Journal of Feline Medicine and Surgery (2009) ■■, ■■–■■
doi:10.1016/j.jfms.2009.06.003

ELSEVIER

jfms

CASE REPORT
Reconstruction of a large diaphragmatic defect in a kitten using small intestinal submucosa (SIS)

Angelo A Andreoni Dr Med Vet*, **Katja Voss** Dr Med Vet Diplomate ECVS

Clinic for Small Animal Surgery, Vetsuisse Faculty, University of Zurich, Winterthurerstrasse 260, 8053 Zurich, Switzerland

A double-layer sheet of small intestinal submucosa (SIS) was used to reconstruct a large chronic diaphragmatic defect in a 4-month-old kitten. The SIS graft was easy to use, postoperative recovery was uneventful, no side effects of the SIS implant were observed, and the SIS graft resulted in restoration of normal clinical function while allowing growth of the kitten without restriction of chest wall development. Herniation of fat through the caval hiatus was diagnosed 29 months postoperatively on a CT scan. The cat was free of clinical signs.

Date accepted: 23 June 2009

A presumably 4-month-old, male, European shorthair cat with a body weight of 1.2 kg was presented because of inappetence, chronic dyspnea and respiratory distress. The owners had found the kitten when it was approximately 6 weeks old. The cat started to display dyspnea 5 weeks before presentation; the owners noticed that the cat never rested lying on its side because it would develop respiratory distress when trying to do so. A barium contrast study performed by the referring veterinarian showed displacement of intestinal loops into the thoracic cavity. A diaphragmatic hernia was diagnosed and the patient was referred for surgery to the author's clinic. The cat showed marked inspiratory and expiratory dyspnea at the time of admission, and had a reduced body condition. Hematology and blood chemistry were unremarkable.

The patient was treated with an intravenous (IV) infusion of lactated Ringer's solution at 2 ml/kg/h, buprenorphine (Temgesic; Essex Chemie: 14 μg/kg IV q 4 h), and oxygen (oxygen box, 2 l/min flow) over night. Anesthesia was induced the next morning with midazolam (Dormicum; Roche: 0.02 ml/kg IV), and propofol (Propofol MCT; Fresenius: 4 mg/kg IV) after pre-oxygenation for 5 min. Anesthesia was maintained with isofluorane (Isoflo; Abbot) in oxygen (high-flow 1 l/min, then low-flow 0.1 l/min) with a semi-circular half-closed system under controlled ventilation, and a constant rate infusion of fentanyl (5 μg/kg/h IV). Intermittent positive pressure ventilation (10–15 mm H_2O) with a positive end-expiratory pressure of 3–5 mm H_2O was maintained throughout surgery. Cefazoline (Kefzol; Teva Pharma: 22 mg/kg IV) was administered preoperatively, and the intraoperative fluid rate was 10 ml/kg/h.

Exploratory coeliotomy through a ventral midline approach revealed a large defect of the ventral portion of the diaphragm (Fig 1a). Small intestinal loops, omentum, liver and part of the stomach were displaced into the thoracic cavity, and were carefully repositioned into the abdomen. The diaphragmatic edges were blunt and retracted, and the central tendon could not be identified. There was no evidence of a hernial sac or of a connection of the diaphragmatic edges with the pericardium. The size of the defect made primary closure impossible. The margins of the diaphragmatic defect were debrided by excision of a thin tissue layer with a number 15 scalpel blade. A 4-ply small intestinal submucosa (SIS) sheet (Vet BioSIS T; Cook Biotech, Wisconsin) was rehydrated in sterile saline solution for 3 min, was then folded to form a double-layer sheet and cut to the desired size, overlapping the defect by approximately 1 cm. The SIS was sutured on to the diaphragmatic defect with preplaced simple interrupted sutures, using polydioxanone 4–0 (Fig 1b). Care was taken not to compress the caudal vena cava during closure. A pediatric feeding tube was placed in the right hemithorax as a thoracic drain. The post surgical pneumothorax was only partially evacuated to allow for slow expansion of the lungs. A routine coeliotomy closure was performed.

