CLINICAL EXPERIENCE

WILEY

Clinical significance of interventional therapeutic bronchoscopy combined with bronchial arterial embolization in the treatment of hypervascular primary airway tumors in children

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ABSTRACT

Importance: Pediatric hypervascular primary airway tumors are progressive, fatal lesions with a low incidence, and the disease is often more serious than that in adults.

Objective: To evaluate the clinical efficacy and safety of interventional therapeutic bronchoscopy combined with conservative treatment and bronchial arterial embolization in children with primary airway tumors.

Methods: We retrospectively analyzed the clinical data of four pediatric patients with hypervascular primary airway tumor between 2017 and 2019 at Beijing Children's Hospital.

Results: Two patients were low-grade bronchial mucoepidermoid carcinoma, one patient was pleomorphic adenoma, and one was bronchial leiomyoma. Interventional therapeutic bronchoscopy combined with bronchial arterial embolization was used for treatment (all four patients received general anesthesia). The tumors were safely resected in all patients via interventional bronchoscopy. There were no severe complications related to the procedures. All patients were followed up for 5–12 months, and one low-grade bronchial mucoepidermoid carcinoma recurred.

Interpretation: Interventional therapeutic bronchoscopy combined with bronchial arterial embolization appears to be a safe and efficient therapeutic method associated with less trauma and fewer complications, including no serious adverse events, in children with hypervascular primary airway tumors without bronchus wall infiltration.

KEYWORDS

Hypervascular primary airway tumor, Bronchial artery embolization, Bronchoscope, Children

INTRODUCTION

Primary airway tumors refer to tumors that arise in the trachea and bronchus, and they can cause central airway stenosis and affect ventilation. The clinical manifestations include cough, hemoptysis, dyspnea, and severe respiratory failure.[1] Asphyxia or even death might occur because of severe obstruction or massive hemoptysis in the absence of timely treatment. Surgical treatment of airway tumors is extremely difficult because the tumors are difficult to locate, and because the tumors, which have high blood content, occupy the airway, it is difficult to perform anesthesia via tracheal intubation before surgery, resulting in additional postoperative complications.[2] In

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recent years, with the continuous improvement of pediatric flexural bronchoscopy, minimally invasive treatment via bronchoscopy has been widely used in pediatrics. For lesions that cannot be excised surgically, local minimally invasive interventional therapy using bronchoscopy is of great importance for improving respiratory distress and quality of life. However, this new method is limited in that it presents great challenges such as intraoperative hemorrhage of hypervascular primary airway tumors. We have explored the use of selective bronchial artery embolization to interrupt or reduce blood supply to tumors without bronchus wall infiltration and further used an electric trap, an argon knife, and cryotherapy to remove the tumors.

METHODS

Ethical approval

This study was approved by the Ethics Committee of Beijing Children's Hospital (2020-Z-133) and informed consent was signed by all patients' guardians.

Patient data

Between 2017 and 2019, four patients with hypervascular primary airway tumors were treated in our hospital. Clinical data were collected for all children including age, sex, clinical manifestation, imaging data, pathological data, treatment, and prognosis.

RESULTS

Patient 1

A 7-year-old girl experienced cough and wheezing for 7 months and continuous hemoptysis for 4 months with a blood volume of 5–10 mL once before hospitalization. Physical examination after admission revealed dyspnea, no facial or lip cyanosis, and coarse crackle lung sounds, whereas other examinations were normal. Enhanced chest computed tomography (CT) uncovered an irregular soft tissue shadow (approximately 9 mm × 9.7 mm × 12.7 mm) on the right posterior wall of the trachea (second thoracic vertebra level) occupying approximately 80% of the lumen without bronchus wall infiltration. After enhancement, the focus was obviously enhanced with a CT value of 213 HU. However, the blood supply and blood vessels were not clear (Figure 1A).

