

Treatment of primary tracheal glomus tumors

Two case reports and a literature review

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Abstract

Rationale: Glomus tumors (GTs) are rare soft tissue neoplasms. Several treatment options have been reported for tracheal GTs including thoracotomy, bronchoscopic electrocautery, Nd: YAG laser, and cryotherapy. However, few studies have evaluated the ideal treatment for tracheal GTs.

Patient concerns: A 30-year old man who presented with cough, and expectoration for 1 month, and who had been diagnosed as having a tracheal neoplasm by cervical, and thoracic computed tomography (CT). The patient was a 47 years old man. He was admitted to our hospital presenting with intermittent hemoptysis for 3 years. Thoracic CT revealed a round tumor on the right posterior tracheal wall.

Diagnoses: Both of them were diagnosed as benign GTs. Histopathology of the tumor showed clusters of round epithelioid cells with eosinophilic cytoplasm, and uniform round to ovoid nuclei surrounding dilated capillaries. Immunohistochemical staining was positive for smooth muscle actin (SMA).

Interventions: The tracheal tumor of first patient was located at the level of C7–T1. Tumor resection was performed under fiberoptic bronchoscopy. The tracheal tumor in second patient was located in the lower trachea. Surgical tracheal resection and anastomosis were performed.

Outcomes: Both of them achieved good results and no recurrence was seen at the final follow-up

Lessons: We recommend choosing the most appropriate approach to manage tracheal GTs based on patients' general condition, and tumor characteristics to obtain an excellent prognosis. Our 2 cases of tracheal GT were managed by different approaches, and both achieved good results.

Abbreviations: CgA = chromogranin-A, CK1 = casein kinase 1, EMA = epithelial membrane antigen, MSA = muscle-specific actin, PCK = pancytokeratin, SMA = Smooth muscle actin, Syn = synaptophysin.

Keywords: bronchoscope, glomus tumors, thoracotomy, treatment

1. Introduction

Glomus tumors (GTs) are rare soft tissue neoplasms derived from modified smooth muscle cells of the normal glomus body surrounding arteriovenous anastomoses^[1–3]. GTs constitute less than 2% of all soft tissue tumors, and are most often located in the dermis, or subcutis of the subungual region^[4]. GTs are rare in visceral organs because of the lack of glomus bodies in extracutaneous sites^[5]; however, several unusual sites have been reported including the gastrointestinal tract, bone, cervix,

mediastinum, stomach, respiratory tract, and other organs^[6]. Within the respiratory tract, the trachea is the most frequent location for GT^[1], with approximately, 40 reported cases, and only 6 of the 40 cases in the superior trachea. The majority of GTs in the superior trachea were located at the level of the superior border of the manubrium or T2–T3 on sagittal views. To our knowledge, only 1 report discusses a case of GT in the trachea at the level of C7–T1, which was treated successfully, using bronchoscopy^[7]. Several treatment options have been reported for tracheal GTs including thoracotomy, bronchoscopic electrocautery, Nd: YAG laser, and cryotherapy^[7–9]. Fernandez-Bussy et al^[6] reported that 67.35% of tracheobronchial GT patients were treated surgically, and 32.65% were treated endoscopically; however, few studies have evaluated the ideal treatment for tracheal GTs. We reported 2 rare cases of primary tracheal GT; one at the level of C7–T1 that was resected using bronchoscopy, and the second in the lower trachea, which was treated by thoracotomy. The size, site, invasion, degree, and corresponding treatment of reported tracheal GTs were also reviewed.

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The study was approved by the Ethics Committee of West China Hospital. Written informed consent was obtained from both patients.

The authors report no conflicts of interest.

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2. Case presentation

2.1. Case 1

The patient was a 30-year old man who presented with cough, and expectoration for 1 month, and who had been diagnosed as having a tracheal neoplasm by the local hospital. He was admitted to our hospital, and cervical, and thoracic computed tomography (CT) revealed a round, exophytic mass (diameter:

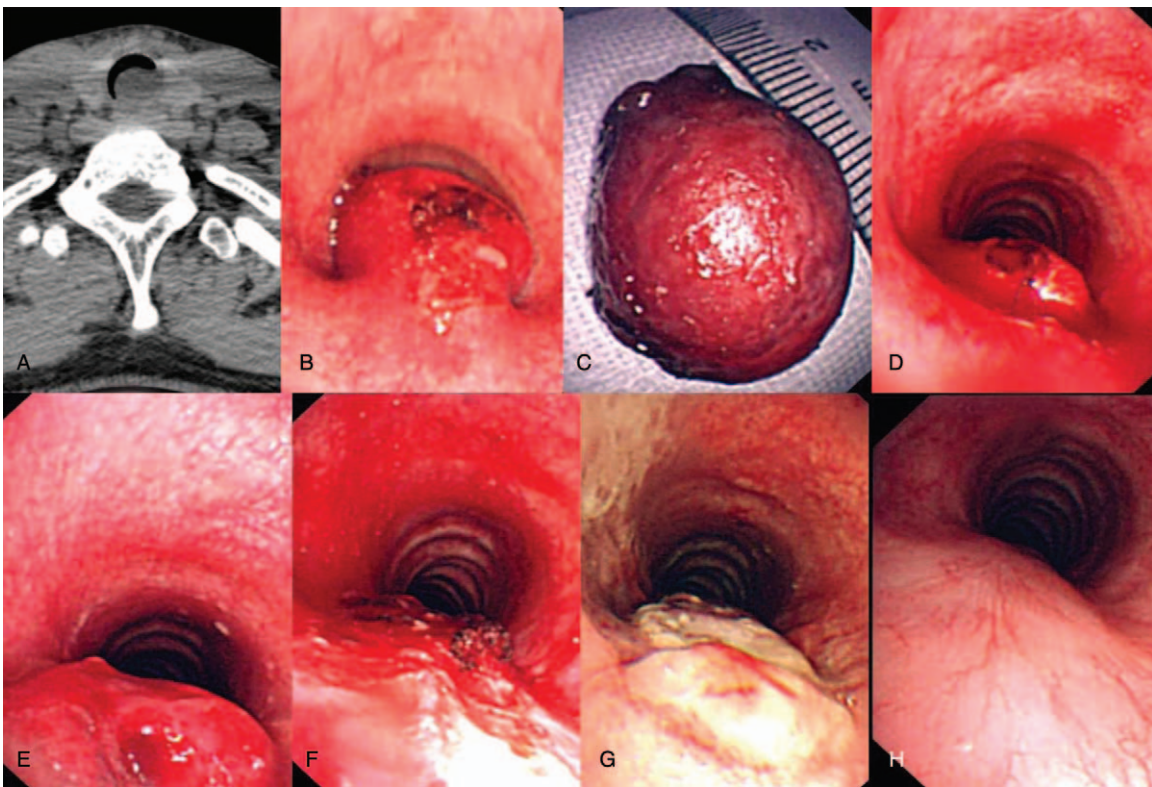


Figure 1. (A) CT scans demonstrate a round, exophytic mass in the trachea of the level of C7-T1, (B) bronchoscopic visualization of the GTs show pedicle attachment, and the obstruction of the trachea, (C) a hemispherical red mass with a diameter of about 2 cm was resected, (D) partial tumor base remained on tracheal wall, (E and F) the remainder tumor base was resected, (G) inflammatory sphacelus was generated on basal wound repeatedly, and debrided under fiber bronchoscope, (H) at 1-year follow up, the tracheal wall was smoothly, and tumor recurrence was not found CT=computed tomography, GTs=Glomus tumors

1.7 cm) in the trachea at the level of C7-T1 (Fig. 1A). A papillary, and highly-vascular tumor was found on the posterior wall of the upper trachea using a fiber-optic bronchoscope. The tracheal lumen was markedly narrowed to a thread-like diameter (Fig. 1B); however, the patient suffered no symptoms of dyspnea. Coagulation function testing, and arterial blood gas analysis results were within normal limits. Because the tracheal tumor was located at the level of C7-T1, it was difficult to remove the tumor by thoracotomy; therefore, tumor resection was performed under fiberoptic bronchoscopy. First, a hemispherical red mass with a

diameter of approximately 2 cm was resected by high-frequency electroexcision (Figs. 1C and D). Two days later, the tumor base was resected again using a high-frequency electrotome and electrocoagulation (Figs. 1E and F). Subsequently, basal inflammatory necrosis was found, and debrided repeatedly under fiberoptic bronchoscopy (Fig. 1G). Histopathology of the tumor showed clusters of round epithelioid cells with eosinophilic cytoplasm, and uniform round to ovoid nuclei surrounding dilated capillaries (Fig. 2A). Immunohistochemical staining was positive for Smooth muscle actin (SMA), and muscle-specific