Buprenorphine (10 μg/kg IV) was administered every 4 hours for postoperative analgesia. The patient was kept in the oxygen cage for 24 h after surgery, and the thoracic drain was removed the following

*Corresponding author. Tel: +41-44-6358437; Fax: +41-44-6358944. E-mail: aandreoni@vetclinics.uzh.ch

1098-612X/09/■■■■■■+■■ $36.00/0

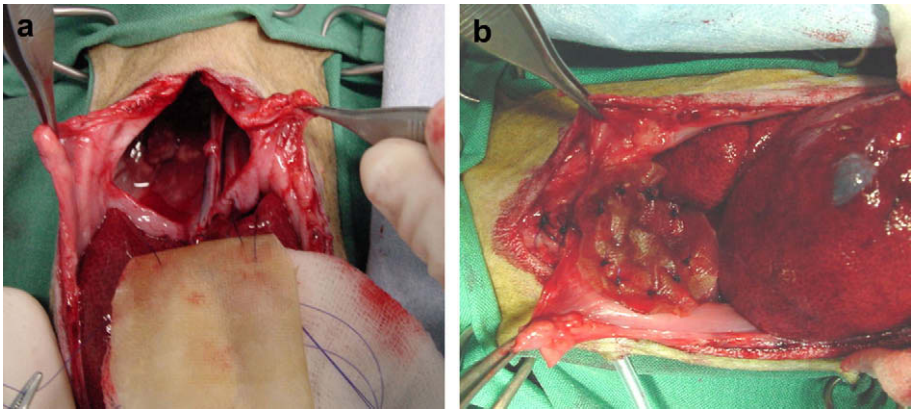

Fig 1. Intraoperative photographs. (a) Note the large diaphragmatic defect, extending from the sternum and ventral aspect of the rib cage to the hiatus of the caudal vena cava, comprising the entire ventro-central part and more than half of the width of the diaphragm. (b) A double-layer SIS has been sutured loosely across the defect, taking care not to compress the caudal vena cava.

morning. The cat was released from the hospital after 3 days.

One week after surgery, follow-up latero-lateral and ventro-dorsal thoracic radiographs revealed a continuous diaphragm. However, there was an alteration of the diaphragmatic outline around the esophageal hiatus, which was interpreted as a possible sliding, hiatal or paraoesophageal hernia. The cat displayed no clinical abnormalities related to these radiographic findings. Six months later the cat was in a good body condition, had grown to a body weight of 3.5 kg, and was free of clinical signs. Follow-up thoracic radiographs showed a nearly normal diaphragmatic shape and no signs of herniation of abdominal contents (Fig 2). Twenty-nine months after surgery the cat weighed 4.8 kg, and was still free of clinical signs. Follow-up thoracic radiographs performed at that time revealed an intrathoracic soft tissue opacity caudal to the heart and ventral to the caudal vena cava. Herniation of abdominal fat through the ventral caval hiatus was diagnosed by computed tomography (CT) scan examination (Fig 3). No further investigations were undertaken as the cat was free of clinical signs.

This case report describes the use of an SIS graft to fill a large diaphragmatic defect in a kitten. Diaphragmatic hernias in cats are caused by trauma in approximately 80% of cases, 5–10% are congenital, and the remaining are of unknown origin.[1,2] The lack of a complete history, and the appearance of the defect made it difficult to differentiate a chronic traumatic from a congenital hernia. Overall, a chronic traumatic diaphragmatic hernia was considered more likely; although the central tendon of the diaphragm seemed to be missing, there was no hernial sac indicating a congenital diaphragmatic hernia, and the absence of a connection of the defect with the pericardium excluded a peritoneopericardial hernia.

Herniorrhaphy by primary closure is usually feasible, but in congenital or chronic cases atrophy and contraction of the diaphragmatic edges may produce a defect in which primary closure cannot be achieved.[3,4] If primary closure cannot be accomplished, other

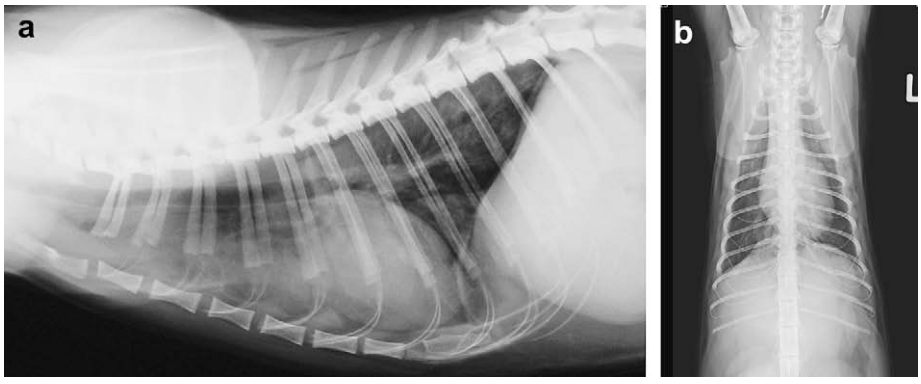

Fig 2. Six-month follow-up radiographs of the thorax. The diaphragm has a normal contour on the latero-lateral radiographs. (a) A slightly abnormal shape with bulging of the left aspect of the diaphragm can be seen on ventro-dorsal radiographs. (b) There are no signs of herniation of abdominal contents.