Surgery was difficult because the tumor was located in the main airway, its basal component was long, and the nature of the lesion was not clear. Tracheal intubation might cause asphyxia because of massive hemorrhage given the rich blood flow of the tumor. The tumor displayed flap-like activity before anesthesia, and normal ventilation could be maintained. However, the loss of flap-like activity in tumors after general anesthesia may block the airway and increase the risk of asphyxia. Therefore, bronchial artery occlusion was performed under local anesthesia to

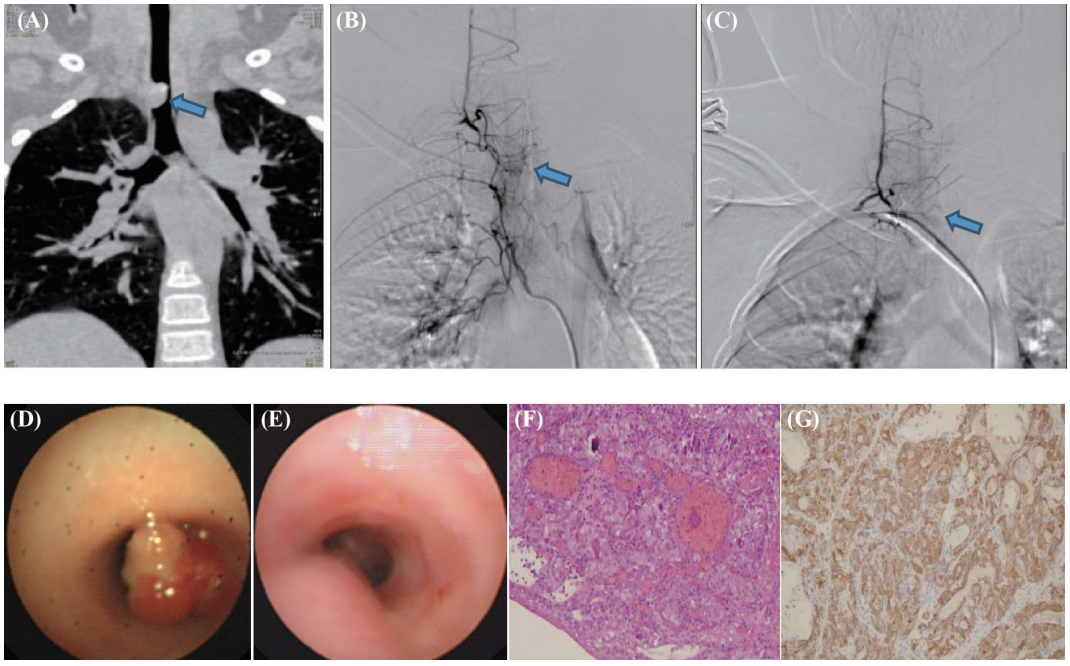

FIGURE 1 Imaging data of Patient 1 with bronchial mucoepidermoid carcinoma. (A) The right posterior wall of the trachea displayed irregular soft tissue shadows projecting into the lumen and occupying a large part of the lumen. (B) Preoperative angiography of the vascular closure of the tracheal tumor. (C) Postangiogram of the tracheal tumor after vascular occlusion. (D) The polyp-like neoplasm in the upper middle of the trachea was obstructed beyond the diameter of the tube (before surgery). (E) After bronchoscopic interventional therapy, the lumen was unobstructed, and the glottis to the carina was well exposed. (F) HE staining revealed the adenoid structure of the subepithelial mucus cells in the bronchial mucosa. (G) Immunohistochemical detection (×20) revealed that the tumor cell foci were positive for CK7.

reduce the possibility of massive hemorrhage, and further invasive resection of the bronchoscopy was performed under general anesthesia.

Under local anesthesia, bronchial arteriography and embolization were performed through the right bronchial artery intubation. Subsequently, under intravenous anesthesia and a laryngeal mask, interventional bronchoscopy was performed. The tumor (5 mm × 8 mm × 15 mm) was removed using a high-frequency electric trap and forceps. The residual base tissue was further subjected to an argon injection and repeated freeze-thaw cycles. The glottis to the protuberance was well exposed (Figure 1B–E). No special discomfort occurred after the operation.

The pathological diagnosis was bronchial mucoepidermoid carcinoma (low grade) based on the findings of positivity for cytokeratin (CK; glandular epithelium), epithelial membrane antigen (EMA), CK7, and carcinoembryonic antigen (Figure 1F, G).

