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Case Report Rapport de cas

Catastrophic gastric rupture in a horse secondary to psyllium pharmacobezoars

Thomas C. Bergstrom, R. Russell Sakai, Jorge E. Nieto

Abstract — A mare was euthanized because of gastric rupture secondary to complete duodenal obstruction by 2 bezoars located in the pylorus and proximal duodenum. Infrared spectroscopy showed that the bezoars were composed of psyllium. The mare had been receiving treatment with a pelleted psyllium product at 4 times the recommended dosage. Veterinarians should be aware that treatment of colic in horses with pelleted psyllium products could be associated with gastric impaction.

Résumé — Rupture gastrique catastrophique secondaire à des pharmacobézoards de psyllium en boulettes chez un cheval. Une jument a été euthanasiée en raison d'une rupture gastrique secondaire à une obstruction duodénale complète par deux bézoards situés dans le pylore et le duodénum proximal. La spectroscopie infrarouge a montré que les bézoards se composaient de psyllium. La jument avait reçu un traitement composé d'un produit de psyllium en boulettes à quatre fois la dose recommandée. Les vétérinaires devraient être au courant que le traitement des coliques chez les chevaux avec des produits de psyllium en boulettes pourrait être associé à une impaction gastrique.

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Case description

A 15-year-old, 401 kg Arabian mare with a body condition score of 5/9 was presented with an approximately 5-hour history of abdominal pain. She had no history of major health issues except for 1 colic episode at 8 y of age that responded to medical management. The patient was part of a herd that was accommodated in a sandy paddock and had a history of sand colic. The patient and herd mates had been inconsistently treated with psyllium pellets in the past due to exposure to sand in their environment and the presence of sand in fecal sediments. The patient was in the 3rd day of a week-long course of psyllium administered by the owner. The mare was being fed 453 g [1.13 g/kg body weight (BW), PO, q24h; recommended dose 0.31 to 0.46 g/kg body weight, q24h] of psyllium pellets (Sand Clear, Fanram Companies, Phoenix, Arizona, USA) in a mixture with commercial grain. The mare's forage was a grass alfalfa mix and she had free access to water. The mare had been receiving routine health care by the referral veterinarian for more than 10 y. On the day of examination, the mare was found to be rolling, pawing, and demonstrating signs of abdominal pain at the evening feeding after appearing clinically normal in the morning. The patient remained uncomfortable in the field with no obvious abnormalities on physical examination by the referring veterinarian and no new feces were noted during the examination. The lack of abnormalities and failure to respond to analgesics flunixin meglumine (Banamine; Merck Animal Health/Intervet, Madison, New Jersey, USA), 1.1 mg/kg BW, IV, once, and butorphanol tartrate (Torbugesic; Zoetis, Parsippany, New Jersey, USA), 0.025 mg/kg BW, IV, once, prompted referral to the UC-Davis William R. Pritchard Veterinary Medical Teaching Hospital (VMTH).

On presentation, the patient was not exhibiting signs of abdominal pain, had a normal heart rate [40 beats/min (bpm); reference interval (RI): 28 to 44 beats/min], mild tachypnea [24 breaths/min (br/min); RI: 8 to 15 br/min], and normal body temperature (37.5°C; RI: 37.2°C to 38.3°C). The remainder of the physical examination revealed reduced borborygmi in the left quadrants and adequate borborygmi in the right quadrants. No feces were passed during the examination or the 40-minute trailer ride before presentation. Results of a rectal examination were unremarkable at the time of presentation. Additionally, the patient had small amounts of mud and bedding material on the dorsum, indicating recent rolling or recumbency. Due to concerns of enterolithiasis, abdominal radiographs were taken and revealed a moderate amount of sand in the ventral colon, but no evidence of an enterolith. An abdominal ultrasonographic examination revealed no significant findings except a slightly enlarged stomach, filled with gas, which extended to the 14th intercostal space. A complete blood cell count revealed a slight leukopenia

