Diaphragmatic and perineal hernias associated with cutaneous asthenia in a cat

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- Cutaneous asthenia is a rare hereditary disorder that results in altered strength or extensibility of connective tissues.
- The most common lesions in affected animals are cutaneous fragility and hyperextensibility.
- The diagnosis depends on clinical findings (skin extensibility index) and light and electron microscopic evaluation of affected tissue.
- Surgical repair of hernias can be performed successfully on an affected cat, and healing of the incision can occur without complications.

An 11-year-old neutered male domestic shorthair cat weighing 5 kg (11 lb) was examined for an acute episode of dyspnea. The cat had a 1-month history of coughing when it was handled and had been medically treated for a left-sided reducible perineal hernia for 3 months with a high-fiber diet and stool softeners. Additionally, hyperextensibility of the cat's skin observed since 9 months of age had resulted in a presumptive diagnosis of cutaneous asthenia (similar to **Ehlers-Danlos syndrome [EDS]** in humans). At 10 months of age, the cat created 2 lacerations on the caudal aspect of its head after scratching with its hind limb, and at that time, onychectomy of all digits was performed to prevent further self-trauma.

Evaluation of thoracic and abdominal radiographs revealed gas-filled intestinal loops within the thorax, consistent with a diaphragmatic hernia. Rectal temperature was 38.5°C (101.3°F), pulse was approximately 180 beats/min, and respiration rate was 60 breaths/min. Examination of the cat occasionally resulted in tachypnea. Borborygmus was auscultated in the thorax, although heart sounds could not be discerned. Intestinal loops were not detected via abdominal palpation. A perineal swelling lateral to the left side of the anus was confirmed to be a left-sided reducible perineal hernia via rectal palpation; the right side of the pelvic diaphragm was intact.

The skin on the ventral aspect of the thorax and abdomen was pendulous. There was marked hyperelasticity of the skin in the thoracic and lumbar regions (**Fig 1**). An extensibility index ([vertical height of skin fold divided by body length from the occipital crest to the tail base] × 100; reference limit, < 19%[1]) of 25% was determined to be consistent with dermatosparaxis.

Surgical repair of the diaphragmatic hernia was recommended. The cat was premedicated by administration of morphine (0.11 mg/kg [0.05 mg/lb], IV), atropine (0.02 mg/kg [0.01 mg/lb], IV), and medetomidine (2.2 µg/kg [1.0 µg/lb], IV). Anesthetic induction was achieved by administration of thiopental (6.6 mg/kg [3 mg/lb], IV to effect). Isoflurane and oxygen in a circle breathing circuit were used to maintain anesthesia. Cefazolin (22 mg/kg [10 mg/lb], IV) was administered after induction of anesthesia, prior to the surgical procedure, and repeated every 90 minutes until completion of surgery.

A standard ventral midline celiotomy was performed. The falciform ligament was ligated with 3-0 polydioxanone and transected distally with Metzenbaum scissors. Observations in the abdominal cavity included a large rent in the right dorsal aspect of the diaphragm extending from the dorsal aspect of the right costal part to its mid body at the level of the caval foramen. The right lateral lobe, right medial lobe, and caudate process of the caudate lobe of the liver, as well as the stomach, duodenum, jejunum, spleen, and mesentery, were herniated into the right hemithorax. Adhesions and pleural effusion were not detected at the time of surgery. Moderate atelectasis was seen in the right lung. Reduction of the abdominal contents was achieved with digital traction. Prior to closure of the diaphragmatic rent, an open-ended, 8-F red rubber feeding tube was placed percutaneously at the level of the 12th rib and positioned in the thoracic cavity at the ninth intercostal space. After visual placement of the tube, the edges of the diaphragmatic hernia were apposed with a simple continuous pattern of 2-0 polypropylene. Biopsy specimens were obtained from