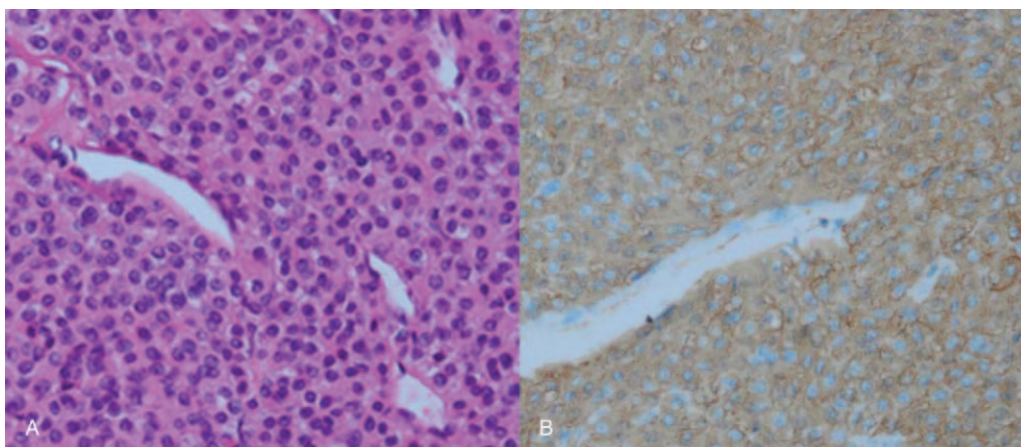


Figure 2. (A) The histopathology results shows uniform polygonal cells with round to ovoid nuclei, and slightly, eosinophilic cytoplasm (magnification, $\times 400$), (B) on immunohistochemical evaluation, tumor cells were stained for SMA (magnification, $\times 400$) SMA = Smooth muscle actin

