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NOTE

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Esophageal smooth muscle hypertrophy causing regurgitation in a rabbit

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ABSTRACT. A five-year-old rabbit was evaluated for a 7 to 8 month history of regurgitation, weight loss, and hyporexia. Previously performed whole body radiographs, plasma biochemistry results and complete blood count revealed had no significant abnormalities. A computed tomography (CT) scan revealed a circumferential caudal esophageal thickening. The animal received supportive care until euthanasia was performed 6 weeks later. Caudal esophageal smooth muscle hypertrophy was diagnosed on necropsy. This case indicates that regurgitation can occur in rabbits and advanced imaging can investigate the underlying cause.

KEY WORDS: computed tomography, esophageal stricture, gastrointestinal disorder, rabbit, vomiting

Regurgitation, a passive retrograde movement of ingesta to the upper esophageal sphincter, is a clinical sign of an esophageal disorder [12]. Esophageal disorders are somewhat common in the dog and have been described as rare in the cat [4]. Vomiting, an active process of ingesta from the stomach (whereas regurgitated material rarely reaches the stomach), must be carefully differentiated from regurgitation when an animal is presented for either clinical sign [12]. Regurgitation can be a clinical sign of esophageal foreign body, esophagitis, esophageal stricture, megaesophagus (with numerous differential diagnoses potentially causing this anatomic abnormality), esophageal dysmotility, and esophageal neoplasia [12]. While it is frequently noted that rabbits cannot vomit, no mention of regurgitation is made when discussing rabbit gastrointestinal disorders [3, 7, 8, 11].

An approximately five-year-old male neutered Dutch rabbit (*Oryctolagus cuniculus)* was referred with a 7 to 8- month history of regurgitation, bruxism, intermittent anorexia, and progressive lethargy. The referring veterinarian diagnosed and treated the rabbit for cuterebriasis in the conjunctiva of the right eye 9 months prior to referral. Approximately two weeks after this diagnosis, the rabbit returned to the primary veterinarian for lethargy and anorexia. The rabbit was a consistent weight at 1.3 kg with a body condition score of 4/9 and was being offered its typical and appropriate diet of approximately free choice timothy hay with one cup of leafy green vegetables and one-quarter cup of rabbit specific pellets per day. Despite conjunctival swelling remaining, an anesthetized ocular examination revealed no further abnormalities. Whole body radiographs revealed a mild to moderate amount of gas in the small intestinal loops, which may have suggested ileus. A biochemistry profile was within normal limits. The rabbit was started on syringe feedings with a critical care mixture (10 m*l* three times a day, Oxbow Animal Health, Murdock, NE, U.S.A.). Treatment with metoclopramide (0.3 mg/kg by mouth every 12 hr; 1 mg/m*l*, compounded at Pet Apothecary, Milwaukee, WI) and meloxicam (0.4 mg/kg by mouth every 24 hr; 1.5 mg/m*l*, Metacam, Boehringer Ingelheim, Duluth, GA, U.S.A.) led to a gradual improvement in the rabbit's appetite and attitude over the next two months, although the bruxism continued and the rabbit's appetite for hay and cecotrophy never returned.

Despite the noted improvements, one to two months following the *Cuterebra* sp. larva removal, the rabbit began to regurgitate. On average, once daily the rabbit would extend its neck and produce approximately 5 to 15 m*l* of green liquid in a passive manner. The liquid was similar in color to the leafy green vegetables the rabbit had been previously offered, but there appeared to be no temporal association between when the rabbit would eat and when the behavior would occur. Continued bruxism, regurgitation, soft feces, and the rabbit eating only leafy green vegetables and pellets, led to empiric courses of metronidazole (20 mg/kg by mouth every 12 hr; 125 mg/m*l*, compounded at Pet Apothecary, Milwaukee, WI, U.S.A.) and sulfamethoxazole and trimethoprim (25 mg/kg by mouth every 12 hr; 48 mg/m*l*, Sulfamethoxazole and Trimethoprim, Hi-Tech Pharmacal, Amityville, NY, U.S.A.) being prescribed, which led to no improvement in clinical signs. Repeated blood tests and whole body radiographs revealed