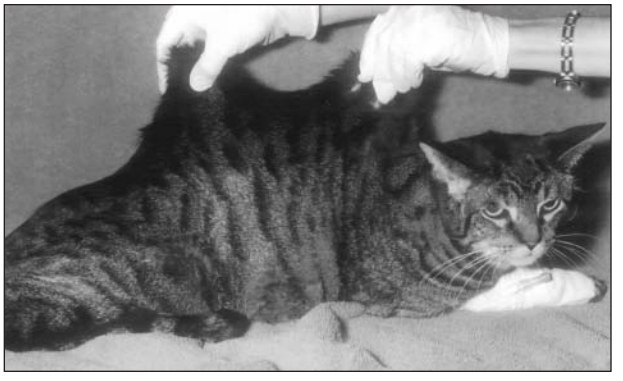

Figure 1—Photograph of a cat with cutaneous asthenia. The skin could be stretched more than 10 cm above the dorsal aspect of the thorax and abdomen.

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the epidermis prior to closure and submitted for histopathologic and transmission electron microscopic examination. The linea alba and subcutaneous tissues were individually closed with 3-0 polydioxanone in a simple continuous pattern. The epidermis was sutured with 3-0 nylon in a simple interrupted pattern. A 3-way stopcock with sterile medical-grade injection ports was placed on the thoracic tube, and a soft-padded bandage was applied to the thorax.

The cat was placed in intensive care for care of the thoracic tube and administration of hydromorphone (0.22 mg/kg [0.10 mg/lb], IV, q 6 h) for pain. The thoracic tube was removed 24 hours after surgery because there was minimal fluid accumulation (< 2 mL/kg/d [0.91 mL/lb/d]) and no accumulation of air in the thoracic cavity. The cat was released from the hospital 3 days after surgery. Lactulose (0.4 mL/kg [0.18 mL/lb], PO, q 12 h) and cisapride (1 mg/kg [0.45 mg/lb], PO, q 12 h) were prescribed for medical management of the perineal hernia. The surgical incision healed without complications, and sutures were removed 22 days after surgery.

Postoperatively, a grade 2/6 systolic heart murmur was detected. Abnormalities determined by use of echocardiography included systolic anterior motion of the mitral valve, a dilated aortic valve annulus in the proximal portion of the aorta (13.1 mm; reference range, 9.0 to 10.0 mm), and mild ventricular hypertrophy. Serum thyroxine concentration was unremarkable (26.8 nmol/L; reference range, 17.0 to 49.0 nmol/L), which ruled out hyperthyroidism as the cause for ventricular hypertrophy.

Histopathologic examination of the skin revealed normal epidermis and slightly thin dermis that contained high numbers of small collagen bundles, compared with a site-matched specimen from a control cat. No collagen abnormalities were detected with Masson trichrome stain. Additionally, Vernhoeff and acid orcein Giemsa stains revealed no abnormalities in the elastin fibers. Electron microscopic findings of the skin were consistent with cutaneous asthenia. The diameter of the collagen fibers was highly variable, compared with a site-matched sample from a control cat.

Four weeks later, the cat was admitted for surgical correction of the left perineal hernia. The cat was constipated despite treatment prescribed previously. The cat received premedication, anesthesia, and cefazolin as administered previously. A standard perineal herniorrhaphy was performed on the left perineum. Surgical observations included retroflexion of the urinary bladder; adipose tissue and the distal aspect of the descending colon were in the surgical field. After the urinary bladder, adipose tissue, and colon were replaced in the abdomen via digital manipulation, it was determined that the musculature of the pelvic diaphragm was weak and had excessive elasticity. Reduction of the contents of the left-sided perineal hernia revealed a perineal bulge consistent with a right-sided perineal hernia; rectal examination before surgery had not revealed any abnormalities of the right perineal region. The decision was made to correct the left-sided defect prior to correction of the right side.

