

## Vocal fold granuloma associated with brachycephalic obstructive airway syndrome in 13 dogs

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### Objective

To clinically and histopathologically characterize the laryngeal mass commonly referred to as *vocal fold granuloma* in brachycephalic dogs and to evaluate treatment responses and follow-up outcomes.

### Animals

13 brachycephalic dogs were included (8 French Bulldogs, 2 Bulldogs, 1 Pug, 1 Boston Terrier, and 1 Cavalier King Charles Spaniel).

### Clinical Presentation

Brachycephalic dogs diagnosed with a vocal fold mass during endoscopic laryngeal examination were retrospectively included.

### Results

11 dogs were referred for consultation of brachycephalic obstructive airway syndrome (BOAS). All dogs exhibited clinical signs of upper respiratory obstruction, and 7 had gastrointestinal symptoms. Twelve dogs underwent surgical resection of vocal fold masses with BOAS surgery. Histopathological evaluation revealed exophytic granulation tissue associated with ulceration and inflammation, as well as varying degrees of mucosal hyperplasia. Postoperative treatment included glucocorticoids and antibiotics. One dog with unilateral laryngeal paresis experienced a recurrence of clinical signs 6 months postoperatively and required a second surgical resection. The median follow-up duration for all 13 dogs was 499 days (range, 95 to 1,708 days). No further recurrence was observed during the follow-up period.

### Clinical Relevance

Laryngeal masses in various brachycephalic breeds, referred to as *vocal fold granulomas*, consisted of granulation tissue rather than true granulomas. Surgical intervention, including conventional BOAS surgery and excision of granulation tissue, combined with anti-inflammatory treatment appeared essential for establishing a diagnosis and addressing underlying causes.

**Keywords:** brachycephalic obstructive airway syndrome, vocal fold granuloma, ulcerative laryngeal disease, proliferative laryngeal disease, granulation tissue

**B**rachycephalic obstructive airway syndrome (BOAS) is a hereditary, early-onset, and lifelong condition affecting dogs with a brachycephalic conformation.<sup>1</sup> The brachycephalic conformation results in airway malformation, such as stenotic nares, an elongated soft palate, tracheal hypoplasia, aberrant

turbinates, and macroglossia.<sup>1,2</sup> Recently, additional anatomical abnormalities have been recognized, including *vocal fold granuloma*.<sup>3</sup>

A similar benign laryngeal lesion has also been documented in human medicine. Although historically referred to as *vocal fold granuloma*, this lesion is not a true granuloma composed of epithelioid macrophages but is characterized by epithelial hyperplasia and inflammatory changes.<sup>4</sup> The first study<sup>3</sup> of vocal fold granuloma in dogs reported granulation tissue formation in vocal folds, and all 6 dogs were French Bulldogs. However, BOAS has been reported in various brachycephalic dogs beyond French Bulldogs,

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such as English Bulldogs, Pugs, Boston Terriers, Pekingese, and Cavalier King Charles Spaniels, and the prevalence of vocal fold granulomas in these other brachycephalic dogs remains unclear.

The present study aimed to clinically and histopathologically characterize the laryngeal mass commonly referred to as a *vocal fold granuloma* in a broader range of brachycephalic breeds beyond French Bulldogs and to evaluate treatment responses and follow-up outcomes.

## Methods

This multi-institutional retrospective study was conducted at AMC Suematsu Animal Hospital (Oita, Japan), Kyoto Animal Medical Center (Kyoto, Japan), and TRVA Animal Medical Center (Tokyo, Japan) between 2020 and 2024. Brachycephalic dogs diagnosed with a vocal fold mass during endoscopic laryngeal examination were included. Data collected were signalment, clinical signs (upper respiratory signs such as stridor, stertor, inspiratory efforts, exercise intolerance, and syncope and gastrointestinal signs such as ptyalism, regurgitation, and vomiting), physical examination findings, imaging findings, endoscopic examination results, histopathological findings, treatment data for BOAS and vocal fold masses, and recurrence information. Severity of stenotic nares (mild, moderate, and severe),<sup>5</sup> pharyngeal collapse (partial or complete),<sup>6</sup> and laryngeal collapse (grades 1 to 3)<sup>7</sup> were evaluated on the basis of previous studies. Under endoscopic examination (Evis Lucera Elite, Olympus Corp; VO-4C, Olympus Corp; and aView 2 Advance, Ambu A/S), the severity of the elongated soft palate, laryngeal collapse, and laryngeal paresis or paralysis was evaluated prior to intubation.

