pISSN 1598-298X / eISSN 2384-0749
J Vet Clin 35(2) : 50-52 (2018)
http://dx.doi.org/10.17555/jvc.2018.04.35.2.50

Journal of Veterinary Clinics
www.ksvc.or.kr

Botulinum Toxin Injection before Surgical Intervention in a Dog with Cricopharyngeal Achalasia

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(Received: February 07, 2018 / Accepted: April 13, 2018)

Abstract : A 6-month-old castrated male poodle presented with a cough, dysphagia, and regurgitation. Cricopharyngeal achalasia (CPA) was diagnosed by clinical history and a fluoroscopic examination. The animal received a botulinum toxin (BTX) injection but symptoms had not resolved by three days after injection. Thus, a cricopharyngeal and thyropharyngeal muscle myotomy was performed and immediately the clinical signs resolved. This report describes successful correction of CPA with myotomy after failure of BTX injection in a dog.

Key words **:** Botulinum toxin, Cricopharyngeal achalasia, Cricopharyngeal muscle myotomy, Dog.

Introduction

Cricopharyngeal achalasia (CPA) is a rare disease in which the upper esophageal sphincter fails to relax during deglutition (5,22). General clinical signs of CPA are repeated swallowing attempts, regurgitation, coughing, aspiration, and weight loss (5,14,20). These are potentially life threatening and reduce the quality of life.

CPA is generally diagnosed by clinical history and video-fluoroscopic study but the diagnosis is often delayed as the condition is not widely recognized among clinicians (5). Treatment for CPA involves, dilation of the cricopharyngeal (CP) muscle, CP myotomy, or botulinum toxin (BTX) injection (5,8). In humans, CP myotomy is considered the most successful and standard treatment, however, BTX injection is preferred over surgical treatments because of the low risk, low cost of the procedure, thus, most patients receive a BTX injection before the myotomy (23). Nonetheless, there is lack of veterinary studies providing information about CPA, particularly BTX treatment. In this report, the dog with cricopharyngeal achalasia was administered a BTX injection. Because there was not sufficient efficacy, myotomy was subsequently performed. This is the first report describing the treatment of CPA with myotomy after failure of BTX injection in a dog.

History

A six-month-old, 2.5 kg castrated male poodle with a cough, and dysphagia was referred to the Veterinary Medical Teaching Hospital, at Kyung-pook National University. The dog had been gagging from 3-month-old and presented repeated swallowing attempts, and continuous regurgitation after just eating commercial solid food at the time of visiting.

Upon physical examination, the dog was bright and alert, but had poor body condition (BCS 2/9). The complete blood count and serum biochemistry profile did not reveal abnormalities, except increased alkaline phosphatase (367 U/I, [RI (reference interval) 47-254 U/I]), inorganic phosphorus (6.9 mg/dl, [RI 1.9-5.0]), and calcium (12.3, [RI 9.3-12.1]). In plain radiographs, only mild bronchitis was noted and abdominal ultrasound revealed no specific abnormality.

In a video-fluoroscopic study on standing posture with iohexol (Bonorex 300; Centrial Medical Service, Seoul, Korea), the narrowed esophageal tract was noted and aspirated contrast material was shown in the airway. Only a small amount of contrast had merely passed through the esophagus and most of the contrast material were regurgitated (Fig 1).

On the basis of the clinical signs and the contrast fluoroscopic study, the dog was diagnosed as CPA. After discussion with the owner, medical treatment with botulinum toxin (BTX) was selected for CPA treatment. Anesthesia was induced with intravenous propofol (6 mg/kg, Provive, Myungmoon Pharm, Seoul, Korea) and maintained with isoflurane (1.5 MAC, Ifran, Hana Pharm, Seoul, Korea). After positioning in dorsal recumbency, the skin of neck was incised about 3 cm from the larynx. The sternohyoid muscle was divided and retracted bilaterally. In total, 10 U of BTX (Meditoxin Inj.; Medtox, Korea, 100 UI diluted in 1 ml of normal saline) was intramuscularly injected at three points of the CP muscle (bilateral and ventral points). For three days after BTX injection, the symptoms, including cough, regurgitation, and improper swallowing, deteriorated. In contrast fluoroscopy, administered iohexol presented around cricopharyngeal region, similar to before BTX injection. Therefore, surgical treatment was conducted. The surgical approach was performed under general anesthesia with the dog in a dorsal recumbency position, and the cricopharyngeal and thyropharyn-

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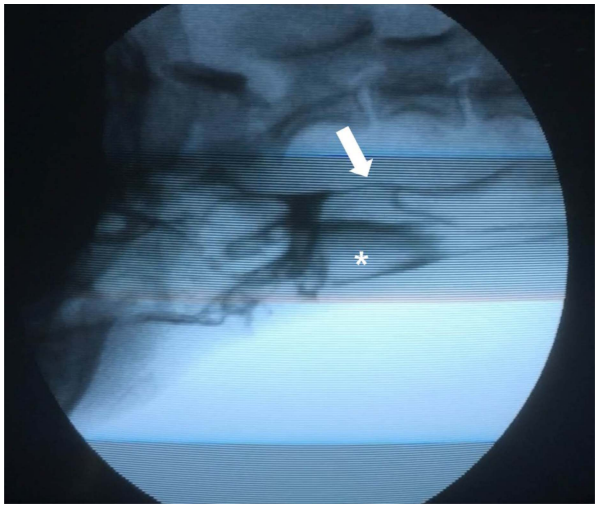

Fig 1. Fluoroscopic image of the dog before surgery. Narrowed esophageal tract (white arrow) and aspirated contrast material (asterisk) are shown.

