【 CASE REPORT 】

# Tracheal Paraganglioma:
# A Case report and Review of the Pertinent Literature

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**Abstract:**
The trachea is a sporadic origin of paraganglioma. The purpose of the present study was to identify the features of tracheal paraganglioma and reveal the effectiveness of computed tomography (CT) and magnetic resonance imaging (MRI) by reviewing both previous and current cases. In cases of tracheal tumors, we need to consider the bleeding risk associated with a biopsy, as the tumor may be paraganglioma, which is hypervascular. If a biopsy is not available, then CT and MRI can aid in making a pre-operative diagnosis. MRI in particular is useful for long-term observations.

**Key words:** tracheal paraganglioma, tracheal tumor, extra-adrenal pheochromocytoma, salt and pepper appearance

## Introduction

A paraganglioma is a tumor derived from extra-adrenal chromaffin cells. The trachea is a rare origin site of paraganglioma. To our knowledge, only 14 cases of primary tracheal paraganglioma have so far been reported. We herein report two cases of tracheal paraganglioma.

## Case Reports

The institutional review board approved all aspects of this study, and informed consent was obtained from the patients.

### Case 1

A 67-year-old woman presented to her primary physician with a 15-month history of a cough and sputum and a 12-month history of hemoptysis. The physician gave her symptomatic treatment. With this treatment, the hemoptysis stopped, but the cough persisted. Two months prior to this presentation, the hemoptysis resumed, so she presented to the otolaryngology department, and laryngoscopy was performed. However, the bleeding origin could not be detected.

For a further examination, she was introduced to our hospital. She had hypertension and was treated with telmisartan. Her vital signs were as follows: blood pressure, 129/89 mmHg; pulse rate, 87 beats/min with regular rhythm; respiratory rate 12 breaths/min; $SpO_2$ 97% while breathing ambient air. Sometimes she had a headache. She had a cough and blood sputum, but her respiratory sounds were normal. The blood test findings were not significant. Chest radiography showed nodular opacity in the trachea. Chest computed tomography (CT) revealed an 1.8×1.4-cm tumor at the posterolateral tracheal wall. The tumor had uniform soft-tissue attenuation and marked enhancement on contrast-enhanced (CE) CT (Fig. 1). The tumor had an intermediate signal intensity on T1-weighted imaging (WI) and a high intensity on T2-WI on magnetic resonance imaging (MRI) (Fig. 2a-c). Dynamic CE-MRI demonstrated a homogeneous and marked enhancement of the nodule (Fig. 3). The intensity of the nodule was approximately equal to that of the nearby vascular structures in each phase. A high intensity