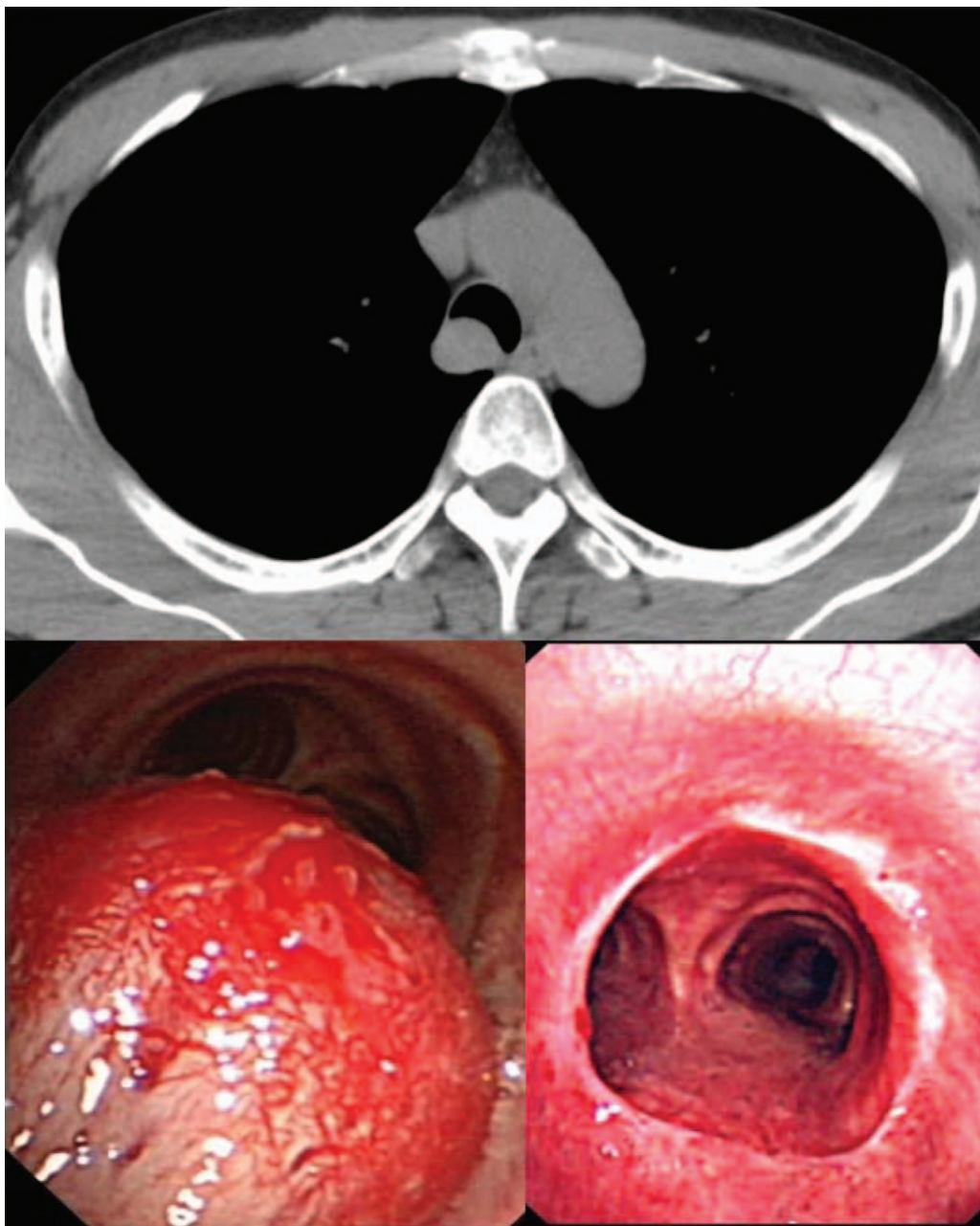


Figure 3. (A) CT scans showed a round like transtracheal mass with a diameter of about 1.8 cm growing at the right posterior wall of the trachea, (B) bronchoscopic visualization showed a red round embossment with hypervascularized and active bleeding at lower trachea, (C) tracheal resection and anastomosis was performed. There was no evidence of tumor recurrence or symptoms at one year follow up. CT=computed tomography

actin (MSA), and negative for desmin, pancytokeratin (PCK), epithelial membrane antigen (EMA), casein kinase 1 (CK1), Syn, and chromogranin-A (CgA) (Fig. 2B). The tumor was diagnosed as GT. At the 1-year follow-up, the patient's upper tracheal posterior wall was smooth with no evidence of tumor recurrence (Fig. 1H).

2.2. Case 2

A 47-year-old man was admitted to our hospital presenting with intermittent hemoptysis for 3 years. CT revealed an approximately, round transtracheal mass with a diameter of approximately, 1.8 cm on the right posterior tracheal wall (Fig. 3A).

Bronchoscopy revealed a red-surfaced mass with hypervascularization, and active bleeding in the lower trachea (Fig. 3B). The patient suffered no symptoms of dyspnea. Blood laboratory testing revealed no coagulation disorders; however, because the tumor had invaded the tracheal wall, we were concerned about the risk of hemorrhage under bronchoscopic resection. Therefore, we performed surgical tracheal resection, and anastomosis, completely, removing the tumor, and corresponding tracheal ring. Microscopically, the tumor was composed of large nests of epithelioid round cells with slightly, eosinophilic cytoplasm, and "punched-out", round nuclei. The nests were surrounded by dilated vessels (Fig. 4A). Immunohistochemistry was positive for SMA and caldesmon, and negative for desmin, EMA, CK1, Syn,

