

# Oesophageal stricture in a cat due to oral administration of tetracyclines

**A three-year-old, male neutered domestic shorthair cat was presented with dysphagia and regurgitation following treatment with oral doxycycline and oxytetracycline for *Haemobartonella felis* infection. Fluoroscopy confirmed the presence of multiple strictures along the entire length of the oesophagus. Balloon dilatation was performed successfully on two occasions and the symptoms resolved. To the authors' knowledge, this is the first report of oesophageal strictures associated with oral administration of tetracyclines in a cat in the UK.**

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## INTRODUCTION

Oesophageal strictures are an uncommon finding in cats (Burk and others 1987). Strictures are usually caused by severe oesophagitis and result in regurgitation, dysphagia and weight loss. The most common causes of oesophagitis include gastric reflux under general anaesthesia, vomiting, foreign bodies and ingestion of caustic agents. However, up to 15 per cent of strictures in humans lack an apparent aetiology (Cronstedt and others 1978). Oral medications have been proven to cause oesophagitis with stricture formation in humans (Carlborg and others 1983) and cats (Carlborg and Densert 1980). Oral tetracyclines, especially doxycycline, appear to increase the risk of oesophagitis, and thus stricture formation, in both man and animals (Carlborg and others 1983).

To the authors' knowledge, this is the first report of a case of oesophageal stricture occurring secondarily to oral administration of tetracyclines in a cat in the UK.

## CASE HISTORY

A three-year-old, male neutered domestic shorthair cat was presented with a two-month history of lethargy and weight loss. Biochemistry demonstrated increased

alkaline phosphatase, alanine transferase (222 U/litre; reference range 30 to 60 U/litre) and hyperglobulinaemia (56 g/litre; reference range 19 to 48 g/litre). Haematology revealed severe regenerative anaemia (haematocrit 8 per cent; reference range 30 to 45 per cent) and the presence of *Haemobartonella felis*. Therapy for *H felis* was initiated with oral prednisolone (Prednidale 5; Arnolds), at 2 mg/kg twice daily, and doxycycline (Ronaxan 20; Merial), at 10 mg/kg orally twice daily. Seven days later, doxycycline therapy was substituted with oxytetracycline (Oxycare 50; Animalcare) at 10 mg/kg orally three times daily. After a further 10 days, the cat developed dysphagia, regurgitation of all solids and some liquids. The oropharynx was examined under sedation, but no abnormalities were detected. A barium swallow study demonstrated retention of a small amount of barium in the oesophagus at the level of the thoracic inlet.

On presentation at the University of Glasgow Veterinary School, the cat was in poor bodily condition, mouth breathing and tachypnoeic with marked respiratory effort. Harsh lung sounds were audible on auscultation, referred from the upper respiratory tract. There were frequent gagging noises and copious amounts of saliva produced. The cat's mucous membranes were pale, but the capillary refill time was normal. The cat initially appeared interested in food and ate willingly, but within one or two minutes regurgitated forcibly.

The haematological changes observed earlier were confirmed; that is, regenerative anaemia (haematocrit 23 per cent) with a leucocytosis ( $20.4 \times 10^9$ /litre, reference range  $5.5$  to  $15.5 \times 10^9$ /litre) due to a mature neutrophilia ( $18.15 \times 10^9$ /litre, reference range  $2.5$  to  $12.5 \times 10^9$ /litre). No red blood cell parasites were seen on the blood smear and platelet numbers were normal. Serum biochemistry revealed a mild increase in alanine transferase (52 U/litre, reference range <35 U/litre), but was otherwise

unremarkable. The cat tested negative for feline leukaemia virus and feline immunodeficiency virus.

General anaesthesia was induced with intravenous propofol (Rapinivet; Schering Plough), at 4 mg/kg, and maintained with isoflurane (Isoflivet; Schering Plough Animal Health) and 100 per cent oxygen. Thoracic and lateral cervical radiographs were normal. Abdominal radiographs revealed gas-distended intestines and stomach. Upper gastrointestinal endoscopy (Olympus WM 30) was performed following radiography. The 5 mm diameter endoscope could not be passed more than 5 cm into the oesophagus, but eventually a 3 mm diameter urinary catheter was passed with difficulty. A barium oesophagram performed under fluoroscopy confirmed the presence of multiple oesophageal strictures. The longest stricture extended over a distance of 2 to 3 cm from just cranial to the thoracic inlet. Two shorter strictures were present in the caudal oesophagus. There was no evidence of distension of the oesophagus cranial to the strictures.