Dogs were anesthetized with IV administration of propofol and placed in sternal recumbency. For easier access during laryngeal surgery, some patients underwent transient tracheostomy. Vocal fold masses were grasped with forceps and resected with Metzenbaum scissors or a surgical energy device (Sonicbeat; Olympus Corp). Repair of stenotic nares, staphylectomy, and removal of everted laryngeal ventricles were performed as needed. All resected vocal fold masses were submitted for histopathological evaluation. Specimens were fixed with 10% formalin, and pathology slides were stained with H&E. Diagnoses were established or supervised by American College of Veterinary Pathologists–certified pathologists. All dogs were privately owned, and informed consent was obtained in accordance with each institution’s guidelines. Because of the retrospective nature of this study, approval from the IACUC was considered unnecessary.

## Results

### Animals

A total of 13 brachycephalic dogs were eligible for this study, including 8 French Bulldogs, 2 Bulldogs, 1 Pug, 1 Boston Terrier, and 1 Cavalier King Charles Spaniel, and consisted of 8 males (6 intact and 2 castrated males) and 5 females (3 intact and 2

spayed females). The median age was 3 years (range, 0.5 to 7 years). The median body condition score was 6 (range, 5 to 8), and the median body weight was 10.3 kg (range, 6.9 to 19.2 kg). Patient information is summarized in **Supplementary Table S1**.

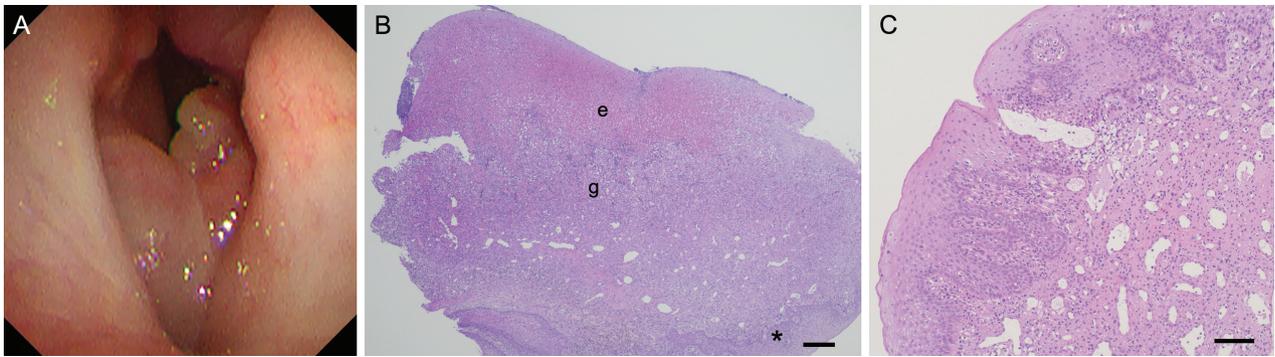
Eleven dogs were referred for BOAS consultation. One dog was presented with upper respiratory obstruction and had received a transient tracheostomy at a primary care hospital before referral. Another dog was referred because of difficulty in intubation before an ovariohysterectomy. All dogs exhibited clinical signs of upper respiratory obstruction. Respiratory signs included inspiratory effort (100% [13 of 13]), stertor (92% [12 of 13]), and stridor (92% [12 of 13]). Exercise intolerance was reported in 89% (8 of 9), cyanosis in 15% (2 of 13), and syncope in 8% (1 of 13). Gastrointestinal signs included vomiting (54% [7 of 13]), regurgitation (31% [4 of 13]), and ptyalism (23% [3 of 13]). Frequency was not recorded. On physical examination, 11 dogs had stenotic nares (mild,  $n = 3$ ; moderate, 4; severe, 2; severity not recorded, 2). All dogs underwent fluoroscopic evaluation. Pharyngeal collapse was observed in 12 dogs (complete,  $n = 7$ ; partial, 4; severity not recorded, 1) and could not be evaluated in 1 dog with a transient tracheostomy. Epiglottic retroversion was observed in 2 dogs. Thoracic fluoroscopy was available for 4 dogs, and hiatal hernia was not detected.