Mucoepidermoid carcinoma is insensitive to radiotherapy and chemotherapy, and no radiotherapy or chemotherapy was provided after surgery. Bronchoscopic cryosurgery was performed once a week for 1 month. The tumor was eradicated, leaving a smooth mucosa, and the interval between cryotherapy sessions was extended to 3 months. Enhanced chest CT and bronchoscopy were performed after 10 months, and no tumor recurrence was observed.

Patient 2

A 6-year-old boy experienced intermittent fever (highest temperature of 39°C) and cough for 2 months. After 1 week of treatment for pneumonia, the patient's fever was abated, but his cough persisted. Twenty days before admission, the patient's cough was aggravated. Chest CT revealed a soft tissue density block shadow in the right trachea and right pulmonary emphysema. A physical examination revealed normal growth, poor nutrition, stable breathing, no concave signs, coarse breath sounds, and right lung inspiratory wheezing. After admission, contrast-enhanced chest CT uncovered a soft tissue density in the left wall of the right main bronchus (CT value, 61 HU). After enhancement (CT value, 151 HU), the focus was obviously enhanced with a clear boundary and diameter of 1.2 cm.

Right bronchus arteriography and embolization were performed through the right bronchial artery intubation under general intravenous anesthesia and a laryngeal mask. After embolization, interventional therapy under bronchoscopy was performed after the occlusion. The tumor (5 mm × 8 mm × 10 mm) was removed using a high-frequency electric trap and forceps. The residual base tissue was further treated with argon injection and repeated freeze-thaw cycles. After the operation, the lumen was unobstructed, and no special discomfort occurred (Figure S1).

The pathological diagnosis was bronchial mucoepidermoid carcinoma (low grade) based on the findings of positivity for CK and EMA and negativity for thyroid transcription factor-1(Figure S1).

Tracheal cryotherapy was performed once a week after surgery. The focus was stable for three consecutive treatments. The patient was transferred to a local hospital for further treatment; however, the tumor recurred after 1 year without regular cryotherapy. The tumor encompassed one-third of the right main bronchial lumen, and regular freezing was performed after bronchoscopy resection.

Patient 3

A 9-year-old girl experienced wheezing with chest tightness and shortness of breath for 3 months. She was treated for bronchial asthma, which was slightly improved. Her cough and wheezing were aggravated for 1 week accompanied by intermittent hemoptysis. Physical examination revealed heavy breathing, mild cyanosis of the lips, all three concave signs, and bilateral wheezing. Other examinations were normal. Contrast-enhanced chest CT illustrated that the right posterior wall of the airway was obviously thickened. The nodular soft tissue was convex in the local airway, and it had an irregular shape. The size of the lesion was approximately 12 mm × 14 mm × 15 mm with a CT value of 34 HU. The focus was obvious after CT enhancement (110 HU), and infiltration outside the trachea was noted.

Protective embolization of the thyroid artery was performed using microcoils. Under intravenous anesthesia and a laryngeal mask, bronchoscopic interventional therapy was conducted. The tumor (5 mm × 8 mm × 15 mm) was removed using a high-frequency electric trap and forceps. The residual base tissue was further treated with argon injection and repeated freeze-thaw cycles. The lumen was unobstructed, and no special discomfort occurred (Figure S2).

The pathological diagnosis was pleomorphic adenoma based on its histopathology, including a variable mixture of epithelial and mesenchymal-like myoepithelial cells in a variably myxoid extracellular matrix. The epithelial elements consisted of tubular structures (Figure S2).

Pleomorphic adenoma is not sensitive to radiotherapy and chemotherapy. Two weeks after surgery, bronchoscopy revealed that the main bronchus was unobstructed, and the local lesion was slightly enlarged. The basal part of the lesion was frozen once a week. After three consecutive treatments, the focus was stable and controlled. The freezing interval was gradually extended to 1 and 3 months. Six months after surgery, no coughing hemoptysis occurred, and contrast-enhanced CT revealed that the invasiveness of the lesion was obviously reduced. No obvious recurrence was found via bronchoscopy.