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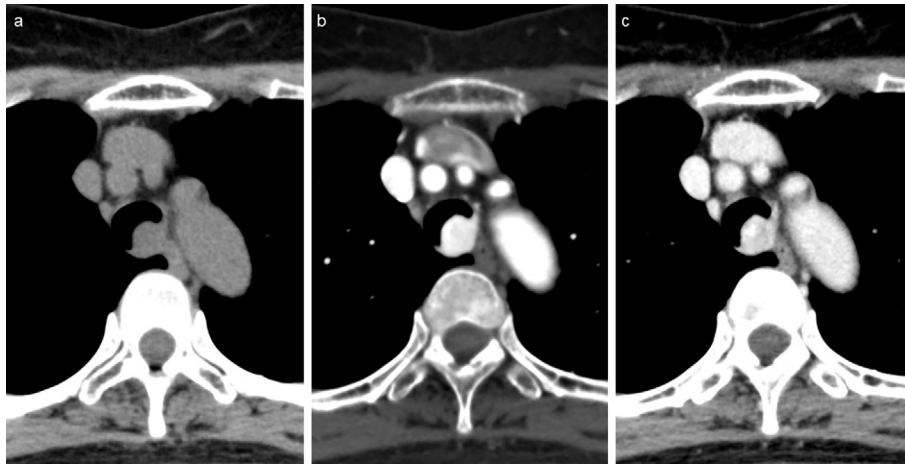
**Figure 1.** (a-c) Axial CT images showed a 1.8×1.4-cm mass arising from the left posterolateral tracheal wall. (b, c) Contrast-enhanced CT images showed marked homogeneous enhancement.
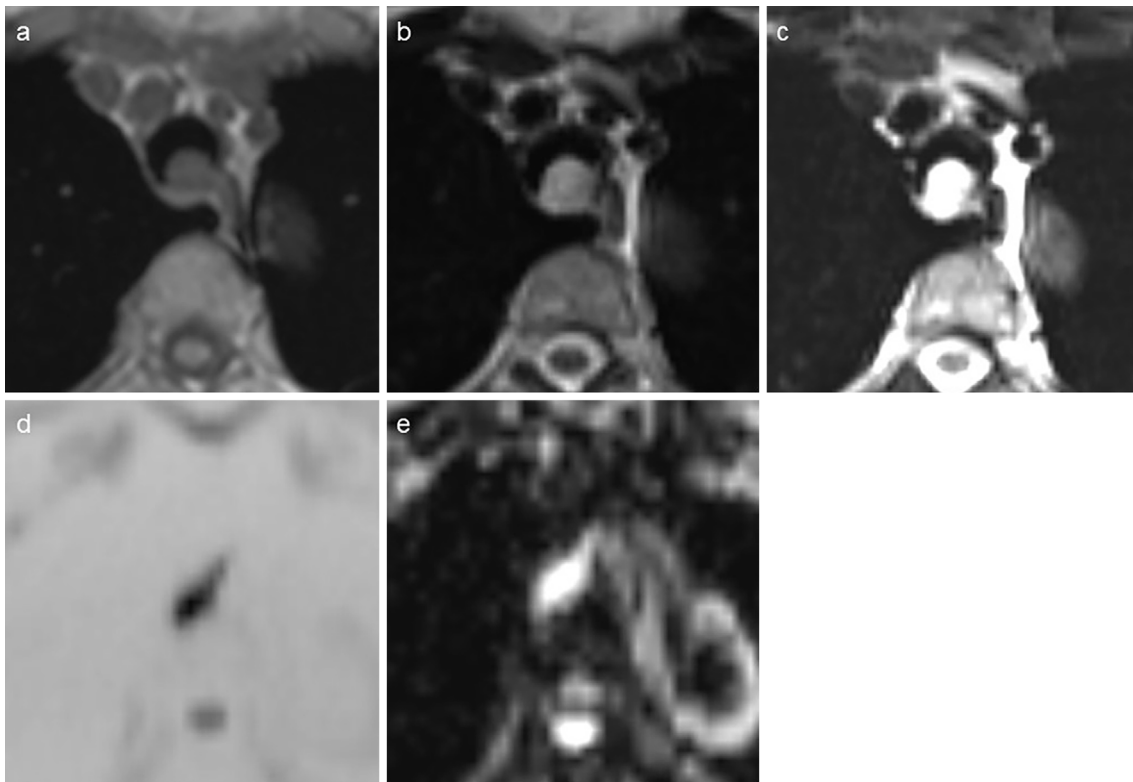


**Figure 2.** The tumor demonstrated iso-intensity on T1-WI (a) and high intensity on T2-WI (b) and a very strong signal intensity on fat-suppressed T2-WI (c). The mass showed a high signal intensity on diffusion-weighted imaging (DWI) (inverse display) with a mean apparent diffusion coefficient (ADC) of $1.98×10^{-3}$ mm$^2$/s (d, e). WI: weighted imaging

was noted on diffusion-weighted imaging (DWI) with a mean apparent diffusion coefficient (ADC) value of $1.98×10^{-3}$ mm$^2$/s (Fig. 2d, e). $^{18}$F-fluorodeoxyglucose (FDG) positron emission tomography (PET) image showed a high uptake in the tumor but no significant uptake in the other organs (Fig. 4). There were no areas of abnormal intensity on brain MRI. Given these findings, we diagnosed the tumor to be a primary tracheal neoplasm without metastasis.

Bronchoscopy revealed a hemorrhagic hypervascular tu-mor in the trachea (Fig. 5). As CT and MRI revealed the hypervascularity of the tumor, we avoided performing a preoperative biopsy due to the risk of bleeding. Under general anesthesia, tracheal resection of five rings with mediastinal lymph node dissection through a median sternal incision was performed. The trachea was reconstructed with end-to-end anastomosis and covered with the stem flap of the right thyroid lobe. The final pathology report revealed the tumor to be a 12-mm paraganglioma that lay against the tracheal
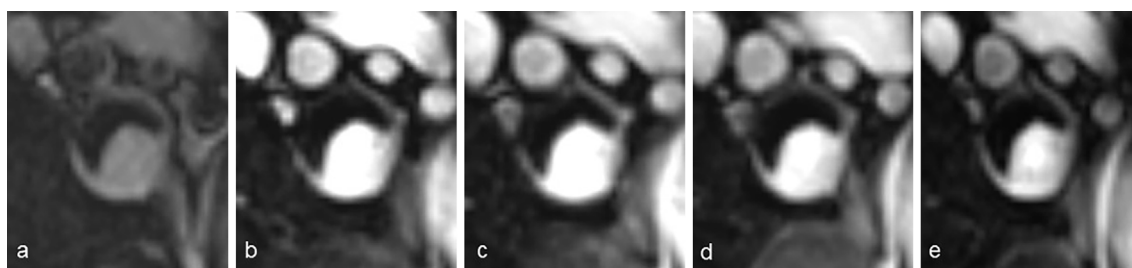
**Figure 3.** (a-e) Dynamic contrast-enhanced MRI images showed marked enhancement with an intensity equal to that of the nearby vascular structures in each phase.
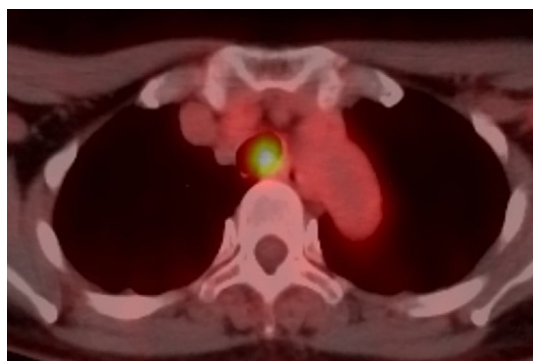