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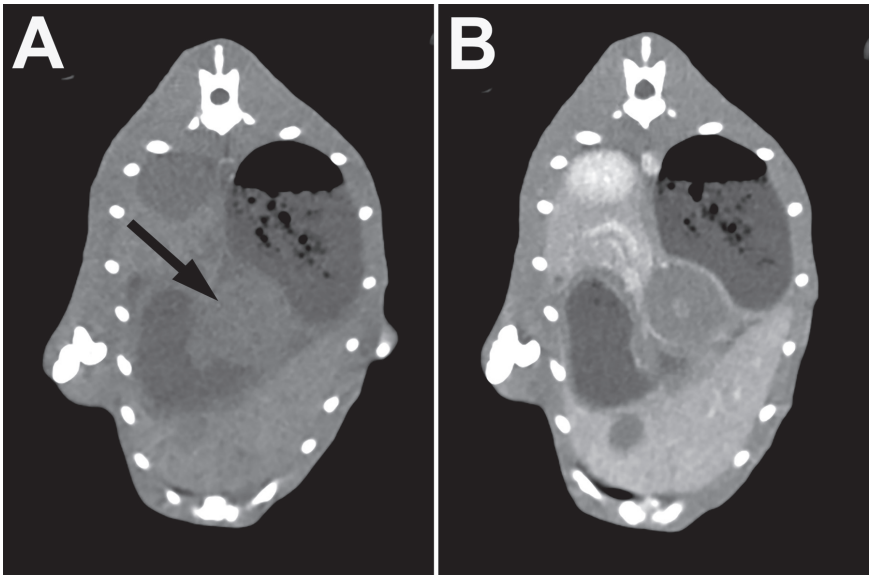

Fig. 1. Transverse precontrast (A) and postcontrast IV (B) CT images in a soft tissue window (W: 350, L: 40) of a circumferential, hypoattenuating soft tissue mass lesion in the caudal esophageal wall (A) at the level of stomach (black arrows). (B) Intravenous positive contrast uptake in the mucosal and serosal esophageal layers delineates the homogeneous mural thickening. Contrast uptake is also in the liver, right cranial pole of the kidney, and small intestinal loops. Right is to the left and dorsal is at the top of the images.

no abnormalities. The owners felt that the rabbit had an adequate quality of life despite the current clinical signs, and therefore the rabbit was continued on meloxicam and metoclopramide. However, progressive lethargy in the last month prior to referral, prompted to owners to pursue further diagnostics.

On presentation, the rabbit was severely underweight (body weight 1.07 kg), scored with a body condition of 1.5/9. The animal exhibited constant bruxism throughout the examination. The rabbit's incisors and cheek teeth on cursory oral examination appeared within normal limits, its abdomen felt empty, and some fecal staining was present in the perianal region. The remainder of the physical examination was unremarkable. A full diagnostic plan for the rabbit was initiated upon presentation, which included a complete blood count, plasma biochemistry panel, and full body intravenous contrast enhanced computed tomography (CT) scan. Because regurgitation was previously unreported in rabbits, the CT scan was elected examine the esophagus and stomach, but also the dental arcades more fully and the pharynx in case dental disease or a pharyngeal abnormality was causing ptyalism or dysphagia leading to fluid exiting the mouth and mimicking regurgitation. The complete blood count revealed no abnormalities. The clinically significant abnormalities of the biochemistry panel included a hypercalcemia (>16 mg/d*l* (>4.0 mmol/*l*) [in-house reference range: 8.0–14.8 mg/d*l* (2.0–3.69 mmol/*l*)]). An ionized calcium was then performed to further investigate the hypercalcemia and it was also found to be slightly elevated (1.87 mmol/*l* [1.57–1.83 mmol/*l*] [10]).

A sedated (0.5 mg/kg midazolam [5 mg/m*l*, Midazolam, Hospira, Lake Forest, IL, U.S.A.] and 0.3 mg/kg butorphanol [10 mg/m*l*, Torbugesic, Fort Dodge Animal Health, Overland Park, KY, U.S.A.] delivered intramuscularly) full body contrast CT scan (2.2 m*l*/kg of iohexol [300 mg/m*l*, Omnipaque, GE Healthcare Inc., Chicago, IL, U.S.A.]) revealed that the caudal esophagus was circumferentially thickened, homogeneous and soft tissue attenuating. There was mild contrast enhancement of the esophageal adventitial wall. The esophageal wall thickening extended from the level of the carina to the region of the caudal esophageal sphincter (Fig. 1). Five hours later the rabbit was syringed 5 m*l* of diluted 1:1 iohexol with tap water and another CT scan was performed directly following administration of the iohexol. The positive contrast column created in the esophagus was severely thinned over the length of the aforementioned caudal esophageal circumferential mural thickening (Fig. 2).