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(4170 cells/μL; RI: 5400 to 14 300 cells/μL) characterized by a neutrophil count of 2990 cells/μL (RI: 2300 to 8600 cells/μL), and lymphopenia of 1010 cells/μL (RI: 1500 to 7700 cells/μL). Blood lactate (1.9 mmol/L), glucose (7.22 mmol/L), electrolytes (potassium 2.9 mmol/L, sodium 136 mmol/L, ionized calcium 1.39 mmol/L, chloride 96 mmol/L), packed cell volume (30%), and total protein (76 g/L) were also measured at the time of admission. A nasogastric (NG) tube was placed and 3 L of net reflux that was not foul smelling and was mixed with approximately 200 to 300 g of well-masticated feed were recovered. The NG tube was left indwelling. Abdominocentesis was not performed due to the risk of enterocentesis, given the presence of sand in the ventral colon.

The mare was hospitalized and administered a 10 L IV bolus of isotonic crystalloids followed by a maintenance rate of 1 to 2 L/h. The patient was quiet when admitted to the intensive care unit with a heart rate of 36 bpm and respiratory rate of 12 br/min. The mare was checked for reflux 2 h after admission and no net reflux was obtained. Four liters of water and 453 g of magnesium sulfate were administered *via* the NG tube; the patient was walked for 10 min then returned to her stall with the NG tube in place. After her walk she was noted to be lying quietly in sternal recumbency with normal heart (36 bpm) and respiratory rates (16 br/min). Approximately 2 h after the administration of enteral fluids, signs of abdominal pain (rolling) were observed and the mare was noted to have full body muscle fasciculations, and a heart rate of 100 bpm. Analgesia/sedation was provided with xylazine hydrochloride (XylaMed; VetOne, Boise Idaho, USA), 0.49 mg/kg BW, IV, and the patient was immediately evaluated for gastric reflux. Approximately 100 g of feed material mixed with clear non-foul smelling fluid was retrieved without net reflux. Repeat abdominal ultrasonography was unremarkable with the exception of a segment of thickened and nonmotile small intestine (7 mm wall thickness) along the left flank at the level of the costochondral junction. At the onset of abdominal pain, blood lactate, packed cell volume, and total protein were measured and found to be 14.5 mmol/L, 63%, and 90 g/L, respectively. Abdominocentesis under ultrasound guidance was performed and brown, sour smelling fluid was obtained with suspected feed material. A second ultrasound-guided abdominocentesis was performed in a different location to ensure enterocentesis had not occurred and similar fluid was obtained. Abdominal fluid was evaluated by a blood gas analyzer (ABL 705 blood gas analyzer; Radiometer America, Westlake, Ohio, USA); pH $<$ 6.3 (below range of analyzer), lactate of 16 mmol/L (RI: $<$ 1 mmol/L), glucose of 0.8 mmol/L (RI: 5.3 to 6.9 mmol/L), and a total protein of 17 g/L (reference value: $<$ 20 g/L). Gastric rupture with septic peritonitis was confirmed and euthanasia was elected.

Necropsy was performed the following day during which a severe, acute, focal full thickness rupture of the greater curvature of the stomach was identified. A 7.5 × 6 × 3 cm black-green bolus of impacted material was removed from the pylorus (Figure 1) and a similar 5 × 4 × 4 cm bolus was removed from the duodenum 15 cm aborad to the pylorus. On cut section both objects appeared to be composed of hay, psyllium, and husk-like structures. Further abnormalities included severe, acute septic peritonitis with serosanguinous fluid mixed with ingesta. The remainder of the gastrointestinal tract was examined grossly and other abnormalities (such as increased mural thickness, other rupture, strangulation) were not identified. Microscopic examination of tissue was not undertaken.