The next day, the cat was anaesthetised (as before) and an oesophageal dilator (8.5 F, 4 cm Balloon Dilatation Catheter, Cooks, inflated balloon diameter 23 mm) was passed into the oesophagus alongside the endoscope. The catheter was positioned centrally in the most cranial stricture and the balloon was slowly inflated with ioversol (Optiray 300; Mallinckrodt UK) under fluoroscopic guidance to a diameter of 20 mm. Inflation was maintained for one minute. This process was repeated in the caudal portion of the oesophagus. Post-dilatation, a small amount of haemorrhage was visualised endoscopically at the dilatation sites.

Postoperatively, the cat's recovery was very slow and, at one hour, a blood sample indicated a haematocrit of 7 per cent. The cat was slowly transfused following blood typing with 30 ml of blood. Within 24 hours, the cat was eating well, regurgitat-

ing only small amounts of solid food. The post-transfusion haematocrit was 18 per cent and *H felis* inclusions were detected. The following therapy was initiated: prednisolone (Prednidale 5; Arnolds), at 1 mg/kg orally twice daily, oxytetracycline (Engemycin 5%; Intervet), at 10 mg/kg subcutaneously once daily, ranitidine (Zantac Syrup; Glaxo), at 2 mg/kg orally twice daily, and aluminium hydroxide gel with lignocaine (Mucaine; Wyeth), at 2.5 ml orally three times daily. The cat continued to regurgitate over the next 10 days, but with reduced frequency.

Endoscopic examination 10 days later identified two small areas of narrowing in the region of the thoracic oesophagus. Further balloon dilatation was performed. The second dilatation was uneventful. No further regurgitation was reported and the cat was discharged three days later with a 21-day course of oral doxycycline (Ronaxan 20; Merial), at 10 mg/kg twice daily, given as a powder with food. One month later, the haematocrit was within the reference range and there was no recurrence of the *H felis* infection. The cat had gained weight and was regurgitating only intermittently.

## DISCUSSION

Oesophageal strictures occur secondarily to a severe oesophagitis, which causes damage to the lamina propria and muscularis layers. Damage to these deeper layers incites fibroblastic proliferation and contraction, leading to stricture formation. In turn, symptoms of regurgitation, dysphagia and weight loss develop, usually five to 14 days after the onset of severe oesophagitis (Leib 2000). The most common causes of oesophagitis include gastric reflux under general anaesthesia, vomiting, foreign bodies and ingestion of caustic agents. In humans, however, up to 15 per cent of strictures lack an apparent aetiology (Cronstedt and others 1978). Oral medications have been proven to cause

oesophagitis with stricture formation in humans (Carlborg and others 1983) and cats (Carlborg and Densert 1980).

In the present case, foreign bodies, ingestion of caustic agents and vomiting were eliminated as possible cause of stricture formation on the basis of history. Gastric reflux may have occurred during sedation prior to referral. However, symptoms of dysphagia and regurgitation were already evident. Gastric reflux may therefore have exacerbated a pre-existing oesophagitis or oesophageal stricture. The history of administration of oxytetracycline and doxycycline during the 17 days prior to symptoms occurring, suggests that tablet administration could have been a causative factor.

There appears to be an increased risk of oesophagitis associated with the administration of oral tetracyclines, especially doxycycline, in both man and animals (Carlborg and Densert 1980, Carlborg and others 1983). In an experimental study, doxycycline and oxytetracycline preparations were shown to produce areas of deep ulceration in the oesophagus (Carlborg and others 1983). Doxycycline capsules appeared more likely to be associated with oesophageal damage than tablets. This is thought to be due to a longer retention time in the oesophagus (Carlborg and Densert 1980). Oesophageal retention time can be minimised by administering capsules and tablets with food or providing a water bolus in quick succession to the tablet (wet swallow). In cats, 90 per cent of tablets reach the stomach within 30 seconds when administered by wet swallow. In contrast, 93.3 per cent of tablets administered by dry swallow fail to reach the stomach within 90 seconds (Westfall and others 2001). Oxytetracycline tablets, as available in the UK, are rarely administered in food due to their size and sugar-coating. It is not standard practice to administer tablets by wet swallow techniques and this case received all medications by dry swallow, thereby increasing the risk of oesophageal retention and its associated complications (oesophagitis and

oesophageal stricture). It would appear, therefore, that tetracyclines should, whenever possible, be administered by wet swallow techniques or with food to minimise the risk of oesophageal damage.