**Figure 4.** $^{18}$F-fluorodeoxyglucose PET showed a high uptake of the tumor. The maximum standardized uptake value (SUVmax) was 7.2.
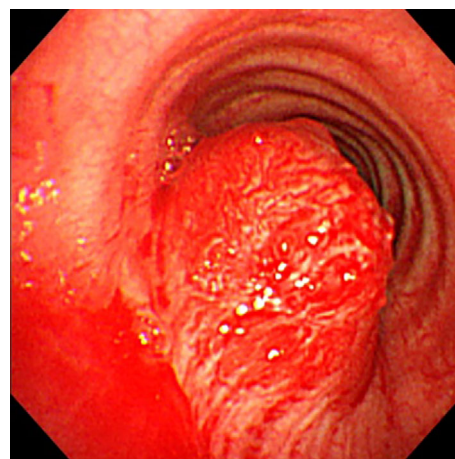


**Figure 5.** Bronchoscopy showed a hemorrhagic tumor with hyper vascularization in the trachea.

submucosa showing cells with abundant pale cytoplasm and hyperchromatic nuclei. Vascular hyperplasia was relatively abundant. The results of immunological staining of the tumor cells were as follows: AE1/AE3, negative; MOC31, negative; Chromogranin A, positive; and S-100, positive (Fig. 6). S-100 was strongly positive in sustentacular cells. The surgical margin was negative. The patient remains disease-free almost four and a half years later.

### Case 2

An 82-year-old man presented to his primary physician with a few years history of a cough. He had been referred to a general hospital because of increasing cough and shortness of breath, and CT showed a tracheal nodule. He was referred to our hospital for further examination and to undergo treatment for the tracheal nodule.

On admission, his vital signs were as follows: blood pressure, 131/71 mmHg; pulse rate, 71 beats/min with a regular rhythm; respiratory rate, 12 breaths/min; SpO$_2$, 98% while breathing ambient air. He had no symptoms of headaches, palpitations, or excessive sweating, but dyspnea on exertion and hemoptysis. Auscultation revealed strider. The blood test findings were not significant, except for C-reactive protein 1.44 mg/dL. Chest radiography showed no abnormalities. Chest CT showed a 1.9×1.5-cm nodule arising from the posterior tracheal wall and protruding into the lumen (Fig. 7). The nodule also protruded posteriorly to the trachea and compressed the esophagus. CE-CT demonstrated a marked enhancement of the nodule, and the attenuation of the nodule was approximately equal to that of the nearby vascular structures in both the early and late phases (Fig. 7b-d). In the early phase, the mass was heterogeneous, and its center was relatively weakly enhanced (Fig. 7b). However, in the late phase, the nodule showed homogeneity and a high degree of enhancement (Fig. 7c). The MR signal was equal to that of the chest wall muscle on T1-WI (Fig. 8a). T2-WI and fat-suppressed T2-WI showed a heterogeneous, hyperintense nodule that appeared even more hyperintense on fat-suppressed T2-WI (Fig. 8b, c, f). The nodule displayed a high signal intensity on DWI with a mean ADC 2.25×10$^{-3}$ mm$^2$/s (Fig. 8d, e). Dynamic CE-MRI showed the same pattern and degree of enhancement as CT. The center of the tumor that showed poor contrast in the early phase of contrast imaging showed a slightly higher signal than the margin on T2-WI (Fig. 8b, c, f). Signal voids were seen at the margin of the nodule on T2-WI (Fig. 9). $^{18}$F-FDG-PET showed a high uptake in the tumor. $^{123}$I-metaiodobenzylguanidine (MIBG) scintigraphy showed no $^{123}$I-MIBG uptake in the nodule.

