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Case Series

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# Invasive tracheal neoplasia in eight cats: descriptive cases and review of the current literature

**James Howard[1], Jade Fisher[2] and M Katherine Tolbert[3]**

## Abstract

*Case series summary* This case series describes eight cases of invasive tracheal neoplasia that were recognized between the years 1989 and 2014 from a single tertiary referral hospital. This is a disproportionately high number of cases compared with the total number of reports in the current literature..

*Relevance and novel information* Invasive tracheal neoplasia is uncommonly diagnosed in domestic cats. Feline tracheal tumors mimic other upper respiratory diseases making diagnosis challenging. Prognosis is guarded to grave, with most cats surviving less than 1 month after beginning treatment. Severe respiratory distress in cats often warrants humane euthanasia. Appropriate clinical suspicion and awareness can expedite diagnoses leading to prolonged survival rates with appropriate treatments. This case series represents the largest number of feline tracheal tumors reported and also describes the first unique histological presentation of what the authors believe to be a poorly differentiated tracheal carcinoma.

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## Introduction

Invasive tracheal neoplasms, tumors arising from luminal and extraluminal tracheal cell lineages that invade the lumen, are rarely reported in veterinary medicine. The largest published review of feline tracheal tumors described 19 feline cases.[1] Only 16 additional case reports have been published, illustrating the infrequency with which this disease is recognized in cats.[2–15]

There are no reported predisposing risk factors associated with invasive tracheal tumors. Cats with tracheal tumors are presented with non-specific upper respiratory signs such as dyspnea, wheezing, exercise intolerance and coughing.[1] Thus, accurate diagnosis is challenging and intervention is often delayed. However, with appropriate diagnostics, tracheal tumors can be promptly identified. This case series describes the largest number of cases reported from one institution.

## Case series description

Eight invasive tracheal tumors were diagnosed between the years 1989 and 2014 at the University of Tennessee Veterinary Medical Center. Cats were excluded (n = 9/17) from this report if they did not have a definitive cytologic or histopathologic diagnosis, or if they had extraluminal tracheal masses without intraluminal invasion. Data collection included signalment, presenting complaint, physical examination findings, treatment, feline immunodeficiency virus/feline leukemia virus status, diagnostic results and outcomes. Descriptive analysis alone was performed owing to small sample size and inconsistent records, which precluded statistical analysis.

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### Case 1

An 11-year-old, female spayed domestic longhair cat weighing 2.95 kg was presented with a 1 day history of respiratory distress that was exacerbated by stress and exercise. Radiographs showed a generalized megaesophagus, an air-filled caudal pharynx and carina compression. Exploratory thoracotomy revealed a tumor, later diagnosed as a tracheal adenocarcinoma, invading the right cranial lung lobe, esophagus and trachea. The cat was euthanized owing to the infiltrative disease.

### Case 2

A 15-year-old, female spayed domestic shorthair cat weighing 3.34 kg was presented with a 14–21 day history of progressive respiratory distress secondary to a previously diagnosed tracheal tumor. The cat was lethargic, cyanotic and maintained an orthopneic posture. There was marked expiratory stridor, wheezing, coughing and gagging. A fluoroscopic-guided debulking procedure was attempted, which resulted in a pneumothorax and hemothorax because of the extensive invasion and necrosis of the tumor. The cat was euthanized. On necropsy, a 2 cm × 2 cm multi-lobulated mass occluded approximately 60–70% of the intraluminal tracheal space. The mass was diagnosed as a low-grade adenocarcinoma.

### Case 3

A 14-year-old, female spayed domestic shorthair cat weighing 6.8 kg was presented for a 1 month history of progressive dyspnea, wheezing, gagging and acute cyanosis. Cervical radiographs showed a 1.5 cm, sessile-based obstructive tracheal mass at the level of C5. Tracheoscopy was performed and no mass was visualized. A cervical exploratory was performed. The mass was identified in the distal trachea near the thoracic inlet. A four-ring tracheal resection and anastomosis was performed. Histologically, the mass was diagnosed as tracheal lymphoma. The cat showed no signs of dyspnea following surgery. Its clinical signs resolved during postoperative monitoring. Long-term response to therapy is unknown as the cat was lost to follow-up.

### Case 4

A 7-year-old, male castrated domestic shorthair cat weighing 9.55 kg was presented in severe respiratory distress, with cyanosis and foaming at the mouth. There was no history of heart disease. Thoracic radiographs showed mild peribronchiolar infiltrates with a bronchointerstitial pattern in the caudodorsal lung fields. A laryngeal examination was performed under sedation, revealing a 2 cm × 2 cm mass caudal to the larynx causing near complete occlusion of the tracheal lumen. Aggressive debulking was performed. The cat improved dramatically following the procedure, with no observable respiratory distress during recovery. The biopsy results were consistent with a salivary gland adenocarcinoma. The cat remained asymptomatic and survived 23 months before being lost to follow-up.