Please cite this article in press as: Angelo A Andreoni, Voss K, Reconstruction of a large diaphragmatic defect in a kitten using small intestinal submucosa (SIS), J Feline Med Surg (2009), doi:10.1016/j.jfms.2009.06.003

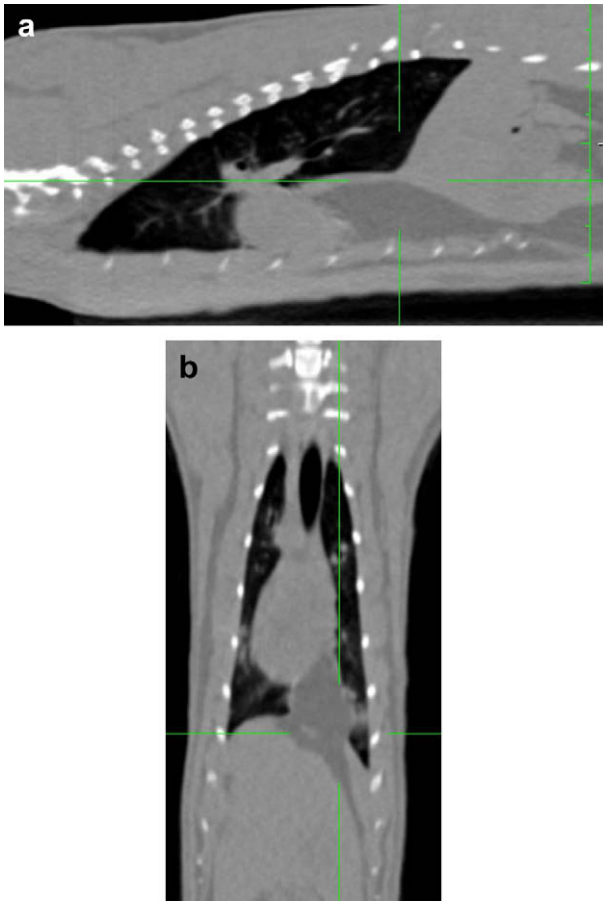

Fig 3. CT-scan with contrast 29 months postoperatively. (a) Sagittal image showing discontinuity of the diaphragm ventral to the caudal vena cava, and herniation of fat into the thoracic cavity. (b) Longitudinal image, showing the caudal vena cava, and herniation of abdominal fat adjacent to it.

means of repair include use of autogenous grafts like omentum, liver or fascia,[3] closure of the defect with muscle flaps,[5] or insertion of prosthetic materials, such as polypropylene mesh, polytetrafluoroethtylene patch or lyophilized dura mater.[6–8]

Synthetic prosthetic materials used for the repair of diaphragmatic defects in infants do not grow with the patient, and their use can be associated with restricted chest wall development and recurrence of the hernia.[7–9] SIS grafts are absorbed with time and the newly formed tissue allows unrestricted growth.[8,10] Clinically, SIS has been applied in neonates for the repair of congenital diaphragmatic hernia and diaphragmatic agenesis.[8] Because of the growth potential of our patient we selected to insert an SIS graft rather than another prosthetic material to occlude the diaphragmatic defect. The kitten grew from 1.2 kg body weight at the time of surgery to 4.8 kg at the latest follow-up at 29 months, without the SIS graft resulting in constriction of the diaphragm or restriction of chest wall development. The use of autogenous grafts like fascia lata[11,12] or flaps of the thoracoabdominal and latissimus dorsi alone or in combination with the serratus anterior muscle in pediatric surgery[13] or of the internal oblique and transversus abdominis muscles in dogs[5,14] would also minimize growth-related complications. However, these are rather complex techniques with prolonged operating times, which could be detrimental in critically ill patients.[8,14]