Surgical repair consisted of a standard perineal herniorrhaphy with elevation of the internal obturator muscle.[2,3] Preplaced, simple interrupted sutures of 3-0 polypropylene were used to appose the edges of the levator ani, coccygeus, external anal sphincter, and internal obturator muscles. After the pelvic diaphragm was repaired, a skin biopsy specimen was obtained from the lateral aspect of the perineal incision and submitted for histopathologic and electron microscopic examination. Surgical closure and anesthetic recovery were without complications. Analgesia was provided with hydromorphone (0.11 mg/kg, IV, q 6 h). Serum copper concentration was 0.64 ppm (reference range, 0.4 to 1.4 ppm). The cat was discharged from the hospital and was prescribed amoxicillin-clavulanate (12.5 mg/kg [5.7 mg/lb], PO, q 12 h) and lactulose. Results of the histopathologic and electron microscopic findings were similar to the previous specimens.

Four months later, the cat was admitted for surgical repair of the right perineal hernia because the cat was constipated despite medical management. A standard right perineal herniorrhaphy was performed while the cat was positioned in sternal recumbancy.[2,3] Upon dissection of the subcutaneous tissue, it was apparent that the musculature of the pelvic diaphragm was weak and had severe elasticity. The distal portion of the descending colon was seen in the surgical field. Digital manipulation was successful in reducing the colonic herniation. The defect was corrected by use of the standard herniorrhaphy with elevation of the internal obturator muscle, identical to the technique used to correct the left-sided perineal hernia.[2,3] After closure of the surgical wound, a bulge was noticed in the left perineal region. Rectal examination revealed that the pelvic diaphragm was weakened on the left side, with herniation of the colon and bladder. Herniation of the bladder was confirmed via cystocentesis. The decision was made to perform a midline celiotomy while performing a colopexy and cystopexy. A standard ventral midline celiotomy was performed. No intra-abdominal abnormalities were detected. The right dorsal diaphragmatic hernia had healed without complications. The colopexy was initiated with a 3-cm seromuscular incision over the antimesenteric border of the mid body of the descending colon and a correlating incision of the transverse abdominis muscle on the caudoventral aspect of the left abdominal wall. The seromuscular layer of the descending colon was sutured to the ipsilateral-incised transverse abdominis muscle with 3-0 polypropylene in a simple continuous pattern. The cystopexy was performed with a 2-cm incision on the ventral and right lateral aspect of the bladder and an incision of the transverse abdominis muscle on the right caudolateral aspect of the body wall. The ipsilateral edges of the incised serous layer of the bladder and the transverse abdominis muscle were apposed with 3-0 polypropylene in a simple continuous pattern. Closure of the linea alba and subcutaneous tissues was performed with 3-0 polydioxanone in a simple continuous pattern; the skin was closed with surgical staples. Recovery was uncomplicated, and analgesia was achieved with hydromorphone (0.11 mg/kg, IV, q 6 h).

Lactulose administration was continued while the cat remained in the hospital. The cat was discharged 4 days after surgery with clindamycin (7.5 mg/kg [3.4

mg/lb], PO, q 12 h) prescribed for 7 days and lactulose as prescribed previously. Six months after surgery, the owner reported that no complications had developed and that the cat was doing well.

A group of rare hereditary disorders that result in altered strength or extensibility of connective tissues is called EDS in humans and cutaneous asthenia in animals.[4-7] Recent molecular and biochemical studies[4,8-11] have led to the definition of 9 types of EDS in humans. Most types of EDS are caused by mutations in genes coding for fibrillar collagen (types I, III, and V) or for enzymes that catalyze the intracellular or extracellular posttranslational modification of collagen fibrils.[4] In humans, EDS leads to hyperextensible and fragile skin and hypermobile joints.[4,9,11] The connective tissue of other organ systems can also be affected, leading to a high risk of blood vessel, intestinal, and uterine ruptures.[4] Nontraumatic hernias have been reported in several types of EDS.[4,12-14]

Hereditary collagen disorders similar to EDS have been described in several species, including cats,[15-22] dogs,[23-27] rabbits,[28,29] mink,[23] horses,[30,31] cattle,[32] and sheep.[33] The disease is rare in cats and has been reported in domestic shorthair, domestic longhair, and Himalayan cats.[5,16,19,20] Two forms of a disorder similar to EDS have been reported in cats. An autosomal recessive form, dermatosparaxis (similar to EDS type VIIC), has been described in Himalayan and mixed-breed cats. Dermatosparaxis is caused by a deficiency of type I procollagen-N-peptidase, which leads to accumulation of partially processed type I procollagen.[18] An autosomal dominant form, similar to EDS types I and II in humans, has also been described, which is believed to be lethal in the homozygous form.[5,16,22,34,35]