### Case 5

An 11-year-old, female spayed domestic shorthair cat weighing 3.18 kg was presented for a 15 day history of stridorous, inspiratory dyspnea. There was an increased end-expiratory abdominal component to its breathing pattern. Thoracic radiographs revealed a soft-tissue mass cranial to the carina. Tracheoscopy was performed and a large, broad-based intraluminal mass was found occluding 80% of the airway. The mass, which extended into the left mainstem bronchi, was debulked and submitted for histologic evaluation. The biopsy samples were indicative of a basal cell tumor arising from the tracheal glands. This is only the second reported case of a tracheal basal cell tumor and the first in a domestic shorthair breed.[7] The cat was euthanized 44 days after initial diagnosis, owing to severe respiratory distress.

### Case 6

A 9-year-old, male castrated Bengal cat weighing 6.7 kg was presented for a 3 month history of progressive coughing, stridor and intermittent orthopnea. Thoracic radiographs performed 1 month prior showed mild tracheal narrowing extending from the thoracic inlet to the level of C2–C3. Nasal CT was pursued at that time to rule out nasal disease contributing to the upper respiratory signs. Tracheoscopy was also performed and showed mild thickening of the tracheal mucosa with small white nodules present within the tracheal lumen with no obstruction.

One month later, the cat was presented with severe dyspnea secondary to an upper airway obstruction. Emergency tracheoscopy revealed a large, proliferative intraluminal lesion near the thoracic inlet. Debulking of the mass was attempted; however, significant luminal obstruction remained after the procedure. Biopsy samples were submitted for evaluation and supportive of a squamous cell carcinoma. Two months later, the cat was represented for worsening respiratory distress. A third tracheoscopy procedure showed almost complete occlusion of the tracheal lumen. A second debulking procedure was attempted with minimal success. The cat was euthanized 110 days following the initial diagnosis.

### Case 7

A 10-year-old, female spayed domestic shorthair cat weighing 9.1 kg was presented for an 11 day history of progressive coughing, stridor, cyanosis and open-mouth breathing. Radiographs showed an intratracheal soft-tissue mass at the level of the third intercostal space. The mass occluded approximately 75% of the lumen. Tracheoscopy confirmed the presence of two tumors. The

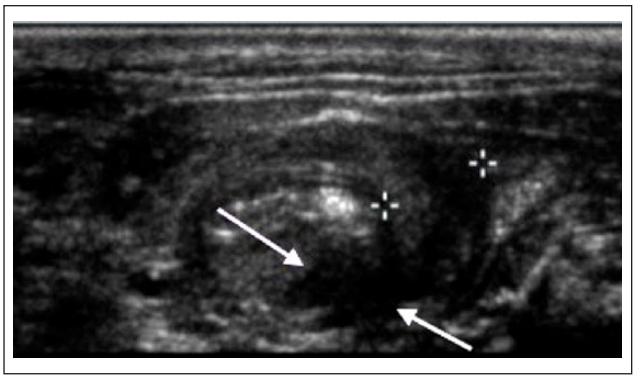

**Figure 1** Transverse image of cervical ultrasound from case 8. Note the degree of intraluminal invasion of the tumor and loss of airway patency. Arrows indicate residual tracheal lumen. Crosses demarcate boundaries of the tracheal wall

**Figure 2** Gross histopathology of the tracheal tumor from case 8. Note the marked expansion of the tracheal wal and surrounding adventitia

first measured 3 cm in diameter and occluded 25% of the tracheal lumen. The second mass was significantly larger, located 1 cm caudal to the first mass. Debulking was attempted, but its location prohibited complete excision. Anesthetic complications necessitated termination of the procedure. Biopsies and impression smears were submitted for evaluation. A high-grade lymphoma was subsequently diagnosed. Palliative treatment (prednisolone, 5 mg PO q12h) therapy resulted in a survival time of 38 days, at which time the cat was humanely euthanized.