SIS shows promise as a graft material because it is biologically safe and easy to handle, has sufficient tensile strength, is infection-resistant, and allows remodeling of replaced tissue.[7,8] Angiogenesis and host cell migration into the SIS three-dimensional collagen matrix followed by differentiation and remodeling can result in tissue that is structurally and functionally similar to the original tissue.[6,7] SIS has mostly been used in tissue engineering studies to create de novo tissues, including diaphragm,[9] abdominal wall,[6,15,16] urinary bladder,[7,17] tendons,[18] and blood vessels.[19] Descriptions of the clinical application of SIS are rare in both human and animal surgery. In veterinary surgery, clinical use of SIS grafts has mainly involved augmentation of tissues or primary reconstructions, rather than application as a defect graft. Clinical studies have shown SIS to be suitable for the repair of full-thickness corneal wounds in dogs, cats, and horses, and for use as conjunctival flaps.[20] In another clinical report, SIS was used in addition to a transversus abdominis muscle flap to repair a large diaphragmatic defect.[14] In this report, the SIS was rather used to minimize the risk of adhesions to the exposed muscle tissue than to provide stability as a primary repair of the defect.[14]

When using an absorbable graft to fill a diaphragmatic defect, the question raises whether the graft will last long enough to allow in-growth of new tissue of sufficient strength. In an experimental study in dogs where SIS was used for repair of perineal hernias, 4-ply SIS sheets were completely remodeled and could not be identified histologically 2 weeks after implantation.[21] This time frame of remodeling and absorption would most likely not be long enough to allow for new tissue bridging a large diaphragmatic defect. However, an in-vivo study in rats with diaphragmatic defects presented evidence of a thin mesothelial surface overlying the SIS patch at 2 weeks after implantation, and the SIS was still present histologically at 4 months.[9] It is possible that absorption of the graft is slower in an area of the body like the diaphragm that is less vascularized as compared to the perineal region where an inserted graft is surrounded by musculature and vessels.[9,21] It also seems that the time to absorption depends on the ply of SIS that is inserted into a diaphragmatic defect: in an experimental study using Beagles a 8-ply SIS could still be histologically recognized 6 months after implantation, while a 4-ply SIS was completely incorporated at that time and could not be identified anymore.[7]

Although surgery was able to restore functional recovery in the kitten in this report without restricting

Please cite this article in press as: Angelo A Andreoni, Voss K, Reconstruction of a large diaphragmatic defect in a kitten using small intestinal submucosa (SIS), J Feline Med Surg (2009), doi:10.1016/j.jfms.2009.06.003

growth of the chest wall, late re-herniation of fat around the caudal vena cava was diagnosed 29 months after surgery. This was identifiable on the 6-month follow-up radiographs. A bimodal distribution of re-herniation has been observed after repair with prosthetic patches in a human study, with the first peak occurring 1–3 months after insertion, and the second between 10–36 months.[8–10] No explanation for the cause was reported in these studies. The amount of falciform fat that was herniated did not affect clinical function in our patient. It is possible that the occlusion of the defect by falciform fat could have prevented herniation of other organs. Adhesion formation between the SIS graft and the liver capsule was observed in experimentally induced defects,[7] which could also have precluded herniation of abdominal organs in the present case.

The exact cause of late re-herniation in our patient remains unknown because we were not able to perform surgical exploration and histopathology of the replaced tissue. The SIS graft was only sutured loosely around the caudal vena cava to avoid compression of the thin-walled vessel. This may have led to incomplete closure of the diaphragm around the hiatus of the caudal vena cava, and may have allowed late herniation of fat. Also a primary insufficiency of the SIS graft cannot be excluded based on diagnostic imaging findings; generalized thinning and multiple defects with liver herniation were noted at necropsy 6 months after surgery in 3/4 patients when a 4-ply SIS was used to graft the diaphragm.[7] These defects were not seen radiographically in any of the cases.[7] It is, therefore, possible that small lesions or defects had been present 6 months postoperatively in our case despite the absence of radiographical signs of re-herniation at that time.

The application of SIS as a defect graft in the repair of a large diaphragmatic defect in a kitten was easy, and allowed unrestricted growth of the diaphragm with the patient. Late re-herniation of falciform fat occurred without impairment of clinical function. Further studies are needed to evaluate if clinical results would be consistent in larger numbers of patients.