Nontraumatic hernias, especially ventral and inguinal, are recognized in humans with EDS types I and VII and cutis laxa.[4,12-14] Dermatosparaxis has been reported in a dog with an inguinal hernia[1] and a cat with a perineal hernia.[15] Although those hernias could have been coincidental, they may have been associated with dermatosparaxis.

Soft tissue hyperextensibility or fragility caused by cutaneous asthenia was considered the most likely cause of the diaphragmatic and perineal hernias in the cat reported here. Although cats with congenital diaphragmatic hernias (usually peritoneopericardial) may not have clinical signs for long periods,[36] this was considered unlikely in this cat because of the location of the diaphragmatic lesion, lack of adhesions within the thoracic cavity, and absence of clinical signs (eg, muffled heart sounds and gastrointestinal signs) until 11 years of age. Additionally, a traumatic hernia was considered unlikely because the cat had no history of trauma and was housed strictly indoors.

Perineal hernias are uncommon in cats and have been associated with megacolon, chronic constipation, perineal masses (adenocarcinoma), and perineal urethrostomy.[37,38] When this cat was examined by the referring veterinarian, it had a perineal hernia and was constipated. It is possible that constipation and tenesmus were present prior to the hernia, but chronic constipation was not reported.

Although humans with EDS may have increased risk of surgical complications (friable blood vessels and soft tissues, delayed wound healing, wound dehiscence, and wide scar formation),[12,39] the cat reported here did not develop any complications during or after surgical repair of the hernias. Only a few studies[39,40] have evaluated wound healing in animals with cutaneous asthenia. Freeman et al[39] reported that there was no important difference in primary intention healing between dogs and cats with cutaneous asthenia (resembling EDS type I) and clinically normal control animals. Because there are clinical differences in skin fragility among the various syndromes of EDS, it is plausible that differences in wound healing are also associated with the various types of molecular or biochemical abnormalities. Delayed wound healing should be considered in animals with cutaneous asthenia, and appropriate decisions on suture type, suture pattern, and duration of application should be made.

Human EDS types I, II, IV, and V can be associated with cardiovascular abnormalities such as valvular prolapse, pulmonary stenosis, mitral regurgitation, aortic aneurysms, atrial septal defect, and tetralogy of Fallot.[41] In the cat reported here, aortic dilatation may have been associated with cutaneous asthenia. Aortic dilatation is an uncommon finding in cats that is sometimes associated with hypertension. Hypertension in this cat cannot be ruled out because blood pressure was not measured prior to administration of anesthetic agents.

A presumptive diagnosis of cutaneous asthenia is often made on the basis of skin hyperextensibility and fragility. A definitive diagnosis of cutaneous asthenia requires histopathologic, electron microscopic, and biochemical studies of the skin. The cat reported here had an elasticity index of 25%, which is consistent with cutaneous asthenia.[1,22] It is not unusual for animals with cutaneous asthenia to have subtle or absent light microscopic changes, as was seen in this cat.[5,22,29,42,43] Of the 2 types of cutaneous asthenia described in cats, the electron microscopic findings in the cat reported here most closely resembled the autosomal dominant form (human EDS types I and II), which often has a bimodal distribution of small and large collagen fibers.[16,20,22] The presence of 2 fiber sizes may represent a heterozygous state in which normal and altered collagen metabolisms exist.[22] Differential diagnoses for cutaneous asthenia include acquired skin fragility and cutis laxa. Feline acquired skin fragility is a relatively rare disorder with several etiologies (eg, spontaneous hyperadrenocorticism, diabetes mellitus, hepatic lipidosis, and administration of corticosteroids and progestins).[42] Acquired skin fragility was ruled out in this cat because the cat was affected at a very young age, did not receive causative medications, and a concurrent systemic illness was not identified.