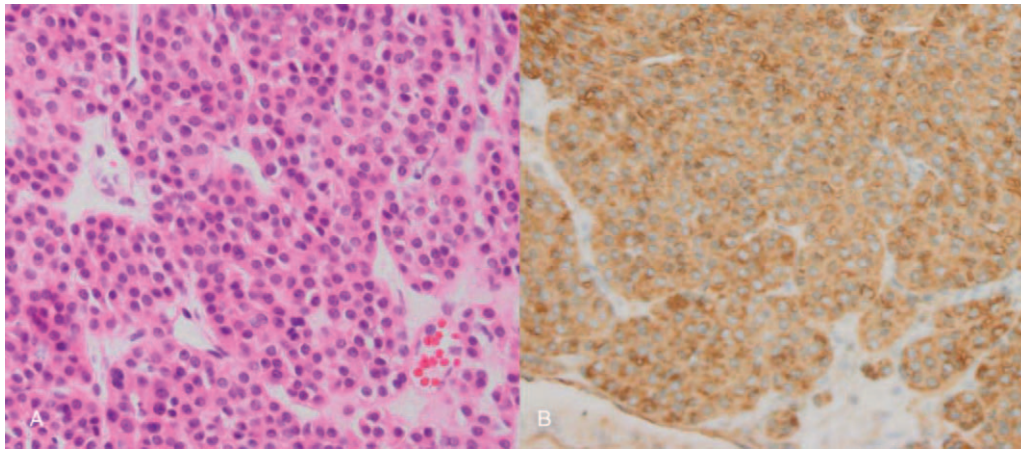


Figure 4. (A) Hematoxylin and eosin staining of glomus tumors showing clusters of glomus cells predominantly around blood vessels (magnification, $\times 400$), (B) immunohistochemical evaluation: tumor cells were stained for smooth-muscle actin (magnification, $\times 400$).

CgA, and S-100 (Fig. 4B). These findings suggested a diagnosis of tracheal GT. No evidence of recurrence or symptoms was noted at 1-year post-operation (Fig. 3C).

3. Discussion

GTs are uncommon mesenchymal tumors that typically develop in the soft tissues of the fingers, hands, or feet, and are reported rarely, in the trachea^[9,7]; therefore, epidemiological data for tracheal GTs is undefined. The first case of tracheal GT was reported in 1950^[10]. Since then, 49 cases of tracheal GT have been reported: 36 cases were reviewed by Fernandez-Bussy et al^[6], 11 cases were later reported, and we report 2 cases. The average patient age was 50.5 years with a range between 10 to 83 years. Patients included 16 women, and 33 men at a ratio of approximately, 1:2, similar to the findings of Fernandez-Bussy et al^[6]. The most common symptoms appearing with tracheal GTs include hemoptysis, cough, and dyspnea^[11]; less common symptoms include stridor, and chest pain^[6]. A small number of patients presented with no clinical respiratory symptoms, and a tracheal mass was found on routine physical exam^[12]; these patients' chest radiographs were reportedly, normal^[9]. Therefore, chest CT, or bronchoscopy should be performed for patients presenting with respiratory symptoms that include hemoptysis, or cough, to prevent a missed diagnosis. Bronchoscopic examination of most tracheal GTs revealed a hypervascular polypoid mass with a pedicle, and tumor size ranged between 0.5 to 4.5 cm^[13,14]. The majority of tumors have been found on the posterior wall of the lower two-thirds of the trachea^[15]; however, tumors on the anterior wall have also been reported^[6]. GT in 7/49 (14.3%) patients was identified in the upper trachea. The highest reported anatomical level for GTs in the trachea is C7–T1, which has occurred in only 2 known cases: 1 in our study and 1 reported by Norder et al^[7].

Tracheal GTs must be differentiated from carcinoid tumors, first. Other differential tumors include tracheal hamartomas, hemangiopericytoma, and paragangliomas. Carcinoid tumors have a less prominent vascular pattern, composed of large nests of polygonal eosinophilic cells with a salt-pepper chromatin pattern, and deposited in a variable collagenous, and myxoid matrix. Immunohistochemically, carcinoid tumors stain positively, for chromogranin, synaptophysin, and cytokeratin, but not react with antibodies to SMA, and show intracytoplasmic

dense-core granules under electron microscopy^[9]. However, microscopical characteristics of benign GTs are medium-sized cells with uniform round to ovoid nuclei, and eosinophilic cytoplasm that are arranged in a nested pattern around dilated, and tangled vascular channels. Moreover, GTs are mesenchymal tumors, which are positive for SMA, MSA, and h-Caldesmon, and have abundant pericellular type IV collagen but are negative for neuroendocrine and epithelial markers^[6,7,9,15].