### *Case 8*

A 10-year-old, male castrated domestic shorthair cat weighing 8.9 kg was presented for a 6 week duration of worsening stridor, wheezing, intermittent coughing and terminal retching exacerbated by exercise and stress. Tracheal auscultation revealed loud referred upper airway sounds. Thoracic radiographs revealed a 3 cm soft-tissue mass at the level of C3–C5 invading and occluding 85–90% of the tracheal lumen. There was a mild bronchial-unstructured interstitial pattern in all lung fields. An esophagram ruled out extraluminal compression by

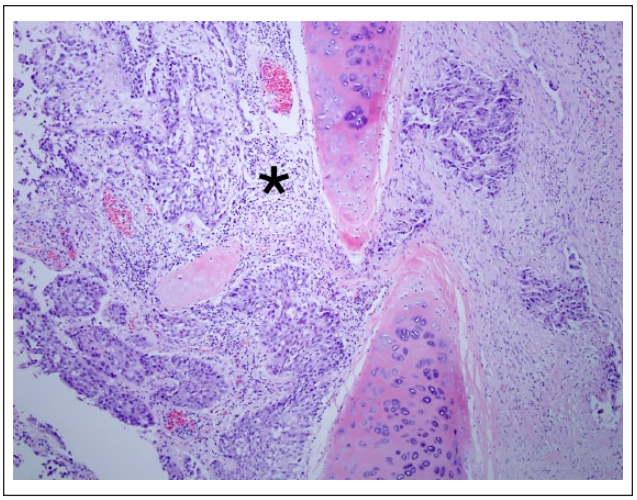

**Figure 3** Neoplastic cells are replacing the mucosa (asterisk) and extending transmurally to expand the adventitia; islands of neoplastic cells are surrounded by a marked scirrhous response

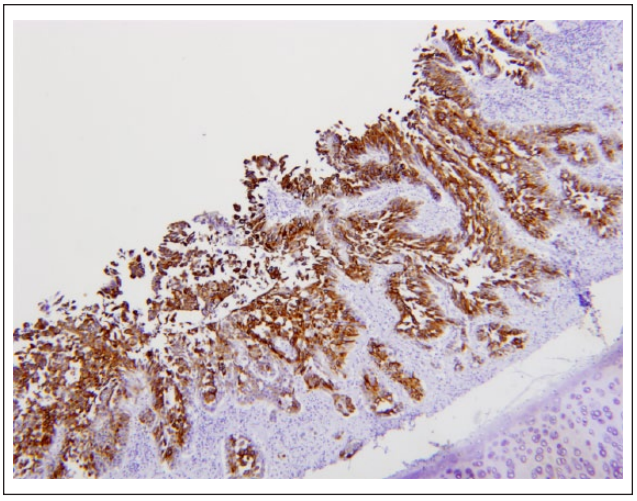

**Figure 4** Tracheal carcinoma. The cytoplasm of neoplastic cells is strongly immunoreactive for cytokeratin

an esophageal mass. Cervical ultrasound showed circumferential involvement of the trachea with intraluminal invasion (Figure 1). Evaluation of fine-needle aspirate samples from the mass was suspicious for a carcinoma. The cat was discharged with directions for hospice care, including piroxicam (2.5 mg PO q24h) and was humanely euthanized 14 days later. Necropsy confirmed the presence of a circumferential tracheal mass with intraluminal invasion (Figure 2). The tumor was submitted for histopathology and subsequent immunohistochemistry (Figures 3 and 4). Samples were fixed in 10% buffered formalin for up to 48 h, trimmed, routinely processed for histology, embedded in paraffin, cut at 5 µm and stained with hematoxylin and eosin.

Immunohistochemistry required additional formalin-fixed, paraffin-embedded sections of the tracheal tumor for staining using anticytokeratin (AE1/AE3) antibodies. These slides were cut at 5 µm on charged slides, air-dried and then heated at 60ºC for 15 mins. Slides were then deparaffinized with xylene and rehydrated through graded ethanols to deionized water. Antigen sites were unmasked using proteinase K (Dako) treatment at room temperature for 5 mins. Slides were then rinsed in Tris-buffered saline/Tween (TBST) at pH 7.6 for 10 mins before being loaded onto the Dako Autostainer, where all procedures are performed at room temperature and all slides are rinsed with TBST between the following steps. Endogenous blocks were performed by treating slides with 3% hydrogen peroxide for 5 mins followed by a serum-free protein block (Dako) for 5 mins. Mouse cytokeratin AE1/AE3 primary antibodies (1:800) were applied and incubated for 30 mins. A horseradish peroxidase-labeled polymer system (Dako EnVision+System) was applied for 30 mins followed by a 10 min application of 3,3′-diaminobenzidine chromogen (Dako). All slides were then taken off the Dako Autostainer, rinsed in deionized water, then counterstained with hematoxylin for 5 s. Slides were blued in ammonia water, then dehydrated through ethanol, cleared with xylene and coverslipped. Negative control slides were processed Universal Negative Control+ mouse serum instead of primary antibodies. Cytokeratin (AE1/AE3) was validated by using respiratory epithelium and the mixed tracheal glands as in internal control within the examined slide.