Plain radiography is often unrewarding in cases of oesophageal stricture (Zawie 1987) and so contrast oesophagrams, fluoroscopy and endoscopy may be required to confirm the diagnosis, particularly if multiple strictures are present (Harai and others 1995). In this case, plain thoracic radiographs were normal and a pharyngeal abnormality was suspected. Endoscopy was therefore performed to allow assessment of the pharynx and cranial cervical oesophagus. Due to the proximity of the stricture to the pharynx, it was not possible to visualise the stricture endoscopically. Endoscopy should, however, provide an opportunity to assess the oesophageal mucosa and identify the presence of active oesophagitis, which may alter management regimens (Harai and others 1995).

An oesophagram performed with fluoroscopy identified the presence of multiple strictures without concurrent oesophageal distension. Fluoroscopy allowed the degree of oesophageal filling to be observed, thereby minimising the potential for oesophageal rupture during contrast administration. Multiple strictures are uncommon in dogs and cats (Leib 2000) but, in this case, may be associated with multiple administration of doxycycline and oxytetracycline tablets over a period of 17 days. The presence of a single stricture could result in increased tablet retention within the oesophagus and therefore predispose to further stricture formation.

Bougienage, balloon dilatation or surgery can be used to treat oesophageal strictures. Of these, balloon dilatation and bougienage are the most commonly used techniques in both man and animals. Surgical treatment was inappropriate in this case due to the extensive nature of the strictures and the poor healing capacity of the oesophagus. Surgical treatment of

oesophageal strictures is associated with a high mortality rate in humans (16.6 per cent) (Starck and others 1984). Although bougienage is associated with a lower mortality rate in humans (1.5 per cent) (Starck and others 1984), it could not have been performed in this case due to the narrow diameter of the stricture. Balloon dilatation is considered more effective and safer than bougienage, since balloon catheters exert radial stretch forces as opposed to the longitudinal shearing forces exerted by bougies. In addition, balloon dilatation causes greatest dilatation in the area of constriction, which helps reduce the risk of oesophageal rupture.

This cat required two dilatation procedures, which is less than the average reported in cats (4.6 dilatations) (Harai and others 1995). In humans, the majority of cases respond to one or two dilatations. The number of dilatations required to resolve clinical signs may be determined by the chronicity or the extent of the stricture.

Balloon dilatation has been associated with complications including oesophageal perforation, mild tearing and bleeding (Harai and others 1995). Although a small amount of haemorrhage was evident after the initial dilatation in this cat, it was not considered to be of clinical significance. However, post-dilatation, the cat developed severe anaemia and required a blood transfusion. This was attributed to a combination of haemorrhage and stress-associated recrudescence of *H felis* infection. This theory was substantiated by increased numbers of *H felis* organisms detected on blood smears collected after the initial procedure. Treatment of the infection was complicated by the concern that further oral tetracycline therapy would exacerbate the oesophageal damage. Enrofloxacin has been reported to be effective against *H felis* (Winter 1993) and might have been used in this patient, although at present it remains unlicensed for this purpose.

The *H felis* infection was initially managed with oxytetracycline administered by

subcutaneous injection and subsequently with oral doxycycline tablets crushed to a powder and mixed with food. The use of powdered medications given in food should reduce the risk of prolonged contact with the oesophageal mucosa (Westfall and others 2001).

## Conclusions

Veterinary surgeons should be aware of the potential for oesophageal damage associated with oral treatment with tetracyclines. Tablets should be administered with food or followed by a water bolus to reduce the risk of oesophageal retention and subsequent oesophagitis.

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