### Endoscopic examination

During the endoscopic laryngeal examination, masses were observed on the left vocal fold in 6 dogs and on the right in 7 dogs. A representative image is shown in **Figure 1**. All masses were located on vocal folds. Three masses were located dorsally, 5 ventrally, and 5 at mid-height. The masses were relatively well demarcated in 85% (11 of 13) of the masses and ill-defined in 15% (2 of 13). Masses had a polypoid appearance in 62% (8 of 13) of the masses and a sessile appearance in 38% (5 of 13). The surfaces were smooth in 11 dogs, but 2 masses appeared multilobular. In 1 dog (dog 7), a similar appearance of a smooth, dome-shaped nodule was also observed in the nasopharynx. An elongated soft palate was observed in 92% (12 of 13) of cases. Laryngeal collapse was observed in 12 dogs and classified as grade 1 ( $n = 11$ ) and grade 2 (1). No cases were classified as grade 3. Left laryngeal paresis was observed in 1 dog (dog 5).

### Surgical interventions, histopathological findings, and treatments

Except for 1 dog, the remaining 12 dogs underwent concurrent surgical resection of vocal fold masses and BOAS surgery. Histopathological evaluation revealed that all masses consisted of granulation tissue, often protruding from ulcerated mucosa, and were accompanied by a variable amount of fibrinosuppurative exudate and neutrophilic inflammation (Figure 1). Adjacent mucosal epithelium was often hyperplastic, and polypoid mucosal hyperplasia was observed in some cases. Additional findings included edema, plasma cell



**Figure 1**—A—An endoscopic laryngeal image of dog 12 showing a polypoid mass in the left vocal fold. B and C—Photomicrographs of a section of the vocal fold mass of the same dog stained with H&E. In panel B, granulation tissue (g) extends outward from the ulcerated mucosa and the surface is covered with exudate composed of fibrin and neutrophils (e). The mucosal epithelium adjacent to the ulcer is thick (asterisk). Bar = 200  $\mu$ m. In panel C, the remaining mucosa is hyperplastic. Bar = 100  $\mu$ m.

and lymphocyte infiltration, hemosiderin-laden macrophages associated with congestion and hemorrhages, and fibrosis. No neoplastic lesions were observed in any of the dogs.

For BOAS surgery, the number of dogs undergoing each procedure was as follows: repair of stenotic nares (92% [11 of 12]), staphylectomy (100% [12 of 12]), and removal of everted laryngeal ventricles (92% [11 of 12]). Tracheostomy tubes in 2 dogs were removed postoperatively.

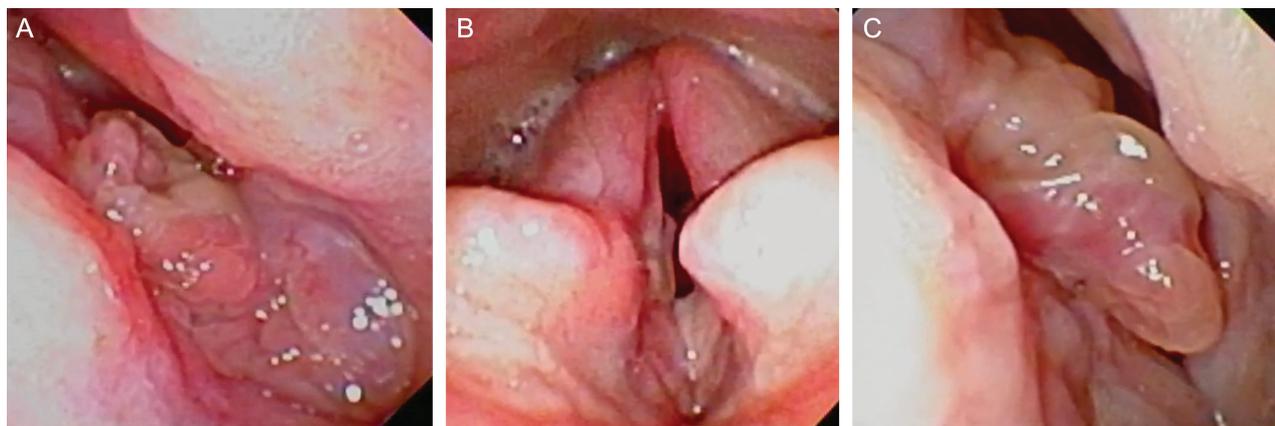
One dog (dog 4) did not undergo surgery and was treated medically with prednisolone (1 mg/kg, SC, q 24 h for 8 days) and maropitant (1.0 mg/kg, SC, q 24 h). For the remaining 12 dogs, prednisolone was also prescribed (0.4 to 1.0 mg/kg, PO or SC, q 24 h for 4 to 10 days). Antibiotics were used as follows: ampicillin (20 mg/kg, SC for 1 to 4 days; n = 7), amoxicillin/clavulanate (12.0 to 19.7 mg/kg, PO, q 12 h for 4 to 9 days; 2), cephalexin (15.6 to 22.5 mg/kg, PO, q 12 h for 5 to 10 days; 2), and amoxicillin (15 mg/kg, PO, q 12 h for 4 days; 1). Other drugs used were maropitant (1.0 mg/kg, SC, q 24 h; n = 11), famotidine (1.0 mg/kg, PO, q 24 h; 1), and mosapride (0.7 mg/kg, PO, q 12 h; 1).

