Bull Vet Inst Pulawy 51, 181-184, 2007

ATROPINE SULPHATE TEST CAN BE AN AETIOLOGIC INDICATOR OF VAGAL BRADYCARDIA DEVELOPED IN A MEGAOESOPHAGUS CASE

İHSAN KELEŞ, NURİ ALTUĞ, ABDULLAH KAYA, CUMALİ ÖZKAN
NAZMİ YÜKSEK, AND LOĞMAN ASLAN[1]

Department of Internal Diseases, [1]Department of Surgery, Faculty of Veterinary Medicine,
University of Yuzuncu Yil, 65080 Van, Turkey
nurialtug@gmail.com

Received for publication October 16, 2006.

Abstract

An acquired megaoesophagus in a calf has been described. The diagnosis of megaoesophagus was made based on clinical and laboratory examinations, using contrast radiography, and necropsy findings. Atropine sulphate was used to enlighten the relationship between damage in the *N. vagus* and bradycardia, which developed in the megaoesophagus case.

Key words: calf, megaoesophagus, atropine.

Megaoesophagus is a congenital or acquired dilatation of the oesophagus resulting from an aperistaltic and/or a neuromuscular disorder in the oesophagus (9, 14, 15). In cattle, it is usually the consequence of such disorders as regurgitation, dysphagia, weight loss, pityalism, and aspiration pneumonia (11, 15).

Congenital megaoesophagus is considered to be a disorder of neuromuscular development. The pathogenesis of the condition is reported to be associated with a stretching of the vagus nerve (14).

Acquired megaoesophagus can result from any condition that causes disruption of the neural reflex control of swallowing or function of the oesophageal muscles (4, 12). It can be caused by any disease that inhibits oesophageal peristalsis by disrupting central, efferent or afferent pathways, or by product of segmental or diffuse motor dysfunction of the oesophagus, or by disease of the oesophageal musculature (oesophagitis, oesophageal neoplasia or obstruction) (4, 9, 12, 15).

Congenital megaoesophagus is caused by a known neurological deficit (14), but the cause is not well defined in acquired megaoesophagus. Furthermore, in clinical diagnosis, the relationship between bradycardia and megaoesophagus has not been determined. In this report, a case of acquired megaoesophagus together with clinical, laboratory, and radiological findings, and results of atropine application was described for the first time.

Material and Methods

The material of the present study was a 3-month-old male Swiss Brown calf showing anorexia, weakness, fullness in the cervical oesophagus region, and vomiting. According to anamnesis, the problem started at weaning period, which was 50 d after birth, and the first symptom was vomiting, but with no problem in drinking water. Later on, even water was observed to be vomited. The animal received some sort of medication by the local veterinarian before being presented to our animal hospital, but the medication had no effect. In our clinic, oesophagus tube was introduced to the animal, and electrocardiogram of the animal was taken. Contrast radiography of the oesophagus was also made.

Routine haematological data (RBC, WBC, haematocrit, and haemoglobin), serum mineral concentrations (Ca, Mg, and P), trace elements (Na, K, and Cl), enzyme activities (ALP, AST, ALT, GGT, LDH and CK), and other biochemical parameters (glucose, urea, blood urea nitrogen, creatinine, uric acid, total-direct and indirect bilirubin, total protein, albumin and globulin) were determined.

To determine the origin of bradycardia (vagal or cardiac) observed in the animal, atropine test was applied. For this purpose, 30 mg of atropine sulphate (Atropin®-VETAŞ / Turkey) were injected subcutaneously. Up to 30 min after the atropine injection, heart rate was observed. Necropsy was also performed after the animal died.

Results

In clinical examination; body temperature was low (36.8°C), respiration rate was high (40/min), and bradycardia (36/min) and dehydration were observed. Furthermore, the oesophagus, especially at the thorax region, appeared filled after eating, and after a while this swallowed feed regurgitated according to anamnesis. The gastric tube could not go further than to the thorax region of the oesophagus, and the tube curled. At the contrast radiography (Fig. 1), contrast substance was observed to accumulate at the cervical dilated region of the oesophagus. Therefore, on the basis of these findings, acquired segmental megaoesophagus was diagnosed.

Laboratory findings are given in Table 1. In the electrocardiography examination of the animal, bradycardia and prolonged QT and ST intervals were found. After atropine application, heart rate increased (41/min). Non-invasive treatment was applied to the animal because of its bad clinical condition. For this purpose; fluid-electrolyte (1.3% $NaHCO_3$, 0.9% NaCl, 5% dextrose) solutions, caffeine (Kafedif® - Ceva Dif/Turkey), penicillin+streptomycin combinations (Reptopen S®- Ceva Dif/Turkey), calcium (Kaldif®- Ceva Dif/Turkey), and vitamin C (Injacom C®- Ceva Dif/Turkey) were applied. But the animal did not respond to the treatment and died on the second day of the treatment.

