Interventional management for benign airway tumors in relation to location, size, character and morphology

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ABSTRACT

Objective: To select minimally stressful methods for patients with benign bronchial tumors, and evaluate interventional strategies in relation to location, size, character and morphology.

Methods: We reviewed the indications and efficacy of various interventional bronchology techniques at our institution, including individual or combined laser resection, electrocautery, argon plasma coagulation and high radiofrequency snaring for the treatment of various types of benign bronchial tumors.

Results: It is essential to treat endoscopically that the tumor is visible and has a stalk and not invade beyond bronchial wall. By using combined techniques, no complications or recurrences were encountered.

Conclusions: Interventional bronchology techniques for benign bronchial tumors can be simple and safe, and therapeutic strategies should be designed in relation to location, size, character and morphology of tumors.

KEY WORDS

argon plasma coagulation; benign endobronchial tumor; high radiofrequency snare; Interventional bronchology; Microwave; Neodymium-Yttrium-Aluminum-Garnet laser

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Introduction

Endobronchial tumors can cause obstruction of the tracheobronchial tree regardless of their benign or malignant character. Tumor removal is thus considered the first treatment of choice to improve respiratory status to dilate and maintain the airway. In particular, treatment of benign airway tumors should employ the method with minimal stress. In patients with inoperable tumors we frequently regard endoscopic treatment as the first treatment of choice, but the indications and decisions regarding the method require careful consideration. Good indications for endoscopic treatment include tumors in which the distal margins can be endoscopically evaluated, and are located within the tracheobronchial tree, as far as the subsegmental bronchi, pedunculation, which can facilitate snaring and resection, if the lesions are not broad based, extend across multiple cartilaginous rings, and if there is no extramural tumor invasion. Furthermore, since a few cases show recurrence or malignant transformation even after resection, careful periodical observation of the resection stump with the bronchofiberscope (BF) is necessary. For this overview study, we selected a variety of interventional therapies for patients compromised due to advanced age or poor general status.

The various techniques we employ include high-power laser irradiation with a neodymium-yttrium-aluminum-garnet laser (Nd-YAG) laser (1-3), microwave (MW) (4,5), argon plasma coagulation (APC) (6-8), high radiofrequency (HRF) snares (9,10) and dehydrated ethanol injection therapy (11). It is important to strictly adhere to the indications of these techniques.

We set out to clarify, based on retrospective evaluation of routine work-up data in our charts and patient treatment data, the efficacy and most appropriate indications for various specifically selected, yet representative of the spectrum of conditions we encounter, with bronchial benign tumors in order to provide a guide to techniques available in interventional bronchology for benign obstructive lesions.

No potential conflict of interest.

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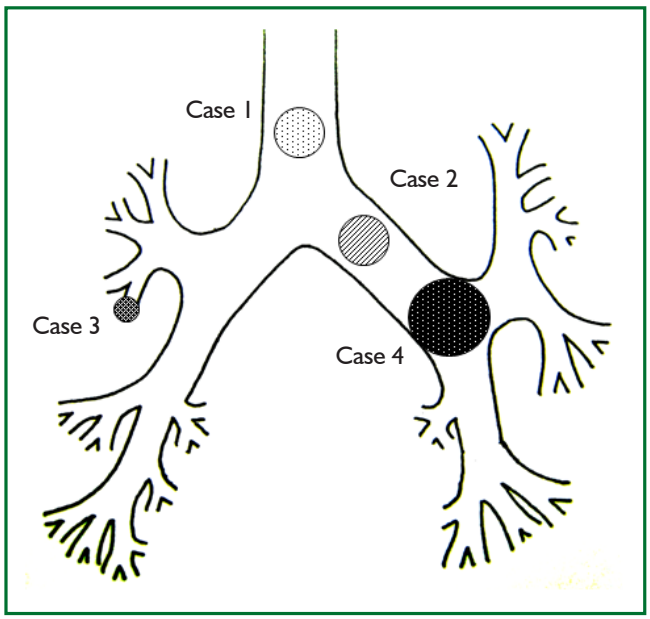

Figure 1. The bronchial map shows the locations of the various types of benign bronchial tumors in this series.

Methods

We examined the efficacy of various interventional bronchology techniques for the treatment of different types of benign bronchial tumors located at a variety of sites in the tracheobronchial tree.

These tumors were located at the level of the trachea (case 1: hamartoma), the main bronchi (case 2: glomus tumor), subsegmental bronchi (case 3: papilloma) and the bifurcation of the left upper and lower lobe bronchi (case 4: lipoma), respectively (Figure 1). We selected the most suitable and safe techniques to achieve complete tumor resection according to the location and tumor characteristics.

All patients provided written informed consent to the procedures, which were all performed as part of the regular preoperative workup, (all data are retrospective) and no patient's identity is revealed. Our Institutional Review Board approved all data collection and analyses.