#### Follow-up information

One dog with left laryngeal paresis (dog 5) underwent surgical resection of the right-side vocal fold mass but experienced recurrence 6 months later. The dog returned on day 276 after the initial resection with worsening inspiratory effort, stridor, stertor, and foamy vomitus. Laryngeal endoscopy revealed recurrence of the vocal fold mass at the same location with a similar appearance (**Figure 2**). The mass was surgically excised again on day 338, and histopathology confirmed a similar lesion to the initial diagnosis. No further recurrence was reported 548 days after the second surgical resection.

Dog 4, which was treated with medication alone, remained asymptomatic for 667 days. Follow-up endoscopy was not performed, and whether the laryngeal mass was completely resolved remained unclear.

The overall follow-up duration for all dogs was a median of 499 days (range, 95 to 1,708 days) after surgery or medical management. For the dogs treated with surgical excision, the follow-up duration was a median of 413 days (range, 95 to 1,708 days).



**Figure 2**—Endoscopic laryngeal images of dog 5. A—At the first visit. An ill-defined, sessile mass with a rough surface is present at mid-height of the right vocal fold. B—After the first surgery, the mass was resected. C—On day 276. A recurrence is observed at the same location, appearing as an ill-defined, sessile mass with a rough surface.

## Discussion

This study identified laryngeal mass formation in various brachycephalic breeds. The most common breed was the French Bulldog, consistent with a previous study<sup>3</sup> in which all dogs were French Bulldogs. In the current study, Bulldogs, a Pug, a Boston Terrier, and a Cavalier King Charles Spaniel were also identified, highlighting the prevalence of this disease beyond French Bulldogs.

As noted in the previous study<sup>3</sup> of French Bulldogs and in human medicine,<sup>8</sup> the term *granuloma* in *vocal fold granuloma* is a misnomer. True granulomatous lesions (granulomas) are characterized by an organized collection of mature mononuclear phagocytes, with or without necrosis, differentiation of macrophages into epithelioid cells and giant cells, and infiltration of other immune cells and frequently associated with foreign bodies or infection.<sup>9</sup> The histopathological evaluation of the *vocal fold granulomas* in this study revealed granulation tissue formation secondary to ulceration, with varying degrees of epithelial hyperplasia, mucosal hyperplasia, inflammatory changes, and fibrosis, findings similar to those observed in human vocal fold granuloma.<sup>10</sup> A comparable misuse of the term *granuloma* in both human and veterinary medicine is exemplified by *pyogenic granuloma* in the oral cavity, which consists of granulation tissue and does not represent granulomatous inflammation.<sup>11,12</sup> The term *vocal fold granuloma* in brachycephalic breeds should be used with the understanding that *granuloma* is a misnomer.