Cutis laxa (previously classified as EDS type IX) has not been reported in cats.[34] Cutis laxa was ruled out in this cat because serum copper concentration was within reference range and elastin abnormalities were not detected.

References

1. Freeman LJ, Hegregerg GA, Robinette JD. Ehlers-Danlos syndrome in dogs and cats. *Semin Vet Med Surg (Small Anim)* 1987;12:221–227.

2. Earley TJ, Kolata RJ. Perineal hernia in the dog: an alternative method of correction. In: Bojrab MJ, ed. *Current techniques in small animal surgery.* 2nd ed. Philadelphia: Lea & Febiger, 1983;405.

3. Bellenger CR, Canfield RB. Perineal hernia. In: Slatter D, ed. *Textbook of small animal surgery*. 2nd ed. Philadelphia: WB Saunders Co, 1993;471–482.

4. Freedburg IM, Fitzpatrick TB. Heritable disorders of connective tissue with skin changes. In: Freedburg IM, Eisen AZ, Wolff K, et al, eds. *Fitzpatrick's dermatology in general medicine*. 5th ed. New York: McGraw-Hill Book Co, 1999;1835–1847.

5. Scott DW, Miller WH, Griffen CE. Congenital and hereditary defects. In: Scott DW, Miller WH, Griffen CE, eds. *Muller and Kirk's small animal dermatology*. 6th ed. Philadelphia: WB Saunders Co, 2001;913–1003.

6. Hegreberg GA. Ehlers-Danlos syndrome. *Am J Pathol* 1975; 79:383–386.

7. Gunson DE. Collagen in normal and abnormal tissues. *Equine Vet J* 1979;11:97–101.

8. Smith LT, Schwarze U, Goldstein J, et al. Mutations in the COL3A1 gene result in the Ehlers-Danlos syndrome type IV and alterations in the size and distribution of the major collagen fibrils of the dermis. *J Invest Dermatol* 1997;108:241–247.

9. Pyeritz RE. Ehlers-Danlos syndrome. *N Engl J Med* 2000; 342:730–732.

10. DePaepe A. Ehlers-Danlos syndrome type IV. *Dermatology* 1994;189:21–25.

11. Byers P. Inherited disorders of collagen gene structure and expression. *Am J Med Genet* 1989;34:72–80.

12. Girotto JA, Malaisrie SC, Bulkely G, et al. Recurrent ventral herniation in Ehlers-Danlos syndrome. *Plast Reconstr Surg* 2000;106: 1520–1526.

13. Iglesias JL, Renard T. Diaphragmatic hernia in an 8-year-old with Ehlers-Danlos syndrome. *Pediatr Surg Int* 1998;13:553–555.

14. Liem MS, van der Graaf Y, Beemer FA, et al. Increased risk for inguinal hernia in patients with Ehlers-Danlos syndrome. *Surgery* 1997;122:114–115.

15. Collier LL, Leathers CW, Counts DF. A clinical description of dermatosparaxis in a Himalayan cat. *Feline Pract* 1980;10(15):27–36.

16. Sequeira JL, Rocha NS, Bandarra EP, et al. Collagen dysplasia (cutaneous asthenia) in a cat. *Vet Pathol* 1999;36:603–606.

17. Scott DV. Cutaneous asthenia in a cat, resembling Ehlers-Danlos syndrome in man. *Vet Med Small Anim Clin* 1974;10: 1256–1258.

18. Counts DF, Byers PH, Holbrook KA, et al. Dermatosparaxis in a Himalayan cat: I. Biochemical studies of dermal collagen. *J Invest Dermatol* 1980;74:96–99.

19. Holbrook KA, Byers PH, Counts DF, et al. Dermatosparaxis in a Himalayan cat: II. Ultrastructural studies of dermal collagen. *J Invest Dermatol* 1980;74:100–104.