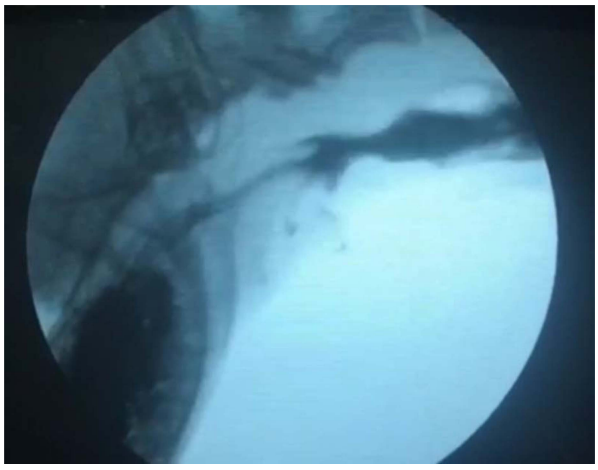

Fig 2. Fluoroscopic image of the dog after surgery. The stricture region could not be seen. The contrast materials were not regurgitated to oral region or aspirated to airway.

geal muscle were transected. After surgery, symptoms were immediately solved. Several hours after surgery, the dog ate commercial canned food with any gagging, cough or repeated swallowing attempts. In contrast fluoroscopy, the contrast solution was amply swallowed and neither regurgitation nor aspiration was observed (Fig 2). The patient was corrected with surgical treatment, and no complication was reported during the six-month follow up period.

Discussion

The CP muscle (upper esophageal sphincter: UES) is a sphincteric structure that separates the hypopharynx from the esophagus (5). Normally, the CP muscle is constantly closed in its resting position to prevent the swallowing of air into the esophagus and the regurgitation of food from the esophagus back into the pharynx (16,21).

CPA is an uncommon cause of dysphagia in which the UES fails to properly relax during swallowing (5,22). This condition is very rare in humans and dogs, and potentially life threatening (5,19). CPA can be treated via CP dilation, the injection of BTX, and CP myotomy (5,8). In the past, many clinicians perform mechanical dilation or myotomy of the CP muscle to resolve symptoms. The CP dilation is often effective and low risk, but the duration of clinical effects is short. CP myotomy shows significant efficacy in CPA but, has some risks such as infection and CPA recurrence due to fibrosis. These complications meant that alternative treatments were required, and the local injection of BTX into the CP muscle in humans was first described in 1994 by Schneider *et al* (18).

BTX inhibits the release of acetylcholine from nerve endings and thus relaxes the muscle complex (13). The therapeutic effects are usually evident by three days after injection, and the duration of benefits generally lasts 3-4 months (6). BTX is inexpensive and a less invasive method compared to other treatments (23). Thus, BTX injection may be preferable to surgical treatments as first option for CPA. In this study, a dog had suffered continuous coughing and regurgitation after feeding. CPA was diagnosed through the video-fluoroscopic study and BTX injection was chosen as treatment for CPA. The dog was injected 10 U of BTX in total and observed for three days after treatment. However, symptoms deteriorated and the patient's condition worsened. According to previous studies, the BTX injection has resulted in mild and minimal side effects, but the temporary worsening of dysphagia, belching, and the worsening of reflux have been reported in humans (7). The reported success rated of BTX injection in humans is 43-100% (mean: 76%) and is not as successful as myotomy (8). Therefore, if BTX treatment fails, CP myotomy can be selected as the second therapeutic choice. Some clinicians believe that if the BTX injection does not attain sufficient improvement, surgical myotomy is also unlikely to be helpful (1,18). However, Zaninotto *et al*. suggested that failure with BTX injection cannot be used as a indicator of an unsuccessful myotomy (23). They found that only 42.8% of patients experienced improved dysphagia with BTX and that 72.7% of patients who did not respond to BTX still benefited from a myotomy. In our study, the patient did not respond to BTX injection. Thus, cricopharyngeal and thyropharyngeal muscle were transected and symptoms were immediately solved. In veterinary medicine, as surgical options for CPA, cricopharyngeal myectomy (or myotomy) with or without thyropharyngeal myectomy (or myotomy) have been reported and no correlation between surgical methods was seen in the occurrence of complications (9,14,15,20).

Although it was unclear why a myotomy might still be useful when BTX fails, insufficient BTX dosage, BTX A resistance, or structural changes in the target muscle are considered as the causes (22). In our study, 10 U of BTX was injected directly into the muscle. This volume was sufficient for the patient compared to previous studies. Thus, the probability that the dose of BTX was insufficient is relatively low, in this study. Some studies have suggested that some patients who were unresponsive to BTX A might respond better to other BTX (B and F) in humans (3,11,12,17). However, BTX resistance in dogs has not yet been reported. The most likely

possibility is structural changes in the CP muscle. BTX is probably ineffective when injected into a rigid, inelastic muscle. The CP muscle is contracted most of the time, thus connective tissue is abundant in CP muscle compared to other muscles (2,10). Particularly, in CPA patients, the CP muscle is more hyperfunction than normal states, thus the connective tissue may be increased and fibrosis can be detected.

CPA is very rare condition in dogs, and reports of CPA treatments particularly BTX injection are limited compared to humans. In human medicine, it is recommended that BTX injection can be applied as a diagnostic test or treatment as a first option because this is safe and more cost-effective than myotomy. However, in dogs, the efficiency of BTX is uncertain (4).

In our case, the dog with no response to BTX was successfully corrected with myotomy. Thus, failure of medical management with BTX cannot be indicate that the patient is not CPA or surgical myotomy would be ineffective. Further studies for injection of BTX in dogs should be performed before clinical application.

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