After the first CT scan was performed (prior to iohexol administration), the rabbit regurgitated approximately 10 m*l* of saliva mixed with spinach greens provided after recovering from sedation. Differential diagnoses for this esophageal lesion, that was most likely responsible for this regurgitation and weight loss, included a neoplastic mural mass, but an esophagitis or esophageal diverticulum could not be ruled out. The hypercalcemia could have also been attributed to a neoplastic cause with hypercalcemia of malignancy. Upper gastrointestinal endoscopy and biopsy were recommended as the next diagnostic step with or without further investigation of the hypercalcemia, but were declined by the owner, as they did not wish to pursue treatment regardless of the diagnosis. The rabbit was discharged with instructions to offer a variety of foods to the rabbit and to restart syringe feedings for nutritional support (15–25 m*l* three times a day, Oxbow Animal Health). All medications were discontinued as the owners did not feel that they provided any relief of clinical signs or discomfort.

Six weeks after the diagnosis, the rabbit had further declined in body condition and energy level and the owner elected humane euthanasia at the primary veterinarian (sedated with dexmedetomidine, ketamine and butorphanol; subsequently given pentobarbital intravenously in the lateral saphenous vein). A complete necropsy was performed. At necropsy, the animal was moderately to

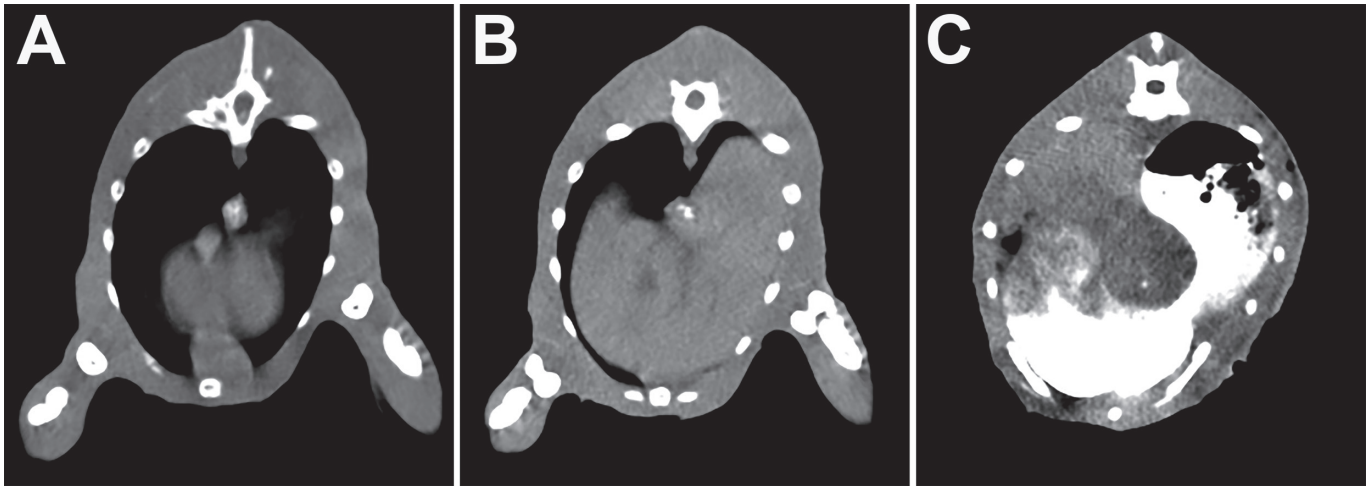

Fig. 2. Transverse cranial to caudal esophagus with oral positive contrast administration. (A) caudal to carina, (B) at level of diaphragm, and (C) at lower esophageal sphincter, CT images in a soft tissue window (W: 350, L: 40). Normal esophageal wall sections (A and B) and at the lower esophageal sphincter (C). Intraluminal thinning of the positive contrast column is noted prior to gastric entry. The mass causes extramural compression of the gastric wall with moderate bulging towards the gastric lumen (C). The stomach contains a large volume of positive contrast media. Right is to the left and dorsal is at the top of the images.