In human medicine, mechanical trauma (eg, intubation trauma and vocal abuse) and chemical injury (eg, gastroesophageal reflux) are implicated in the development of vocal fold granuloma.<sup>8</sup> Similar risk factors are suspected in brachycephalic dogs. First, both primary and secondary airway malformation contribute to negative pressure and increased airway resistance in the upper airway during respiration.<sup>13</sup> Second, brachycephalic dogs are predisposed to gastroesophageal reflux, hypothesized to result from high negative intrathoracic pressure, and reported to improve with esophageal hiatal rim reconstruction, staphelectomy, and alarplasty.<sup>14</sup> This predisposition may explain the prevalence of digestive tract lesions, including esophagitis, hiatal hernia, and pyloric mucosal hyperplasia in these dogs.<sup>15</sup> In this study, all dogs exhibited inspiratory effort and upper respiratory stridor or stertor, suggesting chronic upper airway negative pressure that exposed vocal folds to chronic irritation and mucosal microtrauma.<sup>16</sup> Additionally, 7 dogs showed gastrointestinal signs such as vomiting, regurgitation, and ptyalism. In an experimental study<sup>17</sup> of dogs, exposure of vocal folds to gastric acids resulted in ulcers and subsequent granulation tissue formation. Therefore, both mechanical trauma and chemical injury associated with BOAS likely contributed to the laryngeal mass (ie, granulation tissue) formation in this study.

The treatment of presumed underlying causes is a key therapeutic strategy in human medicine.<sup>18</sup> In brachycephalic breeds with respiratory and gastrointestinal

signs, BOAS surgery is essential to reduce negative pressure and mitigate both mechanical trauma and gastroesophageal reflux-induced injury to the vocal folds. Once BOAS is adequately managed, optimal treatment options for vocal fold granuloma should be determined. In this study, 12 out of 13 dogs were successfully treated with surgical excision followed by postoperative corticosteroids and antibiotics, resulting in a median of 413 days of clinical remission with only 1 recurrence, similar to the previous report.<sup>3</sup> Surgical resection enables histopathological diagnosis, which is crucial for differentiating benign granulation tissue from neoplastic lesions, such as carcinoma, lymphoma, mast cell tumor, chondroma, and other malignancies reported in vocal folds in dogs.<sup>19–21</sup> Differentiation from these neoplasms is important, as they carry poorer prognoses.

In human medicine, nonsurgical treatment is the primary approach for vocal fold granuloma, with various treatment modalities reported,<sup>22</sup> including conservative management without surgical excision or specific medications.<sup>23</sup> However, these findings may not be directly applicable to brachycephalic dogs because human research often includes cases of intubation-related granulomas, which were not observed in this study. Intubation-related granulomas in humans generally have a better prognosis than non-intubation-related granulomas despite similar pathological features.<sup>24</sup> While the pathological characteristics of vocal fold granulomas in dogs and humans are similar, treatment responses may differ because brachycephalic dogs with BOAS have underlying structural abnormalities. Furthermore, as discussed earlier, surgical resection is necessary in dogs to establish the histopathological diagnosis. Surgical excision also reduces the bulk of granulation tissue, which contributes to increased negative pressure in the upper airway. Although these differences are noted between brachycephalic breeds and humans, postoperative medical management with anti-inflammatory medications or potentially proton pump inhibitors<sup>4</sup> seems to be beneficial in brachycephalic breeds to reduce inflammation and gastroesophageal reflux, as these were used in this study. Alternative treatments, such as botulinum toxin injection<sup>25</sup> or a combination of surgical resection and radiation therapy,<sup>26,27</sup> remain unelucidated in veterinary medicine.

One dog with contralateral laryngeal paresis experienced recurrence. Chronic irritation between vocal folds due to laryngeal paresis may lead to recurrent mucosal damage and subsequent granulation tissue formation. A similar association between laryngeal nerve paresis and contralateral granulation tissue formation has been reported in humans.<sup>28</sup> Due to the unilateral nature of the paresis, arytenoid cartilage lateralization was not performed in this case. If a dog with bilateral laryngeal paresis or paralysis experiences recurrent laryngeal granulation tissue formation, surgical intervention for laryngeal paresis or paralysis may be considered.

In conclusion, a laryngeal mass, or *vocal fold granuloma*, was identified in various brachycephalic breeds, with BOAS contributing to its development. The mass

was not a true granuloma but rather granulation tissue associated with ulceration and inflammation. Surgical intervention, including conventional BOAS surgery and granulation tissue excision, combined with anti-inflammatory treatment is essential for the diagnosis and management of the underlying causes.

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The authors have nothing to disclose. No AI-assisted technologies were used in the composition of this manuscript.

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### Supplementary Materials

Supplementary materials are posted online at the journal website: avmajournals.avma.org.