20. Hegreberg GA. Animal models of collagen disease. *Prog Clin Biol Res* 1982;94:229–244.

21. Plotnick A, Brunt JE, Reitz B. Cutaneous asthenia in a cat. *Feline Pract* 1992;20(4):9–12.

22. Patterson DF, Minor RR. Hereditary fragility and hyperextensibility of the skin of cats. *Lab Invest* 1977;37:170–179.

23. Hegreberg GA, Padgett GA, Gorham JR, et al. A connective tissue disease of dogs and mink resembling the Ehlers-Danlos syndrome of man. II. Mode of inheritance. *J Hered* 1969;60:249–254.

24. Barnett KC, Cottrell BD. Ehlers-Danlos syndrome in a dog: ocular, cutaneous and articular abnormalities. *J Small Anim Pract* 1987;28:941–946.

25. Poulsen PH, Thomsen MK, Kristensen F. Cutaneous asthenia in the dog. *Nord Vet Med* 1985;37:291–297.

26. Matthews BR, Lewis GT. Ehlers-Danlos syndrome in a dog. *Can Vet J* 1990;31:389–390.

27. Minor RR, Lein DH, Patterson DF, et al. Defects in collagen fibrillogenesis causing hyperextensible, fragile skin in dogs. *J Am Vet Med Assoc* 1983;182:142–148.

28. Harvey RG, Brown PJ, Young RD, et al. A connective tissue defect in two rabbits similar to the Ehlers-Danlos syndrome. *Vet Rec* 1990;126:130–132.

29. Sinke JD, van Dijk JE, Willemse T. A case of Ehlers-Danlos-like syndrome in a rabbit with a review of the disease in other species. *Vet Q* 1997;19:182–185.

30. Lerner DA, McCracken MD. Hyperelastosis cutis in two horses. *J Am Anim Hosp Assoc* 1978;2:350–352.

31. Solomons B. Equine cutis hyperelastica. *Equine Vet J* 1984; 16:541–542.

32. Hanset R, Lapiere CM. Inheritance of dermatosparaxis in the calf. *J Hered* 1974;65:356–358.

33. Fjolstad M, Helle O. A hereditary dysplasia of collagen tissues in sheep. *J Pathol* 1974;112:183–188.

34. Guaguere E, Alhaidari Z, Fontaine J. Genodermatoses. In: Guaguere E, Prelaud P, eds. *A practical guide to feline dermatology*. Lyon, France: Merial, 1999;16.1–16.11.

35. Minor RR, Wootton JA, Prockop DJ, et al. Genetic diseases of connective tissues in animals. *Curr Probl Dermatol* 1987;17:199–215.

36. Wilson GP, Hayes HM. Diaphragmatic hernia in the dog and cat: a 25-year overview. *Semin Vet Med Surg (Small Anim)* 1986; 1:318–326.

37. Johnson MS, Gourley IM. Perineal hernia in a cat: a possible complication of perineal urethrostomy. *Vet Med Small Anim Clin* 1980;75:241–243.

38. Welches CD, Scavelli TD, Aronsohn MG, et al. Perineal hernia in the cat: a retrospective study of 40 cases. *J Am Anim Hosp Assoc* 1992;28:431–438.

39. Freeman LJ, Hegreberg GA, Robinette JD. Cutaneous wound healing in Ehlers-Danlos syndrome. *Vet Surg* 1989;18:88–96.

40. Freeman LJ, Hegreberg GA, Robinette JD, et al. Biomechanical properties of skin and wounds in Ehlers-Danlos syndrome. *Vet Surg* 1989;18:97–102.

41. Abdelmalek NF, Gerber TL, Menter A. Cardiocutaneous syndromes and associations. *J Am Acad Dermatol* 2002;46:161–183.

42. Fernandez CJ, Scott DW, Erb HN, et al. Staining abnormalities of dermal collagen in cats with cutaneous asthenia or acquired skin fragility as demonstrated with Masson's trichrome stain. *Vet Dermatol* 1998;9:49–54.

43. Brounts SH, Rashmir-Raven A, Black SS. Zonal dermal separation: a distinctive histopathological lesion associated with hyperelastosis cutis in a Quarter horse. *Vet Dermatol* 2001;12:219–224.