TABLE 1 General information and follow-up results of 4 children with primary airway tumor

Patient number	Gender	Age (years)	Time from onset to diagnosis (months)	Main symptoms	The site of the tumor	Pathologic findings	Follow-up time (months)	Recurrence
1	Female	7	7	Cough and wheezing for 7 months, continues hemoptysis for 4 months	The right posterior wall of trachea	Bronchial mucoepidermoid carcinoma (low-grade)	10	No
2	Male	6	2	Intermittent fever with cough for 2 months	The right main bronchial opening site	Bronchial mucoepidermoid carcinoma (low-grade)	12	Yes
3	Female	9	3	Wheeze 3 months, hemoptysis 7 days	The middle section of the trachea	Pleomorphic adenoma	6	No
4	Male	6	12	Intermittent cough for more than 1 year	Right upper lung	Bronchial leiomyoma	5	No

Patient 4

A 6-year-old boy exhibited intermittent cough for 1 year without hemoptysis, wheezing, and fever. He was first diagnosed with an allergic cough and treated. Seven days before admission, the patient's cough was aggravated. Chest CT revealed a soft tissue density shadow in the right main bronchus. After hospitalization, physical examination revealed good nutrition, stable breathing, and no lip cyanosis. Respiratory sounds of the right lung were significantly reduced. Contrast-enhanced chest CT illustrated that the lung texture was thick, and the right lung was translucent. A soft tissue density shadow was found in the initial lumen of the right main bronchus. The boundary was clear, and its size was approximately 8 mm × 9 mm × 11 mm. Upon contrast administration (198 HU), the shadow was obviously enhanced. The lesion was closely related to the lateral wall of the right bronchus.

A stained tumor was visible under the right bronchial artery intubation. A microcatheter was first implanted into the distal part of the bronchial artery and injected with gelatin sponge (350–560 μm). The tumor was no longer visible on radiography.

Under intravenous anesthesia and a laryngeal mask, bronchoscopic interventional therapy was conducted. The tumor was removed using a high-frequency electric trap and forceps. The residual base tissue was further treated with argon injection and repeated freeze-thaw cycles. The lumen was unobstructed, and no special discomfort occurred (Figure S3).

The pathological diagnosis was bronchial leiomyoma. Histopathological analysis of the lesion revealed that leiomyoma cells were arranged in bundles, the nucleus was deeply stained, and no mitosis was observed. Immunohistochemical analysis revealed positivity for SMA and Desmin (Figure S3).

Bronchial leiomyoma is a benign tumor. Two weeks after surgery, bronchoscopy revealed that the main bronchus was unobstructed, and the local lesion was slightly increased in size. The basal part of the lesion was frozen once a week. After three consecutive treatments, the focus was stable and controlled. The freezing interval was gradually extended to 1 and 3 months. No coughing hemoptysis has been observed 5 months after surgery, and enhanced CT illustrated that the invasiveness of the lesion was obviously reduced.

Analysis of the 4 patients

We presented four children (4–10 years old) with hypervascular primary airway tumors. Plain CT revealed an equal density (compared with that of the muscle tissue of the chest wall), whereas contrast-enhanced CT revealed uniform and significant enhancement, indicating that the blood supply to the tumors was abundant. Two patients had tumors in the main trachea, and the other two tumors were located in the right main bronchus (both at the ostial bronchus) (Table 1). Anesthesia was administered before bronchial arteriography, and bronchial artery embolization was performed at the lesion to prevent hemorrhage during surgery. After bronchial artery occlusion, the tumors were excised using a high-frequency electrical snare under a bronchoscope.

No severe complications such as major bleeding and asphyxia were observed. Some patients experienced a small amount of bleeding. The bleeding was stopped after locally spraying 4°C saline and epinephrine. Bronchoscopic cryotherapy was performed once a week after surgery. After 1 month, all of the airway tumors had disappeared, and the cryotherapy interval was extended to 3–6 months. All children were followed up for more than 5 months, and one bronchial mucoepidermoid carcinoma recurred.