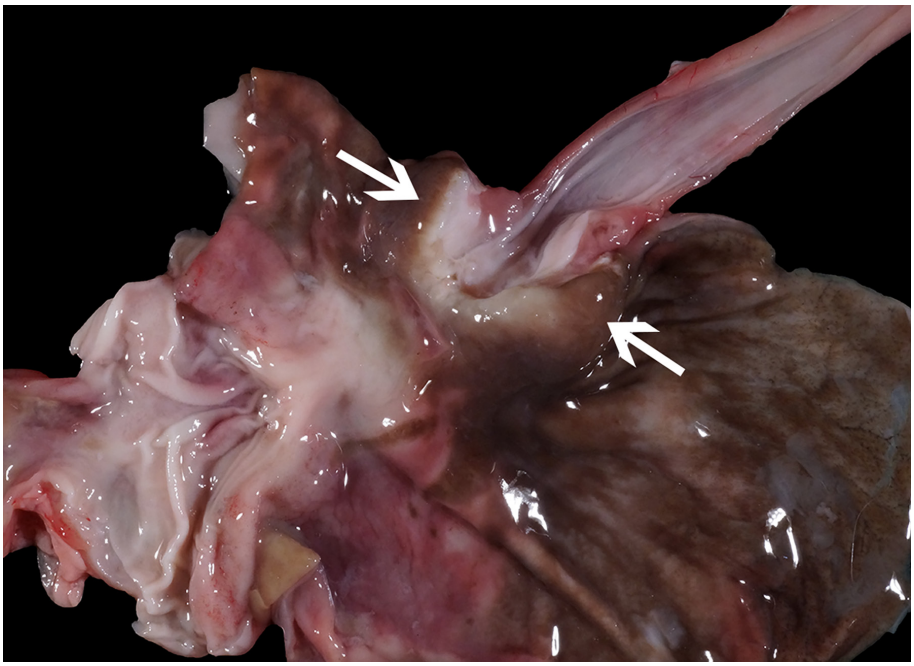

Fig. 3. Gross photograph of the longitudinally opened esophagus, stomach and proximal duodenum. The lower esophageal sphincter is markedly thickened circumferentially (arrows) resulting in a narrowing of its lumen (stricture) and an elevation of the mucosa of the cardia.

severely underweight (1.1 kg). The only other significant finding was a fairly abrupt circumferential firm white thickening of the caudal esophageal wall at the level of the lower esophageal sphincter for a distance of about 1 cm at the level of the esophageo-gastric junction. The wall of the lower esophageal sphincter was circumferentially approximately 1 cm thick and the esophageal lumen was narrowed at this level (Fig. 3). Samples of the normal appearing upper and mid esophagus and of the thickened lower esophageal sphincter were collected for histopathology. The thickening was entirely composed of irregularly interwoven bundles of well-differentiated smooth muscle cells (Fig. 4). Despite the grossly fairly abrupt transition of unaffected esophageal wall to thickened esophageal wall, there was no distinct delineation of the smooth muscle hypertrophy from the unaffected adjacent muscularis at the microscopic level. The histologic sections of the wall of the upper and mid esophagus were unremarkable.

Initial differential diagnoses for the observed regurgitation in this rabbit included ptyalism or dysphagia due to dental disease or pharyngeal issues. The CT scan and witnessing the behavior after the CT scan, however, confirmed that regurgitation was indeed