At necropsy of the animal, the oesophagus was observed to be closed at the *hiatus diaphragmatica* region and thoracal part of the oesophagus was filled with feed. Therefore, thoracal and cervical oesophagus was enlarged (Fig. 2). Thus, the diagnosis of acquired segmental megaoesophagus was confirmed by the necropsy findings. When longitudinal incision of the oesophagus was made, there appeared regions, which were filled with feedstuff containing rough fibre.

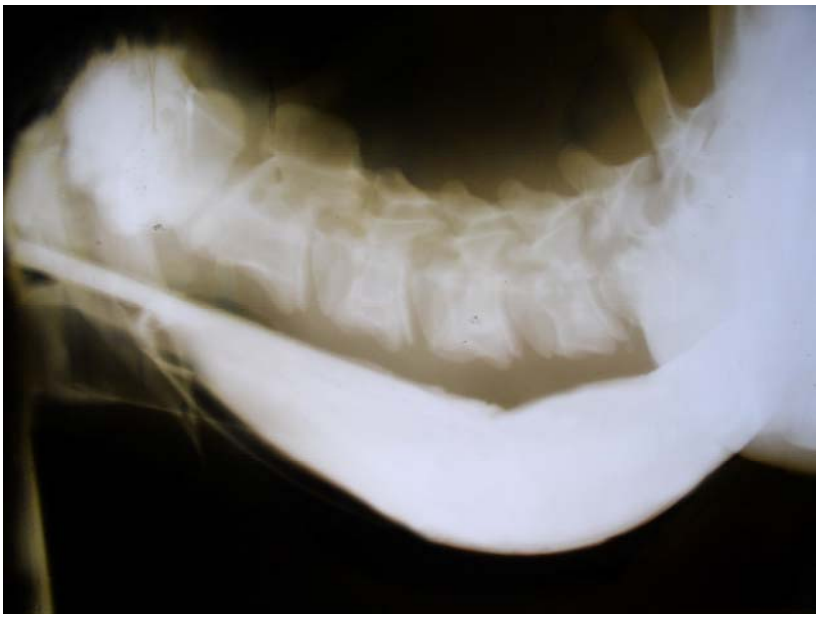

Fig. 1. Positive contrast radiogram outlining the cervical part of dilated oesophagus.

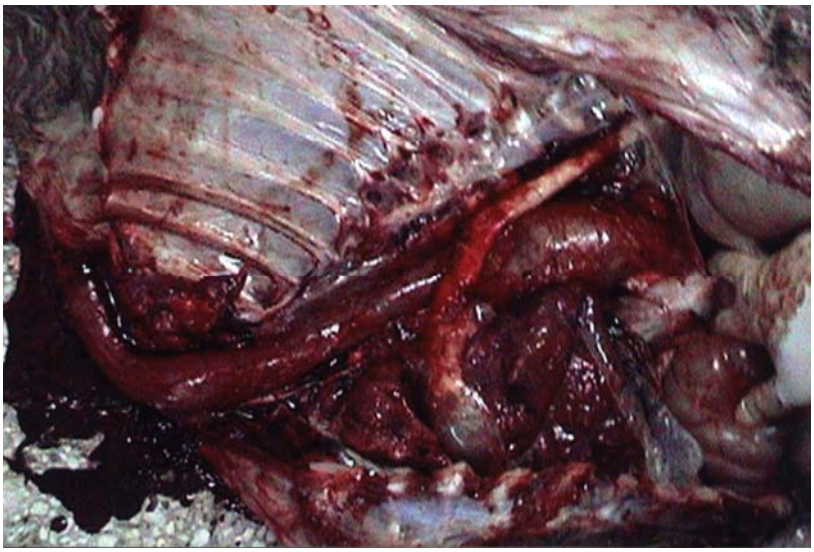

Fig. 2. Appearance of dilated thoracal and cervical oesophagus at necropsy.

Table 1
Important laboratory parameters in a calf with megaoesophagus

Parameter	Case values	Reference values[5,6,7] Min-Max	Mean	Evaluation compared to reference values
Haematocrit (%)	52	24.0-46.0[5]	35.9±3.8[5]	increase
Urea (mg/dL)	103	42.8-64.2[6]	-	increase
Blood urea nitrogen (mg/dL)	48	20-30[6]	-	increase
Creatinine (mg/dL)	2.9	1-2[6] or 0.7-1.1[7]	-	increase
Total protein (g/dL)	5.8	6.7-7.4[6]	7.1±0.18[7]	decrease
Albumin (g/dL)	3.5	3.0-3.55[6]	3.3±0.13[7]	normal
Globulin (g/dL)	2.3	3.0-3.48[6]	3.24±0.24[6]	decrease
AST (IU/L)	128	78-132[6] or 48-100[7]	105±27[6]	increase
LDH (IU/L)	2610	692-1445[6]	1061±222[6]	increase
CK (IU/L)	3546	44-228[7]	-	increase
Sodium (mmol/L)	132	132-152[6]	142[6]	low limit
Calcium (mg/dL)	7.4	9.7-12.4[6] or 7.9-10.0[7]	11.08±0.67[6]	decrease
Phosphorus (mg/dL)	6.5	5.6-6.5[6]	-	high limit