Bronchoscopy revealed a tumor, with increased capillaries on its surface in his trachea. Due to the risk of bleeding, we decided against a biopsy. Tracheal resection and reconstruction were performed. The tumor had not invaded the esophagus. The final pathology report revealed the tumor to be a
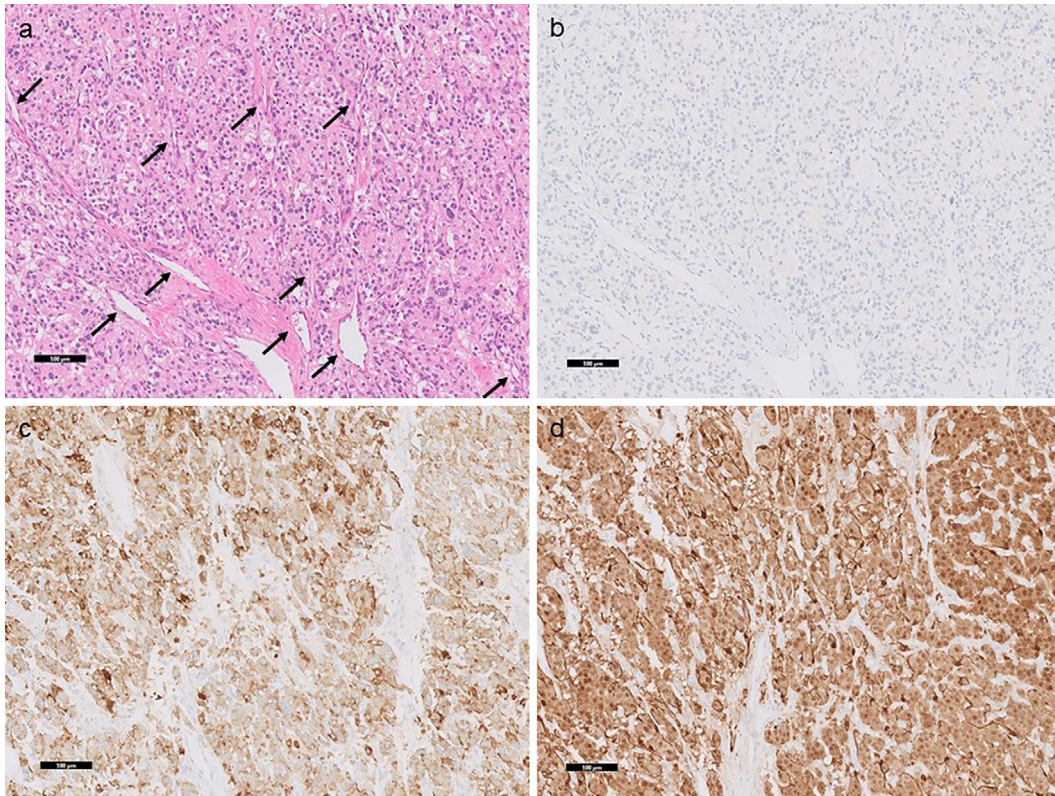
**Figure 6.** The medium-power photomicrograph (×100) showed cells with abundant pale cytoplasm and hyperchromatic nuclei. Vascular hyperplasia was relatively abundant (arrows) (a). In the medium-power photomicrograph (×100), AE1/AE3 was negative, and synaptophysin was strongly positive in tumor cells (b, c). In the medium-power photomicrograph (×100), S100 was strongly positive in sustentacular cells (d).
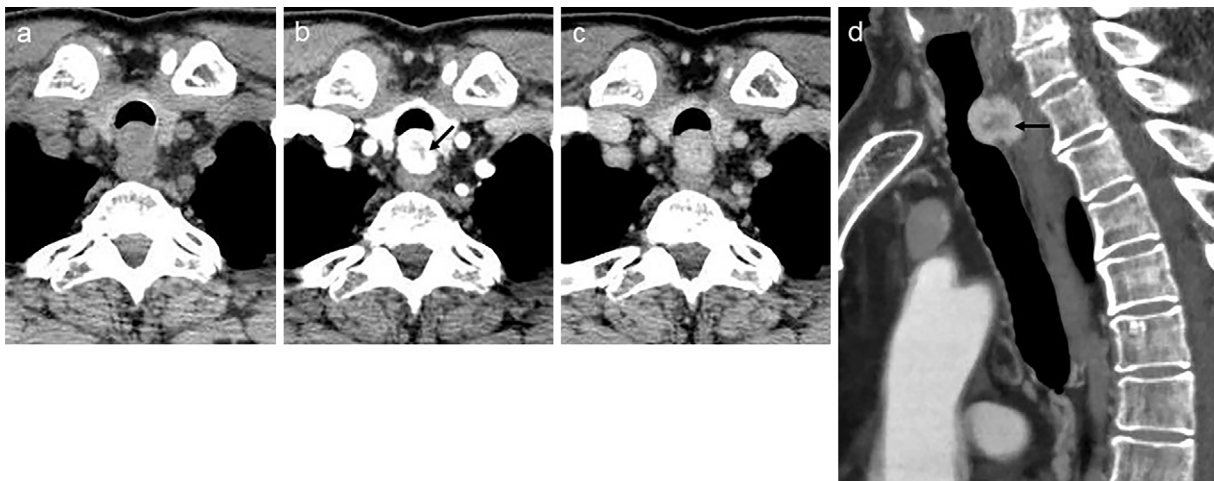


