671–673.
13. **Moser ESJ, Proto A V**. 1987. Lung torsion: case report and literature review. Radiology **162**:639–643.

14. **Neath PJ, Brockman DJ, King LG**. 2000. Lung lobe torsion in dogs: 22 cases (1981-1999). J Am Vet Med Assoc **217**:1041–1044.

15. **Oliveira C, Zamakhshary M, Abdallah MR, Miller SF, Langer JC, Wales PW, Dasgupta R**. 2007. Lung torsion after tracheoesophageal fistula repair: a case report and review of literature. J Pediatr Surg **42**:e5–e9.

16. **Rensing, S., Oerke AK**. 2005. Husbandry and management of New World species: marmosets and tamarins. p 145–162. In: Wolfe-Coote S, editor. The Laboratory Primate. New York: Elsevier.

17. **Seiler G, Schwarz T, Vignoli M, Rodriguez D**. 2008. Computed tomographic features of lung lobe torsion. Vet Radiol Ultrasound **49**:504–508.

18. **Spranklin DB, Gulikers KP, Lanz OI**. 2003. Recurrence of spontaneous lung lobe torsion in a pug. J Am Anim Hosp Assoc **39**:446–451.

19. **Sweeney, J, Oura, T, Wulster, K, Aarsvold S**. 2016. What Is Your Diagnosis? JAVMA **248**:1235–1237.

20. **Tomashefski, J.F., Dail DH**. 2008. Dail and Hammar's Pulmonary Pathology Volume I: Nonneoplastic Lung Disease. Third Edition. (Tomashefski JF, Cagle PT, Farver CF, Fraire AE, editors.). New York: Springer Science+Business Media, LLC.

Figure Legends

Figure 1. Right lateral (A), left lateral (B), and ventrodorsal (C) thoracic radiographs demonstrating right middle and cranial LLT. A vesicular emphysema pattern (circles) is evident in the affected lung lobes. Pleural effusion is noted bilaterally with the heart raised dorsally in the ventrodorsal view.

Figure 2. Evidence of right cranial and middle lung lobe torsion *in situ* (A) and after removal of the pluck (B). The cranial and middle lobes of the right lung are homogeneously dark red-brown, enlarged, and edematous (arrows). The left (unaffected) lung lobes are pale pink, non-collapsible and edematous.

Figure 3. Lung (histological sections): (A) Demarcation between infarcted (arrowhead) and non-infarcted (asterisk) lung parenchyma with kinking of the main bronchial stem to the right affected cranial lobe with mild bronchial epithelial thickening (arrow); hematoxylin & eosin stain; magnification, 2X. (B) Subcapsular distention of the affected lung filled with hemorrhage and moderate amounts of fibrin and pleural thickening; hematoxylin & eosin stain; magnification, 10X. (C) Pulmonary necrosis with acute diffuse hemorrhage of the right cranial lung lobe. Numerous red blood cells are present in the alveolar and interstitial spaces associated with acute edema, and in some areas, moderate fibrin formation; hematoxylin & eosin stain; magnification, 200X. (D) The left lung lobe parenchyma has diffuse atelectasis but is otherwise normal; hematoxylin & eosin stain; magnification, 200X.

Tables

Table 1. Serum chemistry results for a 6-y-old male common marmoset with lung lobe torsion

Parameter	Result	Reference range[a,b]
Alkaline phosphatase (U/L)	34	125 ± 64
AST (SGOT) (U/L)	82	112 ± 112
ALT (SGPT) (U/L)	21	13 ± 24
Creatine Kinase (U/L)	**1036**	543 ± 0
Total Protein (g/dL)	**4.20**	5.1 ± 0.6
Albumin (g/dL)	**2.80**	6.8 ± 1.0
Globulin (g/dL)	1.40	1.7 ± 0.5
Blood urea nitrogen (mg/dL)	**31.00**	19.5 ± 5
Creatinine (mg/dL)	0.40	0.7 ± 0.2
Cholesterol (mg/dL)	92.00	176 ± 73
Glucose (mg/dL)	**660.00**	177 ± 65
Calcium (mg/dL)	8.30	9.5 ± 1.1
Phosphorus (mg/dL)	**12.20**	5.3 ± 1.9
Chloride (mEq/L)	101.00	103 ± 11
Potassium (mEq/L)	3.00	4.9 ± 2.6
A/G Ratio	2.00	
Sodium (mEq/L)	144.00	147 ± 8
Na/K Ratio	48.00	
Anion Gap (mEq/L)	**26.00**	5.0 ± 1.5

[a]Mean ± standard deviation for adult common marmosets (*Callithrix jacchus*) were obtained from Rensing & Oerke, 2005.
[b]Mean ± standard deviation from MIT marmoset colony (Adult (>2 yr) Indoor n=41 (unpublished)).