We used an Efer-Dumon rigid bronchoscope (Efer, La Ciotat, France) for cases 1 and 2, with general anesthesia, employing deep sedation by intravenous 1-2 μ/kg of fentanyl citrate and 1.5 - 3.0 mg/kg of propofol and inhalation anesthesia with N_2O/O_2, with spontaneous respiration. For cases 3 and 4, we employed local anesthesia of approximately a total of 10 ml of 2% xylocaine given by a Jackson spray in synchrony with the patient's inhalation, before inserting the PENTAX EB1830 flexible bronchoscope and giving additional xylocaine via the working channel as needed (Table 1).

Both the rigid and flexible instruments can be used in combination with a variety of ancillary therapeutic methods, each with their own merits and demerits (Table 2).

Results

Case 1: Tracheal hamartoma (Figure 2)

A 58-year-old man was admitted to a local hospital with a diagnosis of pneumonia. Chest computed tomography (CT) revealed an intratracheal mass. Chest CT and BF findings showed a pedunculated polypoid tumor with a smooth surface but irregular shape near the right wall of the carina. The tracheal tumor was diagnosed as tracheal hamartoma by biopsy. Because of its morphology and size, we removed the tumor by first strangulating and resecting with an HRF snare, then debulking the residual tumor with an Nd-YAG laser. Finally we used APC to coagulate the base of the lesion to prevent tumor recurrence. Our experience has shown that, to avoid perforation of the airway wall, APC is safer than Nd-YAG laser irradiation to ablate the tumor bed after resection. The results of pathological diagnosis were hamartoma (12,13), as shown in Fig 2. There has been no recurrence during the 112 months of outpatient follow-up.

Case 2: Bronchial glomus tumor in the left main bronchus (Figure 3)

A tumor was detected on the chest CT of a 39-year-old man with cough and bloody sputum, and the BF findings revealed a smooth lesion occupying more than 90% of the left main bronchial lumen. The left main bronchus tumor appeared to be a pedunculated polypoid lesion with a smooth, red mucosal surface. Transbronchial fine needle aspiration cytology (TBAC) did not yield a definitive histological diagnosis of the tumor. We therefore performed an exploratory procedure under general anesthesia with spontaneous respiration using a rigid scope. When we resected the distal root of the tumor with electrocautery, there was marked bleeding (@ 200ml) from the stump. Hemostasis was achieved by a combination of YAG laser and MW coagulation. The cytological findings of preoperative TBAC showed close clusters of round or polygonal small cells. On intraoperative frozen section, atypical small round tumor cells showed hyperplasia with amorphia. It was difficult to establish a definitive diagnosis, because of its featureless structure, nevertheless carcinoid or adenoid cystic carcinoma were nominated as likely differential diagnoses. Moreover, no other distinguishing structures could be seen pathologically. However, cells with small circular nuclei, slightly acidophilic bright cytoplasm, as well as many capillaries were recognized in the tumor tissue. The tumor cells were hyperplastic when they surrounded blood vessels, and neither ductal structures nor organic patterns could be seen in the tissue. No evidence of malignancy such as strong dyskaryosis or prominent nuclear

Table 1. Details of treatment, reasons for technique and outcome of each case

Case	Anesthesia	Instrument	Reasons	Outcome
Case 1. Hamartoma	General anesthesia	Rigid scope HRF snare YAG Laser APC	Morphology Size Location	No recurrence during 112 months
Case 2. Glomus tumor	General anesthesia	Rigid scope YAG Laser MW	Morphology Bleeding Location	No recurrence during 86 months
Case 3. Papilloma	Local anesthesia	Flexible scope only HRF snare Forceps	Morphology Small size	No recurrence during 87 months
Case 4. Lipoma	Local anesthesia	Flexible scope only HRF snare	Morphology Size Location	No recurrence during 51 months

Table 2. Merits and demerits of various interventional techniques for benign bronchial tumors

	Merits	Demerits
Nd-YAG laser	1. Powerful tissue cauterization 2. Suitable for emergencies	1. Generation of smoke 2. Use with oxygen inhalation is limited 3. Risk of hemorrhage or perforation of the irradiated area
Microwave solidification Argon plasma coagulation	1. Effective in a broad-based lesion 2. Little hemorrhage and perforation, and no smoke generation. 3.Safe under the oxygen inhalation (FiO_2<40%)	1. Limited tissue (superficial layer) cauterization 2. Difficulty of treating tumors located at acute angle bifurcation
High frequency snare	1. No histologic heat denaturation or lysis (histologic diagnosis is possible) 2. Low possibility of hemorrhage and perforation in the irradiation area	1. Heat denaturation of the bronchial wall may extend deeply
Dehydrated ethanol injection therapy	1. Hemostatic effect 2.No need of of expensive facilities	1. Cough induced 2. When tissue is weak, effective injection of the target dehydrated ethanol is impossible

division could be seen. The results of immunohistochemical staining for muscle actin (HHF35) and α-smooth muscle actin (SMA) were positive, but negative for cytokeratin AE1/AE3 and CAM5.2, epithelial membrane antigens (EMA), chromogranin, synaptophisin and neural cell adhesion molecule (NCAM; CD56). Since some benign tumors recur after treatment, it is essential to fully grasp the histological character and establish a pathological diagnosis. Finally, the tumor was diagnosed as a bronchial glomus tumor (14-16). No recurrence of the tumor has been seen during the 86 months of follow-up.