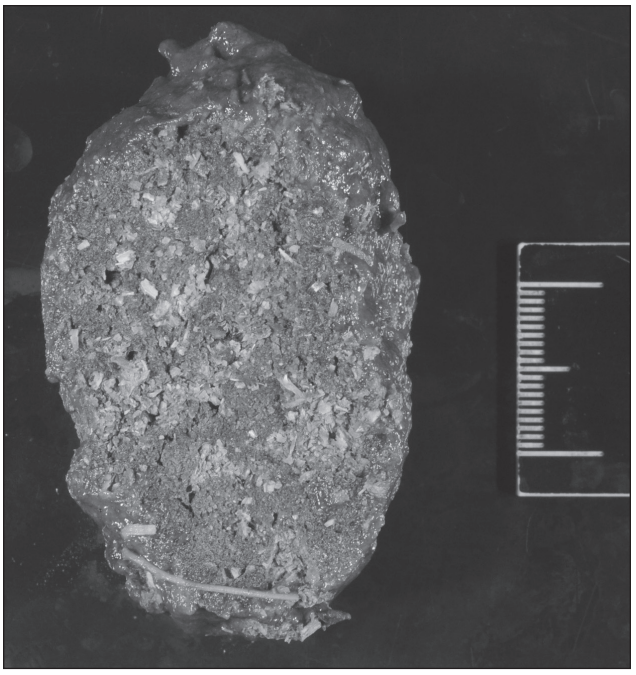

Figure 1. This 7.5 × 6 × 3 cm black-green bolus of impacted material was removed from the pylorus and is representative of the second smaller bolus removed from proximal duodenum. On close inspection husk-like structures are apparent.

Infrared spectroscopy of wet and dried portions of the bezoar was performed and the resulting spectra compared with that of a sample of the same brand of psyllium pellets fed by the owner. Infrared spectroscopy is a method used in analytical chemistry in which an unknown sample is exposed to infrared radiation. The bonds in the sample will absorb the infrared radiation at specific wavelengths unique to that chemical structure. The absorbance of these specific wavelengths is measured and results in an absorbance spectrum. This spectrum can then be compared to known samples and used to identify the chemical composition. This technique has been used in human medicine to identify bezoars composed of psyllium (1). In this case, the infrared spectroscopy absorbance spectrum of wet and dried portions of the bezoars matched a sample of psyllium pellets fed by the owner (Figure 2).

Discussion

We report a case of an equine patient suffering a gastric rupture secondary to pyloric and proximal duodenal obstructions by psyllium pharmacobezoars. The hygroscopic properties of the psyllium caused the pellets to swell and congeal together in the stomach and form 2 bezoars. These bezoars moved aborad and caused obstruction of gastric outflow that initiated a gastric impaction and secondary gastric rupture. Equine gastric ruptures can be caused by problems within the stomach (severe gastric ulceration, excessive feed intake, fermentation of