The neoplasm in this case was a carcinoma representative of epithelial origin with defined cellular nests but no definitive glandular structures to further categorize it as an adenocarcinoma. It is possible that this neoplasm was a poorly differentiated adenocarcinoma or may represent a malignant transformation of tracheal epithelium consistent with a primary tracheal carcinoma. The latter would represent a unique tumor described in the cat.

## Discussion

Eight invasive tracheal tumors represents an inordinately high number of cases diagnosed at one institution over a 25 year period of time. In comparison, only 35 case reports of feline intraluminal tracheal neoplasms from multiple practices have been reported in the last four decades. Misdiagnosis and failure to pursue diagnostic tests to evaluate for tracheal neoplasia might be contributing factors for the small number of reported cases.

Extensive intraluminal occlusion is necessary for recognizable clinical signs. Tracheal tumors, however, are often slow growing and clinically silent, which might be the main contributor to delayed diagnoses. Common clinical signs reported in cats with invasive tracheal tumors are dyspnea, wheezing, stridor, dysphonia, coughing, cyanosis and, rarely, hemoptysis.[1,16] The most common presenting clinical signs in this series were stridor (88%), wheezing (75%), cough (50%), dyspnea (50%) and cyanosis (50%). A large percentage of cats presented with progressive clinical signs (75%). Other less commonly described clinical signs were dysphagia (13%) and gagging (25%).

Survey radiography remains the most widely available, first-tier imaging modality for diagnosing tracheal tumors. Tracheal tumors show no predilection for thoracic or cervical tracheal epithelium; thus, complete tracheal radiographs should be considered. Air within the tracheal lumen provides excellent natural contrast enhancement for tumors. All cats presented in this report showed radiographic evidence of abnormal tracheal narrowing or compression, even if an occlusive mass was not obvious.

Tracheoscopy and biopsy remain the gold standard for diagnosing and evaluating the extent of tracheal tumors.[17] Tracheoscopy was used for definitive diagnosis in 50% of our cases, to localize and determine the extent of invasion. Flexible tracheoscopy is preferred when the patient is stable and complete evaluation of the airway is necessary.[18] Rigid tracheoscopy is utilized and recommended in emergent situations. This allows for rapid evaluation of the proximal airway and can be accomplished with intravenous sedation and flow-by oxygen. If no tumor is found, bronchoalveolar lavage and cytological brushings can be performed to evaluate for inflammatory cells, infectious agents and neoplastic cells from tumors not recognized during tracheoscopy.

Although CT might be unable to determine the degree of tissue invasion, CT remains a valuable diagnostic for intraluminal tumors.[11] Indication for its use include patients with clinical signs and no radiographic evidence of disease, surgical planning, evaluation of peritracheal tissue invasion, radiation planning and assessment of the trachea distal to an occlusive lesion. Intranasal tumors can cause dynamic tracheal collapse and mimic clinical signs associated with tracheal disease including coughing, wheezing and respiratory distress.[19] Thus, nasal CT should be considered in selected cases.

As in other reports,[1] lymphoma and adenocarcinoma were the most common diagnoses in our series (50%). Other less common neoplasms include tracheobronchial neuroendocrine carcinoma, basal cell carcinoma, histiocytic sarcoma and plasmacytoma.[4,7,9,12] To our knowledge, this case series describes the first potential case of primary tracheal carcinoma and the second case report of basal cell carcinoma in a cat (Table 1).

Treatment options necessitate individualized patient analysis to optimize outcome. Resection and anastomosis (R&A) is the treatment of choice and can successfully ameliorate clinical signs for patients with certain tumor types.[16,20] One cat in this study underwent a four-ring tracheal R&A. Postoperatively, its dyspnea resolved and no respiratory distress was evident prior to discharge. A