Discussion

Etiology of megaoesophagus had been implicated in congenital and acquired conditions (9, 15). Any condition that results in disruption of the neural reflex controlling swallowing or affects function of the oesophageal muscles can be responsible. Especially, main disease categories involved are neuropathies and myopathies (4, 8, 9).

Megaoesophagus should be suspected when clinical signs of regurgitation occur shortly after eating (11, 15). In the present case, both information obtained from anamnesis and clinical observations revealed the case as megaoesophagus due to both regurgitation and excess of feed in the oesophagus. Regurgitation is the hallmark of an oesophageal disease, which is a passive act that does not require a neurological reflex for the retrograde evacuation of oesophageal contents (8, 11, 15). At the contrast radiography, barium sulphate accumulated at cervical oesophagus and dilatation in this region was observed. Therefore, thoracal oesophagus could not be observed by contrast radiography because barium sulphate did not pass to thoracal oesophagus. Therefore, acquired segmental megaoesophagus was diagnosed. It has been reported that in cattle, the obstructions are usually in the cervical oesophagus, just above the larynx, at the thoracic inlet, at the base of the heart or at the cardia (11). Furthermore, it is suggested that in megaoesophagus, passage of different sizes of stomach tubes is beneficial (9). This aids in establishing the presence or absence of obstruction causing segmental megaoesophagus (1, 9). In this case study, at necropsy, the oesophagus was filled with feedstuff, containing rough fibre, at the inlet of the *hiatus diaphragmatica* region.

In the present case, physical examination revealed dehydration, increase in respiratory rate, decrease in rectal temperature, and bradycardia. Additionally, laboratory findings showed increases in haematocrit value, urea, blood urea nitrogen, and creatinine contents, and AST, LDH, and CK activities, whereas decreases in total protein, globulin, and Ca concentrations. As for other parameters, Na was in the lowest and P was in the highest physiological reference values (6, 7).

Dehydration in this case was due to regurgitation and dysphagia as reported by other authors who studied megaoesophagus (9, 11, 12). Furthermore, increase observed in the haematocrit value, and urea and blood urea nitrogen concentrations, were also due to disturbances in fluid-electrolyte balance and kidney function disorders, which occurred after dehydration (6).

It is reported that the development of aspiration pneumonia is the most serious potential complication in animals with megaoesophagus, which can be life threatening (8, 9, 11). In this case, although pathological sounds at the lung auscultation was not observed, an increase in respiration rate could develop due to feed aspiration or compensation of the vascular system deficiency, which occurred as a result of bradycardia and dehydration (9).

Previous studies on megaoesophagus, hyperproteinaemia have been reported (9). But, total protein and globulin levels were low in the present study, whereas albumin level did not change. Kaneko *et al.* (6) suggested that albumin and globulin levels decrease due to malnutrition. Furthermore, globulin levels also decrease as a result of chronic pulmonary and immune deficiency diseases. Therefore; in this study, hypoproteinaemia occurred due to decrease in globulin level, which possibly developed as a result of malnutrition after anorexia and regurgitation, and/or lung disorders and immune deficiency.

In this case, serum Na concentration was in the lowest, and P in the highest physiological reference values, but Ca levels were significantly lower than physiological values (Table 1). Although all details are not known, it seems that early in the course of renal failure there were analytically imperceptible hyperphosphataemia and hypocalcaemia (6). The

hyperphosphataemia was due to decreased glomerular filtration. Hypocalcaemia might be a direct physiological effect of hyperphosphataemia (Ca x P = constant), a deficiency of the form(s) of vitamin D, or both as reported by Kaneko *et al.* (6).

Hyponatraemia has been described in acute renal failure in cattle (6). In this case, Na levels were also in the lowest physiological reference limits, which showed kidney function disorders.

Determination of muscle originated enzymes (CK, AST, LDH) in domestic animals was reported to be practical and reliable index in muscle damage (3, 11). In this study, CK, LDH, and AST values were found to be increased (Table 1). This situation might be the sign of oesophageal damage. Similarly, some authors reported increase in CK values in animals with megaoesophagus (4, 9). Furthermore, Ross and Rebhun (12) also reported increase in CK and AST values in a cow with megaoesophagus suffering from acute pharyngeal myopathy.