**Figure 7.** (a-c) Axial CT images showed a 1.9×1.5-cm mass arising from the posterior tracheal wall. (b, c) Contrast-enhanced CT images showed a marked enhancement, equal attenuation to the nearby vascular structures in both the early and late phases. Axial (b) and sagittal (d) CT images in the early phase showed a heterogeneous mass with a relatively weak contrast area (arrows) in the center of the mass. (c) The CT image in the late phase showed homogeneity and a high degree of enhancement for the mass.

paraganglioma that arose from the membranous portion of the trachea and protruded into and out of the trachea. The tumor cells had abundant pale cytoplasm and hyperchromatic nuclei. Vascular hyperplasia was relatively abundant, and spindle-shaped cells were also found in the tumor. Slightly large vessels were seen at the margin of the tumor. There was a myxoid matrix in the center of the tumor (Fig. 10). The results of immunological staining of the tu-
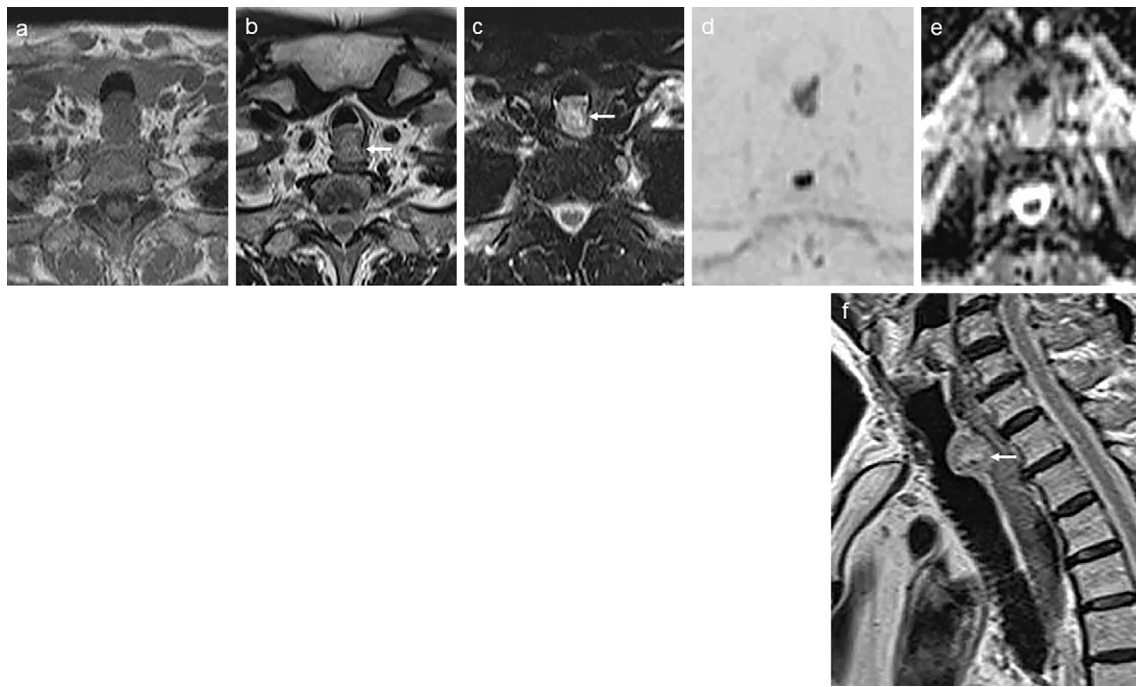
**Figure 8.** (a) The MR signal was equal to that of the chest wall muscle on T1-WI. T2-WI (b, f) and fat-suppressed T2-WI (c) demonstrated a heterogeneous hyperintense mass. The center of the tumor showed a slightly higher signal (arrow) than the margin on T2-WI and fat-suppressed T2-WI. The mass showed a high signal intensity on diffusion-weighted imaging (DWI) with a mean apparent diffusion coefficient (ADC) of $2.25 \times 10^{-3}$ mm$^2$/s (d, e). WI: weighted imaging
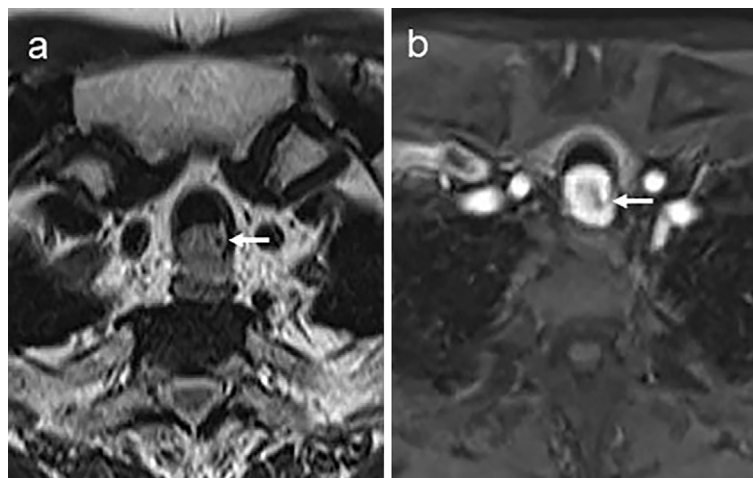