DISCUSSION

In recent years, improvements in clinical technology have significantly increased the diagnostic accuracy for airway tumors. With the continuous development of the interventional technique of respiratory endoscopy, minimally invasive treatment of airway diseases has gradually become the first choice in clinical therapy.[3]

However, compared with that in adults, pediatric tracheobronchial tumors are rare, resulting in less treatment experience. Pleomorphic adenoma in the trachea, also known as a salivary gland type mixed tumor, is a type of salivary adenoma. It commonly arises in the parotid, sinus, nasal septum, and cleft palate. This rare primary tracheobronchial benign tumor often arises in the main airway. To our knowledge, all case reports involved only adults.[4,5] Tracheobronchial mucoepidermoid carcinoma, a type of salivary adenocarcinoma, originates from the submucosal glands of the bronchial wall. It accounts for less than 1% of primary pulmonary malignant tumors and 0.1%–0.2% of children with primary respiratory system malignant tumors, primarily arising in school-age children. Tracheobronchial mucoepidermoid carcinoma can be divided into low, moderate, and highly malignant types.[6] It is usually a low-grade lesion in children with limited growth and metastasis in the respiratory tract.[7,8] Bronchial lymphoma originates from smooth muscle cells between the bronchial rings. It is a rare tumor with a low recurrence rate after resection.

At present, surgical resection is the first choice for the treatment of bronchial malignancies, especially for patients with endotracheal infiltration. However, both surgical trauma and complications are severe. Tumors usually grow along the submucosal long axis or lumen of the bronchus, leading to incomplete resection and local recurrence. In this report, two children were diagnosed with bronchial mucoepidermoid carcinoma without obvious internal infiltration on contrast-enhanced CT; thus, we resected the tumor via bronchoscopy. Large tumors or polyps in the airway are the most troublesome problem in the performance of respiratory endoscopy. Generally, hard tracheoscopy combined with a variety of interventional techniques is used in adult therapy.[9] Rigid tracheoscopy can be performed rapidly and effectively, and the device is small. However, it is difficult for tracheoscopes to pass through the narrow part of the tumor, and it can damage both the tumor and trachea. In addition, the use of rigid tracheoscopy in children with respiratory disease is limited. Flexural bronchoscopes are soft, small in diameter, and easy to bend and rotate. They can safely pass through the narrow section of the trachea. It should be noted that bronchial arterial embolization may not block all blood-supplying arteries of the tumor, and it is necessary to closely monitor bleeding and prepare hemostatic drugs. In addition, collateral circulation may occur in tumor blood-supplying arteries may occur 1 week after bronchial arterial embolization, and thus, airway interventional therapy is best performed within 1 week after bronchial closure. After tumor resection, lung images should be reviewed to prevent pneumothorax.

The physiological airway of children is narrow. Interventional therapy using a bronchoscope in children requires tracheal intubation and a laryngeal mask under general anesthesia. For tumors located in the large airway, the tumor is often rich in blood, and asphyxia caused by bleeding can quickly become life-threatening. Bronchial artery embolization is a vascular interventional therapy that was developed on the basis of selective tracheal intubation and angiography. An embolic agent is selectively injected into the bronchial artery through the catheter, thereby blocking diseased blood vessels such as malformed and dilated vessels, and its immediate hemostatic effect is good.[10-12] Therefore, for hypervascular tumors in the large airway, it is better to first embolize the bronchial artery under local anesthesia. Bronchoscopy was then performed after the blood supply was eliminated, and the tumor volume was reduced. In this study, the blood supply of the tumor was rich. Gelatin sponge particles combined with spring steel rings were chosen for embolization. Gelatin sponge particles consist of non-toxic and non-antigenic protein glue with good accessibility. They cannot reach the bronchopulmonary artery anastomosis branch during embolization, which prevents bronchial ischemic necrosis and reduces the risk of spinal artery embolism. Particles smaller than 560 μm are generally chosen for children. The results revealed that an immediate hemostatic effect were achieved in all four patients, as well as improved ventilation with a small amount bleeding and no obvious adverse reactions. The good condition provided an important guarantee for general anesthesia and successful bronchoscopy.

In conclusion, pediatric hypervascular primary airway tumors in children can be treated via interventional therapy based on the combined use of bronchoscopy and bronchial artery embolization. This multidisciplinary cooperation model results in less trauma and fewer complications without resulting in serious adverse reactions after surgery, supporting its utility in clinical practice. Further large-sample and long-term follow-up studies are required to investigate the efficacy and safety of this treatment.

CONFLICT OF INTEREST

None of the authors of this article have any conflicts of interest to disclose.

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SUPPORTING INFORMATION

Additional Supporting Information may be found online in the supporting information tab for this article.

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