Previous studies report that the vast majority of tracheal GTs are benign and non-invasive^[6,9]; however, 2 consecutive cases of malignant tracheal GT have been reported^[11,16]. GTs are divided into benign GTs, GTs of uncertain malignant potential, and malignant GTs based on the World Health Organization's classification^[3]. Histologically, the malignant GTs was also composed of groups of uniform, rounded cells with centrally, placed round nuclei, and amphophilic to lightly, eosinophilic cytoplasm. However, malignant GTs are characterized by size > 2 cm, and subfascial, or visceral location, rich in small blood vessels, invasive growth, marked nuclear atypia, or atypical mitotic figures, and elevated mitotic activity ($> 5/50$ per high-power field)^[7]. Braham et al^[11] described malignant tracheal GTs based on a high mitotic index, deep location, and size of 2.5 cm diameter. Another case of tracheal GT was considered malignant based on a tumor size of 2.5 \times 1.2 cm, nuclear atypia, and mitotic activity^[16]. However, the diagnostic criteria for malignant GTs are based on atypical GTs of the skin^[15]; therefore, it is not known whether the same criteria are applicable to tracheal GTs. We consider that the degree of nuclear atypia, and mitotic activity could be used to estimate the malignancy of tracheal GTs, but that the criteria related to tumor size, and deep location are unsuitable because most previously-reported tracheal GTs with diameter > 2 cm were benign.

The treatment of tracheal GTs includes primarily tracheal resection, and anastomosis by thoracotomy, and tumor resection by bronchoscopy^[6]. Other complementary therapies including radiochemotherapy and cryotherapy^[7]. Sleeve resection with tracheal reconstruction can achieve complete tumor resection, and this approach does not require adjuvant treatment, and has an excellent prognosis^[11]. Surgical treatment have the corresponding indications, and the majority of reported tracheal GTs were removed surgically. However, surgery can be associated with severe complications including deep vein thrombosis, or pulmonary infection secondary to bed rest, post-operation^[15],

which is the main cause of post-operative mortality [17,18]. Endoscopy is considered minimally, invasive, has less surgery-related complications, shorter length of hospital stay, and can be repeated; however, tumor recurrence with incomplete resection is a concern [9]. Therefore, the ideal management of tracheal GT remains unclear, and unfortunately, given the rarity of this tumor, there is currently, no standard approach for treating patients with tracheal GT [7].

Sakr et al [9] considered that endoscopic intervention has limited indications including that the lesion be strictly, confined to the airway lumen without extension into the airway wall; histology confirms that the tumor is benign; or the patient is not fit, or willing to undergo surgical resection. We agree that tumors > 2-cm diameter are not suitable for endoscopy. Because endoscopy has a limited surgical view, and excision ability, large tracheal tumors increase the intervention difficulty, and are more likely, to result in incomplete resection, and increased complication rates. Endoscopic intervention can be used for primary tumor biopsy, and as a temporary measure to stabilize patients before surgery to immediately, restore airway patency in urgent situations [7-9,15].

Patients not fit to undergo surgical resection include those with a tumor located high in the trachea (e.g.; at C7-T1), and those unable to tolerate operation. For these patients, endoscopic intervention can be considered. In addition, if the basilar part of tracheal GTs is wide, surgical tracheal resection, and anastomosis is not recommended. Because the resection of trachea too much will lead to high tension of anastomotic stoma, and increased anastomotic complications.

In summary, tracheal GTs has invaded the tracheal wall; tumor diameter is greater than 2 cm, and located in the middle, or distal trachea; the tumor has malignant characteristics, and rich vascularity; and the basilar part of tracheal GTs is widely, were the indications of surgical treatment. The benign tumor is strictly, confined to the airway lumen without extension into the airway wall; tumor diameter is less than 2 cm; the tumor is located in the upper trachea; and the patients are considered unacceptably high risk for anesthesia, and surgery were the indications of endoscopic intervention. For the tracheal GTs with malignant, and invasive characteristics located in the upper trachea, or the patient contraindicated for the anesthesia, and surgical treatment, besides the endoscopic intervention, complementary treatment including radiochemotherapy, and cryotherapy should also be performed to reduce the tumor recurrence rate. However, adjunctive radiochemotherapy may not be necessary for patients with completely-resected malignant tracheal GTs. Two cases of malignant tumor completely, resected by surgery alone achieved a good prognosis at the final follow-up [11,16].

4. Conclusion

The majority of tracheal GTs are benign. We recommend choosing the most appropriate approach to manage tracheal GTs

based on patients' general condition, and tumor characteristics to obtain an excellent prognosis. Our 2 cases of tracheal GT were managed by different approaches; both achieved good results, and no recurrence was seen at the final follow-up.

Author contributions

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Methodology: Li Guo, Ke Wang, Hui Zhu.

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