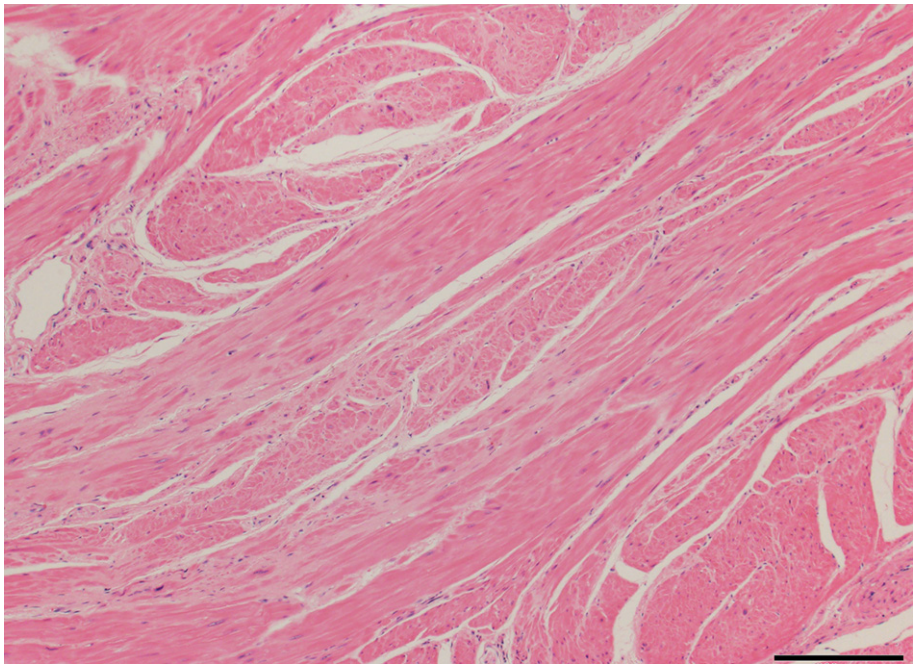

Fig. 4. Photomicrograph of the lower esophageal sphincter. The thickening is entirely composed of interwoven bundles of smooth muscle cells with mild increase of a collagenous extracellular matrix. H & E stain; bar=200 μm.

occurring. It is unclear what led to the smooth muscle hypertrophy of the lower esophageal sphincter and stricture in this rabbit, but in domestic dogs and cats, esophageal strictures leading to regurgitation are most often caused by reflux occurring during an anesthetic event [6, 12]. Because of this, esophageal strictures in dogs and cats are most often in the caudal third of the esophagus, as was seen in this rabbit [1]. For these animals, clinical signs usually emerge within 2 weeks of an anesthetic procedure, but it has been noted that sometimes clinical signs (most often regurgitation and increased appetite) don't manifest for 4 to 6 weeks [12]. While the anesthetic episodes this rabbit's diagnostics at the referring veterinarian fit with this clinical picture, an esophageal stricture due to gastric reflux from anesthesia seems like an unlikely occurrence in a rabbit, due to the increased tone of the lower esophageal sphincter in rabbits [7, 11].

Rather than an esophageal constriction secondary to an esophagitis, as seen in dogs and cats, this rabbit appears to have a smooth muscle hypertrophy more similar to a syndrome seen in horses [2]. Horses with this condition histologically have circular smooth muscle layer of the caudal esophagus thickened with no fibrosis or inflammation noted [2]. This rabbit's histology revealed a similar lesion. Horses with this smooth muscle hypertrophy may be asymptomatic, but Friesian horses (*Equus caballus*) appear particularly prone to a caudal esophageal smooth muscle hypertrophy that sometimes leads to regurgitation, weight loss, choke, and may lead to a proximal megaesophagus [5, 9]. Unlike in the horse, however, the entirety of the rabbit esophagus has striated skeletal muscle, and the thickening found in the rabbit was found to occur rather abruptly, while in horses where this occurs it is usually a gradually progressive thickening that occurs as the muscle moves caudal down the esophagus [11].

It is unknown if this rabbit had an intermittent megaesophagus secondary to this muscular hypertrophy, because no fluoroscopic images of the rabbit eating were captured; megaesophagus was never diagnosed on radiographs or the rabbit's CT scan and was not apparent at necropsy. Given that the rabbit's regurgitation had no association with food intake, it seems likely that some distension of the proximal esophagus may have occurred from food remaining within the esophagus until it was regurgitated.

Neoplasia was initially considered the most likely differential diagnosis for the rabbit's esophageal lesion with leiomyoma a probable differential diagnosis. However, leiomyomas occur as solitary nodules that are raised above the mucosal or serosal surface and do not occur as circumferential thickenings. Furthermore, leiomyomas are usually well delineated from the adjacent musculature on a microscopic level, even though they are non-encapsulated masses. Therefore, this rabbit's lesion was considered to be a hypertrophy rather than a leiomyoma.

Esophageal disorders should be considered as an underlying cause for rabbits evaluated for regurgitation. This rabbit's owners did not wish to pursue further diagnostics, indicating that they would not pursue treatment regardless of diagnosis. Without a biopsy and definitive diagnosis of the mass effect in the esophagus, it was not possible to give an exact prognosis to this rabbit's owners, but with his continued regurgitation it was not believed that he would recover from his weight loss and discomfort. It appears that when the esophageal lumen is occluded to the degree seen in this rabbit that prognosis for a good quality of life is not excellent. It is unclear if techniques such as ballooning of the esophagus [6] or others might have been successful for this rabbit since a neoplastic cause was not present, if diagnostics had been pursued earlier. In future rabbit cases with regurgitation, advanced diagnostics, such as CT scans, may be necessary to differentiate the cause of regurgitation from similar syndromes in this species and further cases with more investigation and diagnostics are necessary in order to better elucidate prognosis.

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