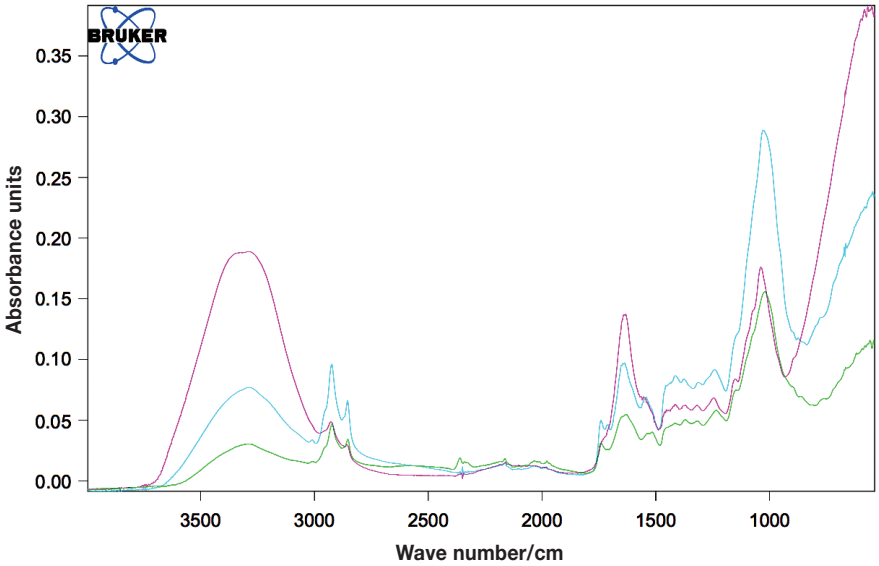

Figure 2. The infrared spectroscopy analysis indicates that the infrared spectra of wet (red) and oven-dried (blue) samples of the bezoar match the infrared spectrum of the sample of the Sand Clear Natural Psyllium Crumbles (green) for Horses.

ingesta, or obstructions of the pylorus), or due to physical or functional obstruction aboral to the stomach (2,3). A bezoar is an aggregate of inedible or undigested material formed in the alimentary tract of mammals (4). The materials that compose bezoars can include plant matter (phytobezoar), hair (trichobezoar), a combination of plant material and hair (trichophytobezoar), or milk proteins (lactobezoar) (4). Reports of bezoars composed of medications, pharmacobezoars, were published in the human literature as early as the 1930s (5). Various medications have been reported to form pharmacobezoars in humans including aluminum hydroxide, sucralfate, enteral feeding formulas, enteric-coated aspirin, and psyllium (1,5–11).

Pellet and powdered formulations of psyllium are commercially available and are used in horses to treat sand impactions (12). In 2007 the Food and Drug Administration (FDA) ruled that granular formulations of psyllium were no longer recognized as safe and effective for human use due to their propensity to cause esophageal obstruction and bezoars (13). This ruling documented 98 choking-related and esophageal obstruction events due to a psyllium product and 78 of these events were related to psyllium in granular formulation (13). These instances of esophageal obstruction occurred when ingested psyllium granules swelled after contact with water and became lodged in a hollow viscus (9,13,14). In the veterinary literature there are no reported instances of alimentary tract obstruction associated with either formulation of psyllium. Additionally, there is disagreement on the efficacy of psyllium in horses as 1 study demonstrated a lack of efficacy (15) and others demonstrated that psyllium is useful in resolving sand impactions (16–18). Most studies administer psyllium in the powdered formulation at a dose of 1 g/kg BW without reported incidences of morbidity or mortality (17,18). In the present case, a dose of 1.13 g/kg BW, PO, q24h of the psyllium pellets formulation resulted in an obstructing pharmacobezoar that initiated a gastric outflow obstruction followed by gastrorrhexis. This pelleted dosage (by weight) is approximately 4 times the manufacturer's recommended dosage (0.31 g/kg BW to 0.46 g/kg BW, PO, q24h), indicating that off-label use of psyllium pellets should be discouraged. The concentration of psyllium husk in the commercial psyllium pellets formulation is 72%.

Vague clinical signs on presentation made diagnosing this mare's gastric impaction particularly difficult. Due to the small amount of reflux, low heart rate, and comfort of the mare at presentation we did not assume she was in imminent danger of stomach rupture. Since abdominocentesis was not performed at admission, it is unknown if changes in the peritoneal fluid were present indicating ongoing gastric wall damage. Other initial clinical findings suggestive of a gastric impaction and gastrorrhexis were the mild leukopenia and slightly enlarged stomach on ultrasonography. A retrospective study found that 33% of horses diagnosed with gastric impactions had leukopenia which, in conjunction with the other findings in this case, was suggestive of gastric impaction (19). However, the clinical findings in this mare were nonspecific and the initial blood analysis was unremarkable. Without the complete history of treatment with psyllium pellets at the time of clinical examination, an obstructing psyllium pharmacobezoar was not considered. Given the nonspecific nature of clinical findings associated with gastric impactions, gathering a complete history of any treatment with psyllium pellets is of the utmost importance in diagnosing an obstructing psyllium pharmacobezoar (19,20). Despite suspecting a gastrointestinal rupture based on clinical examination, other than a focal region of thickened small intestine, ultrasonography abnormalities were limited. The thickened small intestine was likely due to vascular congestion and edema secondary to intraluminal obstruction. Additionally, serosal exposure to gastric contents likely contributed to the increased bowel wall thickness. The lack of additional abnormalities