**Figure 9.** (a) A signal void was seen at the margin of the mass on T2-weighted imaging (arrow). (b) It was identified as a vessel by a contrast-enhanced study (arrow).

mor cells were as follows: AE1/AE3, negative; CD56, negative; chromogranin A, negative; synaptophysin, positive (weak); GFAP, negative; and S-100, negative. S-100 was weakly positive in sustentacular cells. The patient has had no recurrence for 7 months.

## Discussion

A paraganglioma is a tumor derived from extra-adrenal chromaffin cells. Its location is usually the sympathetic paravertebral ganglia of body, and parasympathetic ganglia of the glossopharyngeal and vagal nerve in the neck and head (1). The trachea is a rare origin site of paraganglioma. As the cells are typically responsive to $O_2$ and $CO_2$ tension, the tumor is sometimes called chemodectoma (2).

We searched the previous case reports in the related English literature. In the first step, we used the keywords "paraganglioma", "chemodectoma", or "extra-adrenal pheochromocytoma", with "trachea" or "tracheal" added as heading terms. In the second step, we searched for case reports of tracheal paraganglioma or chemodectoma manually among 58 reports found in the first step. We ultimately identified
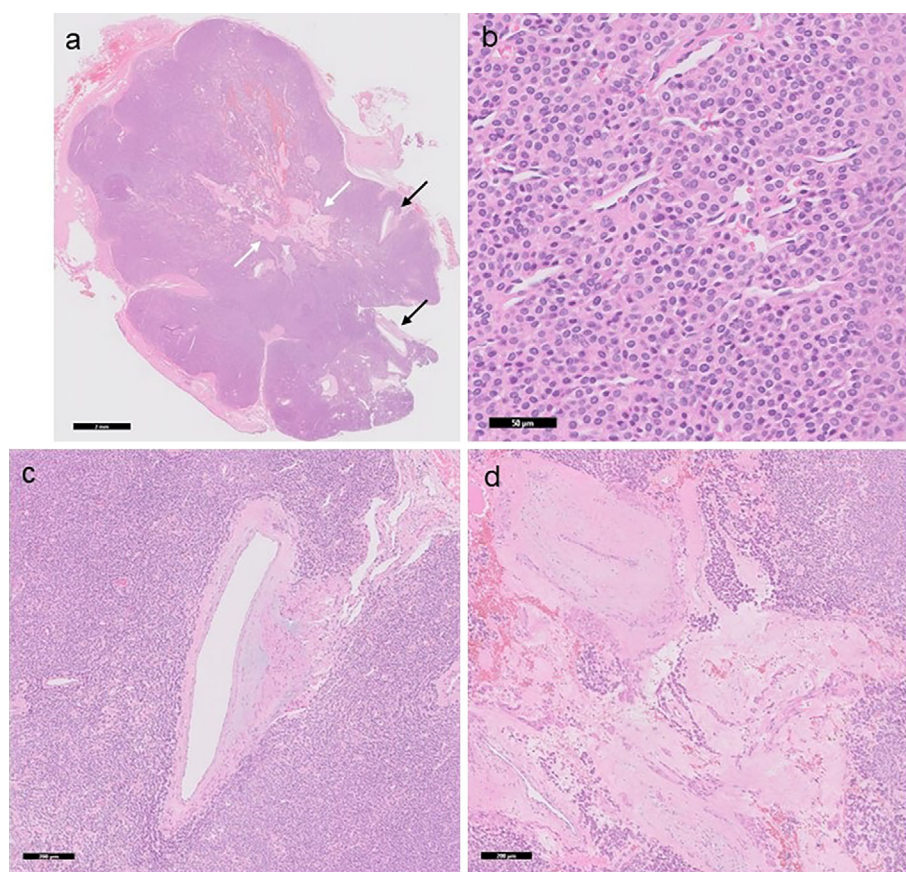
**Figure 10.** (a) The loupe magnification (×5) cut in a cross section similar to the axial section of CT and MRI showed slightly large vessels at the margin of the tumor (black arrows) and a myxoid matrix in the center of the tumor (white arrows). (b) In the high-power photomicrograph (×200), the tumor cells had abundant pale cytoplasm and hyperchromatic nuclei. Vascular hyperplasia was relatively abundant, and spindle-shaped cells were also found in the tumor. (c, d) The medium-power photomicrograph (×50) showed slightly large vessels at the margin of the tumor (c) and myxoid matrix in the center of the tumor (d).