**Table 1** Tracheal neoplasm cellular characteristics

| | Cell type | Pattern | Immunohistochemistry |
|---|---|---|---|
| Squamous cell carcinoma | Squamous epithelial cells ± keratin pearls | Islands, cords and trabeculae | Cytokeratin AE1/AE3+ |
| Adenocarcinoma | Cuboidal polygonal cells ± cilia | Glands and acini containing secretory product | Cytokeratin AE1/AE3+ |
| Basal cell tumor | Poorly differentiated basal cells | Islands, cords and trabeculae | Cytokeratin AE1/AE3+ |
| Lymphoma | Lymphocytes | Sheets and cords | CD3+ (T cell) or CD20+ (B cell) |

recent study states that ⩽50% of the tracheal length can be resected without decreasing its intraluminal diameter.[21] However, marked bronchial changes were noted at ⩾30% resection of the trachea; thus, the potential for lower respiratory complications should be discussed with the client.[21] Tension and dehiscence are life-threatening complications and patients must be closely monitored in the postoperative phases of healing. The literature suggests that the prognosis for surgical resection can be promising with some tumor types. Although one cat was presented with malignant B-cell lymphoma and only survived 25 days following resection, two previously reported cats with adenocarcinoma underwent surgical management, and survival times were 12 months, with the second cat being asymptomatic at its 3 month reevaluation.[22] Additionally, a 32 month survival time was documented in a cat with basal cell carcinoma after R&A coupled with radiation therapy.[7] Extensive tumor invasion limits the usefulness of surgery if surrounding tissues are severely affected.[23] However, surgery still offers the best chance of survival in patients with extensive disease.[24] Anesthetic risks and appropriate ventilation must be addressed as many patients present in severe respiratory distress.[6]

Bronchoscopic debulking can offer immediate improvement in clinical signs. In cases presented in this series that underwent bronchoscopic debulking (3/8), all patients improved following the procedure. Survival times varied between 44 days and 23 months. Interestingly, the severity of presenting clinical signs did not appear to influence survivability outcome. The patient presenting in the most severe respiratory distress survived the longest after an aggressive debulking procedure. Cauterizing wire snares can mitigate the life-threatening risks of hemorrhage and hemothorax as post-procedural complications. Reported survival times using a wire snare technique varies between 1 and 35 months.[12] One case in this series was euthanized following a hemothorax secondary to an attempted fluoroscopic guided-debulking procedure. As such, non-cauterizing methods should be avoided.

Intraluminal stenting is described in the literature in three cats presented for intraluminal tracheal stricture.[5] There were no complications associated with the stenting procedures and survival times were 6 weeks, 32 weeks and 44 weeks. Stenting should be avoided if surgical resection is an option. No cats had stent placement in our series. Prior to stent placement, advanced imaging is recommended for accurate choice of the implant. Radiographs consistently underestimated tracheal diameter in a cadaveric canine study.[25] This study showed that reliance on radiographic measurements would contribute to stent shortening in the clinical patient as it expanded within the tracheal lumen.[25] Additional cadaveric studies are necessary to determine if the same should be anticipated for cats; however, data extrapolation for surgical planning based on experience in dogs is currently advised.

Permanent tracheostomies have been evaluated as a treatment option and should be approached with extreme caution. Tracheostomy procedures are associated with high morbidity and mortality rates in cats, with a reported mean survival time of 20.5 days.[26] In a similar study, there were life-threatening complications in 40% of cases with a mean survival time of 3.3 days.[27] In this series, no cats were treated with permanent tracheostomies.

Staging is a necessary component for developing successful treatment strategies in all cancer patients and those with tracheal tumors are no exception. Chemotherapy and radiation treatments are recommended at the authors' institution for localized, non-resectable tumors, as well as for patients with metastatic disease. These treatments are not curative but might delay local recurrence and further metastasis. Chemotherapy and definitive or palliative radiation were recommended in 75% (6/8) of cases in this series, but no protocols were pursued as front-line therapy.

Palliative care options exist and are indicated based on the severity of disease and owner's expectations. Primary therapies include steroids, antibiotics, bronchodilators and non-steroidal anti-inflammatories (NSAIDs). NSAIDs are predominately the treatment of choice for carcinomas as these downregulate COX expression and might limit the rate of metastatic disease.[28,29]

Prognostication is difficult for cats with tracheal tumors given the scarcity of reported cases. Guarded outcomes might be related to delayed diagnosis and progression of disease.[30] Inappropriate treatment selection might also play a role in poor survival times. Tumor type and extent of invasion are important factors when

selecting for treatments. Median survival time in one study was 15.5 days (range 1–1109 days).[16] Cats in this series survived between 0 and 700 days. Overall, the prognosis for cats with neoplastic tracheal disease remains guarded to grave, regardless of the tumor type.

## Conclusions

Cats with tracheal tumors are often presented with non-specific upper respiratory signs, which can make accurate diagnosis challenging. In cases reported in this series, radiographs and tracheoscopy with biopsy were the most useful diagnostic modalities available to the practitioner. Many treatment options exist, but overall prognosis for tracheal tumors in cats remains guarded. Increases in clinical suspicion, accurate diagnoses and reporting might lead to a higher prevalence than previously described, resulting in improved treatment protocols and outcomes in the future.

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