could be explained by the acute nature of the rupture and lack of time for more diffuse abnormalities to develop. Infiltrative small intestinal disease has been reported to predispose to gastric impaction and rupture (19); however, histology was not performed and the exact cause for the bowel thickening cannot be confirmed.

Gastroscopy may have been helpful in diagnosing the gastric impaction. A gastroscopy/duodenoscopy, after complete gastric lavage, could have identified the bezoars at the pyloric antrum or proximal duodenum. Gastroscopy in human patients has been used to identify psyllium pharmacobezoars (1). Surgical exploration may have been recommended had an abdominocentesis been performed at presentation, which indicated the presence of bowel damage or ischemia. The gastric impaction would have been apparent at surgery but whether a proximal duodenal obstruction would have been identified or treatable is unknown. In general, gastric impactions are treated medically when possible at our institution.

In horses, persimmon phytobezoars are known to cause gastric impactions and ruptures in a similar mechanism to the psyllium pharmacobezoar described in this case (21–23). Persimmons have a high concentration of tannin monomers that polymerize and form a phytobezoar in the presence of hydrochloric acid in the stomach (24). A retrospective study found that horses suffering from gastric or enteric persimmon phytobezoars present with variable clinical signs including chronic weight loss, anorexia, diarrhea, and colic (21). In that study, 4 of 11 treated patients required surgery to relieve obstructions; all patients required intensive medical treatment, and survival was greater for gastric (7/8) than enteric phytobezoars (1/5) (21). Two patients with enteric phytobezoars were euthanized due to gastric rupture (21), indicating that alimentary tract obstruction by a bezoar is a medical emergency associated with mortality, especially in cases of enteric obstructions. Similarly, the mare in this report was at increased risk for mortality due to the duodenal bezoar. Additionally, this case illustrates that horses with psyllium pharmacobezoars may initially show only mild clinical signs of discomfort, making diagnosis challenging.

In humans, treatment of psyllium bezoar is mainly endoscopic division and removal with forceps or snare (1). In horses the treatment of obstructing psyllium pharmacobezoars must consist of resolving the obstructing bezoar and addressing the gastric impaction. Enteral fluid therapy is a commonly used treatment for gastric impactions and has been associated with good success, as 90% (18 of 20) of horses treated with enteral fluids survived to discharge in 1 study (19). However, in cases of obstructive psyllium pharmacobezoars enteral fluid therapy must be administered cautiously in the event the gastric outflow is completely occluded. Fasting is another important aspect of treatment as feeding increases stress on the gastric wall. In cases in which extended fasting is required, patients should receive supportive fluids and if necessary, partial or total parenteral nutrition. Dissolution therapy with carbonated cola and serial monitoring with gastroduodenoscopy should be considered, as cases of persimmon phytobezoars have been successfully treated in this manner (23). Other potential medical treatments include nasogastic intubation with mineral oil, cellulase, dioctyl sodium succinate, or intrabezoar injection with water or N-acetylcysteine. Surgical correction has resulted in successful removal of gastric and duodenal persimmon phytobezoars (22). However, surgery to resolve gastric impactions has been shown to have a poor outcome as 1 study found 5 of 6 horses with gastric impactions treated surgically were euthanized (20). If a diagnosis of a bezoar is made in a horse, it may be beneficial to remove as much gastric contents as possible before surgery using an NG tube, to reduce the risk of abdominal contamination during gastrostomy. Surgery should be considered if no improvement is observed after medical treatment.