only 14 English-language reports, starting with the first case reported by Zeman in 1956. We experienced the fifteenth and sixteenth cases. We have summarized these cases in a table (Table) (2-15).

The sex distribution among the 16 total cases was as follows: 8 males, 7 females, and 1 sex not stated. The patients' ages ranged from 8 to 82 years old (median, 51 years old) (Table). Our cases were older than median age. The age of the onset of whole extra-adrenal paragangliomas tended to be in the 40s to 50s, and sex predilection was roughly equal (16). This trend is characteristic of tracheal paragangliomas.

Our patient presented with cough and hemoptysis. The previous report pointed out that tumor growth is not limited to the trachea, leading to the presentation of dysphagia, pain, hemoptysis, or hoarseness (9). Our case review showed that 11 patients presented with dyspnea (11/16, 68.8%) while 8 presented with hemoptysis (8/16, 50.0%). Strider or wheeze was present in 6 patients (6/16, 37.5%), 2 presented with hoarseness (2/16, 12.5%), and 1 presented with dysphagia (1/16, 6.25%).

The diagnosis of paraganglioma can be made by a bi-

opsy (8), but due to hypervascularity, a biopsy of paraganglioma carries a high risk of bleeding (11-13). Indeed, a biopsy was strictly avoided in six patients because of the risk of bleeding, and three of six patients who underwent a biopsy demonstrated significant bleeding. Previous reports stated that a thoracic surgeon should be involved in any such biopsies and that these procedures should be performed with a rigid bronchoscope (13, 14). Previous reports stated that tracheal paraganglioma tends to arise from the membranous trachea (15). Indeed, tumors reportedly arise from the posterior or posterolateral wall of the trachea, including the membranous trachea in 12 cases (12/16, 75.0%). The maximum tumor size ranged from 1.4 to 3 cm (mean, 2.0 cm) in cases where the size was mentioned (Table). In one case, the volume was not stated clearly but simply expressed as "extended below the vocal cord down to the trachea".

The imaging findings of paragangliomas may be similar to those of pheochromocytoma (17). The radiological features of paragangliomas are similar regardless of the occurrence location (16). On non-contrast enhanced CT, paragangliomas typically show a mass of >10 Hounsfield units (HU) (17). On CE-CT, paragangliomas typically show avid

**Table.  Case Reports of Primary Tracheal Paraganglioma.**

| Reference | Age | Sex | Symptom | Location | Size(cm) | NE-CT | CE-CT | NE-MRI | CE-MRI | PET | Biopsy | Treatment | Recurrence |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| (3) | 45 | Male | Hemoptysis | Left lateral | - | - | - | - | - | - | - | Surgical excision | No (at 3 Y) |
| (4) | 67 | Female | Dyspnea Hoarseness Dysphagia | Below right vocal cord extending down trachea | - | - | - | - | - | - | - | Surgical excision (died during operation) | - |
| (5) | 56 | - | Dyspnea Strider | Posterior | - | - | - | - | - | - | Performed with excessive bleeding | Surgical excision | No (at 6 W) |
| (6) | 55 | Female | Hemoptysis | Posterior | 2×1.5×1 | - | - | - | - | - | Performed | Surgical excision | No (at 6 M) |
| (7) | 55 | Female | Hemoptysis | Anterior | 3 | - | - | - | - | - | Performed with excessive bleeding | Surgical excision | No (at 12 M) |
| (8) | 77 | Female | Dyspnea Hemoptysis | Posterior | 2 | ○ | ○ | - | - | - | Performed | Endoscopic ablation with pre-embolization, stenting and radiation | Yes (at 2 Y) |
| (2) | 41 | Male | Strider Dyspnea | Right posterolateral | - | - | - | - | - | - | - | 1st: Surgical excision 2nd: Endoscopic resection | 1st: Yes (at 9 M) 2nd: No (at 12M) |
| (9) | 50 | Female | Dyspnea Cough | Left lateral | 1×2 | ○ | ○ | ○ | ○ | - | Avoid at the risk of bleeding | Surgical excision | No (at 3 M) |
| (10) | 22 | Male | Dyspnea Hemoptysis | Posterior | 2 | ○ | ○ | - | - | - | Avoid at the risk of bleeding | Surgical excision | - |
| (11) | 29 | Female | Hemoptysis Dyspnea | Posterior | 1.5×1.3 | ○ | - | - | - | - | Avoid at the risk of bleeding | Surgical excision | No (at 6 M) |
| (12) | 40 | Male | Hemoptysis Strider | Posterior | 1.4 | ○ | - | - | - | - | Performed with excessive bleeding | Surgical excision | - |
| (13) | 35 | Male | Cough Dyspnea Hoarseness | Posterior | - | ○ | ○ | - | - | - | - | Surgical excision | - |
| (14) | 52 | Male | Cough Dyspnea Strider | Posterior | 2.3×1.7×2.0 | ○ | ○ | - | - | ○ | Avoid at the risk of bleeding | Surgical excision | No (at 9 M) |
| (15) | 8 | Male | Wheeze Dyspnea | Posterior | 1.7×1.2×1.6 | ○ | ○ | ○ | - | - | Performed | Surgical excision | No (at 3 M) |
| current case1 | 67 | Female | Cough Hemoptysis | Left posterolateral | 1.8×1.4 | ○ | ○ | ○ | ○ | ○ | Avoid at the risk of bleeding | Surgical excision | No (at 4.5 Y) |
| current case2 | 82 | Male | Cough Dyspnea Strider | Posterior | 1.9×1.5 | ○ | ○ | ○ | ○ | ○ | Avoid at the risk of bleeding | Surgical excision | No (at 7 M) |