In the present case bradycardia was present. In vagal indigestion in cattle, bradycardia occurring due to vagal damage is well known by clinician's entity (11). *N. vagus* has a breaking effect on heart rate and *N. accelerentes* has the opposite one. Most parts of the gastrointestinal tract such as the pharynx, oesophagus, and stomach receive parasympatic innervation by way of the vagus nerve, except the terminal portions of the colon. Therefore, *N. vagus* has the regulatory effect on digestive system functions (2, 10). Thus, damages occurring on the *N. vagus* or its branches, cause disturbances in the digestive system functions and heart rate. On the other hand, bradycardia may also occur as a result of defects in the heart internal impulse system**.** Therefore, to differentiate the origin of bradycardia, whether it is of vagal origin or heart internal impulse system, atropine application have been suggested (11, 13). For this purpose, atropine sulphate was applied to the animals having bradycardia, and heart rate was listened up to 30 min in 5 min intervals. If the heart rate after atropine application increased up to 7-16%, the origin of the bradycardia might be considered to be vagal. If it did not, it indicated heart internal system defects (13). Because atropine has an anticholinergic effect, therefore, when it attracts to preganglionic parasympathetic fibres, gets rid of acetylcholine (2, 10). Thus, while vagal effects decrease, heart rate increases. In the present case, after atropine application, heart rate of the calf increased above 14%. Therefore, bradycardia observed in the present study was considered to be of vagal origin.

In a previous study, megaoesophagus and bradycardia were reported to be present in a cow and were thought to be sequelae of vagal nerve injury due to initial pharyngeal traumatic insult. But it is not put forward in certainty (12). In the present study, the relationship between acquired megaoesophagus and vagal damage was determined for the first time. Therefore, similarly as reported for congenital megaoesophagus (14), damages occurring in the vagus nerve or its branches may also play a role in the etiology of the acquired megaoesophagus.

In conclusion, in animals suspected of megaoesophagus, radiographic and endoscopic examinations can give certain diagnosis. But, the role of *N. vagus* can be evaluated by the atropine test. Furthermore, in megaoesophagus cases with severe dehydration and deterioration in the kidney functions, these symptoms should not be overlooked and treatments in this direction should be taken into consideration.

References

1. Anderson N.V., Vestweber J.G., Voisin A.J., Mills L.J.: Hiatal hernia and segmental megaesophagus in a cow. J Am Vet Med Assoc 1984, **184**, 193-195.
2. Cunningham J.G.: Textbook of Veterinary Physiology. Philadelphia, W.B Saunders Co., 2002.
3. Fry J.M., Allen J.G., Speijers E.J., Roberts W.D.: Muscle enzymes in the diagnosis of ovine weaner nutritional myopathy. Aust Vet J 1994, **71**, 146-150.
4. Hopper K., Beck C., Slocombe R.F.: Megaesophagus in adult dogs secondary to Australian tiger snake envenomation. Aust Vet J 2001, **79,** 672-675.
5. Jain N.C.: Essentials of Veterinary Hematology. Philadelphia, Lea & Febiger, 1993.
6. Kaneko J.J., Harvey J.W., Bruss M.L.: Clinical Biochemistry of Domestic Animals. California, Academic Press, 1997.
7. Meyer D.J., Harvey J.W.: Veterinary Laboratory Medicine. Philadelphia, W.B Saunders Co., 1998, pp. 345-359.
8. Mirakhur K.K., Rathor S.S.: Megaesophagus in a calf. Indian Vet J 1989, **66,** 259-260.
9. Ndikuwera J., Odiawo G.O., Usenik E.A.: Idiopathic megaesophagus in a pregnant heifer. Vet Rec 1990, **126**, 165-166.
10. Qian B., Danielsson A.: Vagal regulation of the gastrointestinal neuroendocrine system. Scand J Gastroenterol 1996, **31**, 529-540.
11. Rodastits O.M., Blood D.C., Gay C.: Veterinary Medicine. London, Bailliere Tindall, 1995.
12. Ross C.E., Rebhun W.C.: Megaesophagus in a cow. J Am Vet Med Assoc 1986, **188,** 623-624.
13. Turgut K., Ok M.: Kedi ve Köpek Gastroenterolojisi. Konya: Bahçıvanlar Basım Sanayi A.Ş., 2001.
14. Ulutas B., Sarierler M., Bayramli G., Ocal K.: Macroscopic findings of idiopathic congenital megaesophagus in a calf. Vet Rec 2006, **158,** 26-27.
15. Vestweber J.G., Leipold H.W., Knighton R.G.: Idiopathic megaesophagus in a calf: clinical and pathologic features. J Am Vet Med Assoc 1985, **187,** 1369-1370.