No case of equine gastric rupture secondary to a psyllium pharmacobezoar has been reported. A cursory search of the UC-Davis VMTH records revealed 2 additional cases, which potentially suffered gastric ruptures secondary to pyloric obstructing psyllium bezoars. The first case occurred in the year 2000 after a 25-year-old Appaloosa gelding collapsed with tachycardia and signs of endotoxemia. Necropsy revealed a severe acute gastric rupture with 2 bezoars identified 10 cm aboral to the pylorus that resembled congealed psyllium and feed. However, no further testing was conducted to identify the composition of the bezoars and no history of psyllium use was provided. A second case occurred in 2013 when a miniature horse was suspected to have a gastric rupture and was euthanized. The owner believed the animal had free access to psyllium pellets. On necropsy, a rupture along the greater curvature was described in addition to 1 large bezoar composed of granular, rubbery material admixed with grain at the pylorus weighting 1.3 kg. No attempt to identify the composition of this bezoar was made. Our confirmed case and these suspected cases warrant further investigation into the potential for psyllium pharmacobezoars to result in secondary gastric ruptures. It is possible that horses resolve these obstructions with medical therapy and this phenomenon has so far gone unrecognized.

Underlying alimentary tract disease has been identified in horses affected by gastric impaction. Postmortem examinations on horses euthanized for gastric impaction found that 6 of 7 horses had thickening of muscular layers in the stomach wall (20). Lymphoplasmacytic inflammatory bowel disease has also been identified in horses suffering from recurrent gastric impactions (19). These pathologies could indicate chronic abnormal gastric motility and a predisposition to gastric impaction. No muscular hypertrophy or other gross pathology was identified in the present case but histological examination was not performed. Regardless, any pathology reducing gastric motility due to mechanical, neural, or hormonal alterations could predispose horses to formation of a psyllium pharmacobezoar. Dental disease also has been identified in as many as 50% of horses with primary gastric impactions (19). A brief dental examination on this horse revealed sharp enamel points in premolars and molars. The mare had received regular preventive medicine including dental floating by the same veterinarian for over 10 y. In addition, no asymmetries in the muscles of mastication were identified and the feed retrieved from nasogastric intubation was appropriately masticated. It is the opinion of the authors that horses with poor dental care are more likely to inadequately masticate psyllium pellets thus predisposing them to the formation

of a psyllium pharmacobezoar. In addition, reduced water intake may also facilitate the formation of bezoar. Finally, the mare in the present case report was diagnosed with a moderate amount of sand in the ventral colon. The clinical significance of this finding to the gastric rupture is unknown but could have predisposed this mare to gastric rupture. Any underlying gastrointestinal conditions that reduce gastric motility could predispose horses to formation of a psyllium pharmacobezoar. Therefore, in horses with diagnosis of such diseases psyllium pellets should be administered with caution.

The present case, morbidity and mortality associated with impactions by equine phytobezoars (21), difficulties in diagnosing equine gastric impactions, and the FDA ruling (13) on granular psyllium underscore that care must be taken when using psyllium pellets. Veterinarians and horse owners should be aware of the potential risks of psyllium pellets, especially when administered at a higher dose than the manufacturer's recommendation. This case suggests that in horses with recent treatment of psyllium pellets and signs of colic a psyllium pharmacobezoar must be considered. Additionally, off-label use of psyllium pellets should be discouraged as the horse herein was fed 4 times the manufacturer's recommended dosage of pellets. Further studies are warranted on both pelleted and powdered psyllium to attain a better understanding of the risk factors for the development of pharmacobezoars in horses.

In summary, this is the first reported case of gastrorrhexis secondary to an obstructing psyllium pharmacobezoar. The fatality and the immediate prior treatment with psyllium pellets, at higher than the recommended dose by the manufacturer, demonstrate the need for further investigation to determine the safety of this product in equine medicine.

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