-: Not stated or performed, CE: Contrast enhanced, M: Month, NE: Non-enhanced, W: Week, Y: Year

contrast enhancement and delayed washout due to a rich capillary network (17). On CE-CT and CE-MRI, small paragangliomas show homogenous and intense enhancement due to their hypervascularity, but large paragangliomas with necrosis and hemorrhaging show no such findings (16). On MRI, they have a low to intermediate signal intensity on T1-WI and high signal intensity on T2-WI (16). Signal flow voids, known as a "salt and pepper appearance", can be seen in large tumors (>4 cm) (18). As three reported cases were relatively small tumors, a "salt and pepper appearance" was not seen. However, the second case we reported was not a large tumor, but flow voids were seen on MRI. The signal voids at the margin of the mass on T2-WI was thought to represent slightly large vessels supplying the tumor. DWI was performed only in our cases. The tumor had a high intensity but no decreased ADC. Because both CE-CT and MRI can evaluate not only the morphology but also the vascularity of the tumor, they help assess the bleeding risk at the biopsy. Furthermore, MRI does not involve any radiation exposure, so it seems to be the best imaging modality to use when performing long-term observations.

Surgical excision was performed in 15 cases as the first treatment. One patient died from massive bleeding during the operation. Another one developed recurrence nine months after the surgery and needed endoscopic tumor resection. The remaining 13 patients had no recurrence. Endoscopic treatment was performed in 1 case, which required additional treatment (stenting and 40-Gy radiation). Surgical excision seems to be the optimal treatment if proper airway management and resection with a sufficient margin are done. No metastasis was found in five cases surveyed before surgery. An incomplete resection of the paraganglioma may result in recurrence, but it generally follows a benign course.

The microscopic morphology of paraganglioma is almost the same as that of pheochromocytoma, regardless of the location (16). Paraganglioma is typically composed of nesting tumor cells surrounded by fibrovascular stroma, a structure called the "Zellballen pattern" (11, 15, 19). Immunobiologically the following neuroendocrine markers are often positive in the tumor cells: synaptophysin, chromogranin A, neuron-specific enolase, and CD56. Cytokeratin staining is often negative in the tumor cells. The sustainer cells in fibrovascular stroma are positive for S100 (15). In our case 1, an alveolar pattern of the tumor cells was noted. The tumor cells were positive for chromogranin staining. The sustentacular cells were positive for S100 staining. In our case 2, the tumor cells were positive for synaptophysin staining. The sustentacular cells were positive for S100. Given the above findings, our patients were diagnosed with primary tracheal paraganglioma.

## Conclusion

Tracheal paraganglioma is a rare disease whose main symptom is hemoptysis, stridor, and dyspnea. Sexual differences are not significant. This lesion usually presents in one's 40s to 50s. Tumors are often found in the posterior

wall of the trachea and are rich in blood vessels and easily hemorrhagic. Because a biopsy carries a high risk of bleeding, it is necessary to carefully consider whether or not this procedure should be performed. Evaluating cases of avid enhancement on CE-CT and MRI is useful for the preoperative diagnosis. Although the clinical course is generally benign, if worsening respiratory symptoms are noted as the tumor grows, then surgical resection is mainly selected as the treatment of choice.

**The authors state that they have no Conflict of Interest (COI).**

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