References

1. Wilson 3rd GP, Hayes Jr HM. Diaphragmatic hernia in the dog and cat: a 25-year overview. *Semin Vet Med Surg (Small Anim)* 1986; **1**: 318–26.
2. Wilson 3rd GP, Newton CD, Burt JK. A review of 116 diaphragmatic hernias in dogs and cats. *J Am Vet Med Assoc* 1971; **159**: 1142–5.
3. Hunt GB, Johnson KA. Diaphragmatic, pericardial, and hiatal hernia. In: Slatter D, ed. Textbook of small animal surgery 3rd edn. Philadelphia: WB Saunders, 2003: 471–86.
4. Keep JM. Congenital diaphragmatic hernia in a cat. *Aust Vet J* 1950; **26**: 193.
5. Helphrey ML. Abdominal flap graft for repair of chronic diaphragmatic hernia in the dog. *J Am Vet Med Assoc* 1982; **181**: 791–3.
6. Dejardin LM, Arnoczky SP, Clarke RB. Use of small intestinal submucosal implants for regeneration of large fascial defects: an experimental study in dogs. *J Biomed Mater Res* 1999; **46**: 203–11.
7. Sandoval JA, Lou D, Engum SA, et al. The whole truth: comparative analysis of diaphragmatic hernia repair using 4-ply vs 8-ply small intestinal submucosa in a growing animal model. *J Pediatr Surg* 2006; **41**: 518–23.
8. Smith MJ, Paran TS, Quinn F, Corbally MT. The SIS extracellular matrix scaffold-preliminary results of use in congenital diaphragmatic hernia (CDH) repair. *Pediatr Surg Int* 2004; **20**: 859–62.
9. Dalla Vecchia L, Engum S, Kogon B, Jensen E, Davis M, Grosfeld J. Evaluation of small intestine submucosa and acellular dermis as diaphragmatic prostheses. *J Pediatr Surg* 1999; **34**: 167–71.
10. Moss RL, Chen CM, Harrison MR. Prosthetic patch durability in congenital diaphragmatic hernia: a long-term follow-up study. *J Pediatr Surg* 2001; **36**: 152–4.
11. Newman BM, Jewett TC, Lewis A, et al. Prosthetic materials and muscle flaps in the reapair of extensive diaphragmatic defects: an experimental study. *J Pediatr Surg* 1985; **20**: 362–7.
12. Suzuki K, Takahashi T, Itou Y, Asai K, Shimota H, Kazui T. Reconstruction of diaphragm using autologous fascia lata: an experimental study in dogs. *Ann Thoracic Surg* 2002; **74**: 209–12.
13. Samarakkody U, Klaassen M, Nye B. Reconstruction of congenital agenesis of hemidiaphragm by combined reverse latissimus dorsi and serratus anterior muscle flaps. *J Pediatr Surg* 2001; **36**: 1637–40.
14. Liptak JM, Brebner NS. Hemidiaphragmatic reconstruction with a transversus abdominis muscle flap after resection of a solitary diaphragmatic mesothelioma in a dog. *J Am Vet Med Assoc* 2006; **228**: 1204–8.
15. Clarke KM, Lantz GC, Salisbury SK, Badylak SF, Hiles MC, Voytik SL. Intestine submucosa and polypropylene mesh for abdominal wall repair in dogs. *J Surg Res* 1996; **60**: 107–14.
16. Ko R, Kazacos EA, Snyder S, Ernst DM, Lantz GC. Tensile strength comparison of small intestinal submucosa body wall repair. *J Surg Res* 2006; **135**: 9–17.
17. Caione P, Capozza N, Zavaglia D, Palombaro G, Boldrini R. In vivo bladder regeneration using small intestinal submucosa: experimental study. *Pediatr Surg Int* 2006; **22**: 593–9.
18. Gu Y, Dai K. Substitution of porcine small intestinal submucosa for rabbit Achilles tendon, an experimental study. *Zhonghua Yi Xue Za Zhi* 2002; **82**: 1279–82.
19. Lantz GC, Badylak SF, Hiles MC, et al. Small intestinal submucosa as a vascular graft: a review. *J Invest Surg* 1993; **6**: 297–310.
20. Bussieres M, Krohne SG, Stiles J, Townsend WM. The use of porcine small intestinal submucosa for the repair of full-thickness corneal defects in dogs, cats and horses. *Vet Ophthalmol* 2004; **7**: 352–9.
21. Stoll MR, Cook JL, Pope ER, Carson WL, Kreeger JM. The use of porcine small intestinal submucosa as a biomaterial for perineal herniorrhaphy in the dog. *Vet Surg* 2002; **31**: 379–90.

Please cite this article in press as: Angelo A Andreoni, Voss K, Reconstruction of a large diaphragmatic defect in a kitten using small intestinal submucosa (SIS), J Feline Med Surg (2009), doi:10.1016/j.jfms.2009.06.003