Case 3: Papilloma in the right subsegmental bronchus (Figure 4)

We recognized a small polypoid mass, protruding from the left

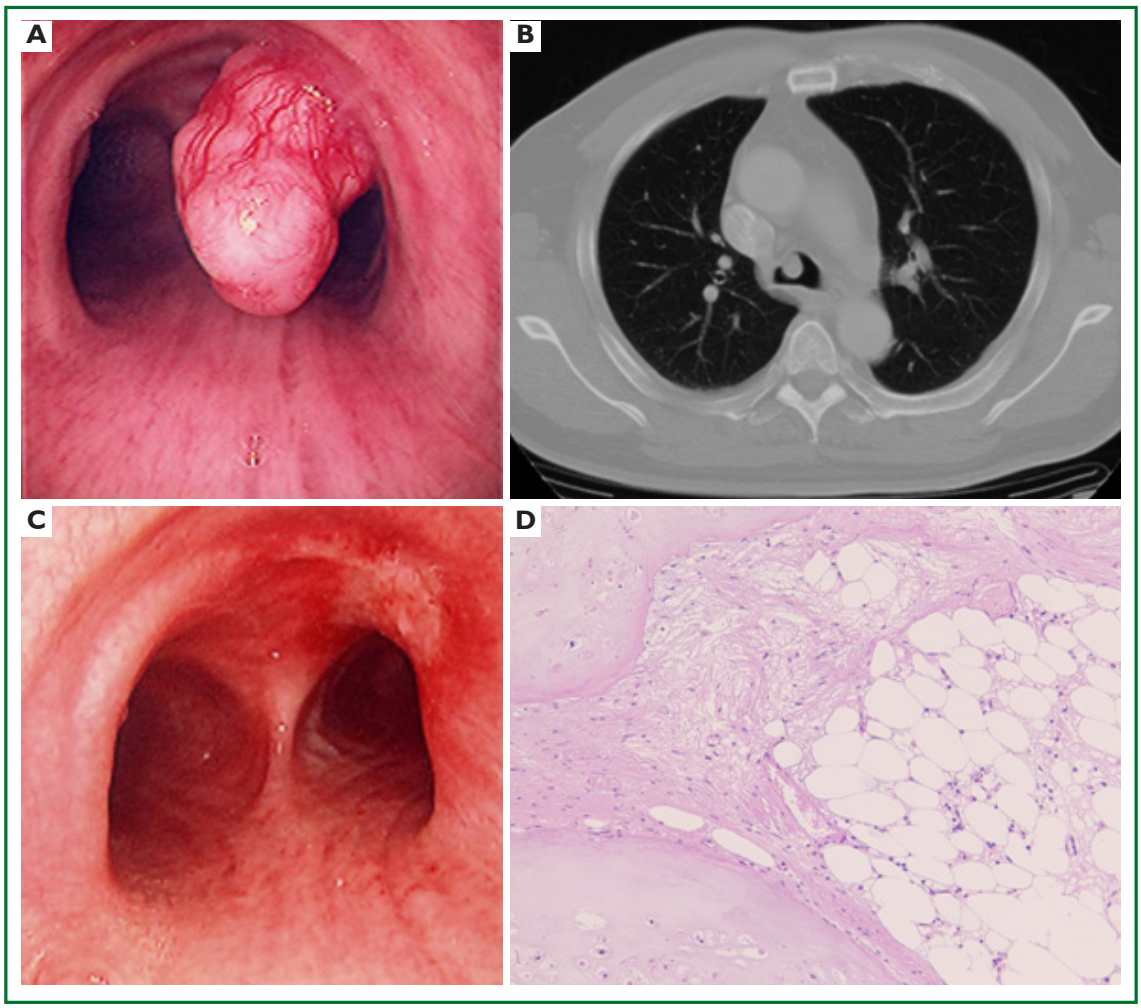

Figure 2. Case 1: BF and chest CT findings show a polypoid tumor in the trachea (A and B). C shows the BF findings after tumor resection. The diagnosis was tracheal hamartoma (D) (hematoxylin and eosin stain, 40 × magnification).

wall of the right B3b in a 52-year-old woman, causing obstructive pneumonitis of the right upper lob on chest CT. BF revealed a tumor with an irregular smooth surface. Biopsy yielded a pathological diagnosis of papilloma (17-19). Polypectomy was performed under local anesthesia. Since initial use of the HRF snare did not remove the entire lesion, the residual lesion was removed by forceps because of the proximity of a blood vessel, via the BF. We have been following up this recurrence-free patient for 87 months.

Case 4: Lipoma in the left main bronchus (Figure 5)

The chest CT of a 58-year-old man showed a round mass 2 cm in diameter in the left main bronchus with a density level similar to fat tissue. BF findings showed a round polypoid tumor with a distal border between the tumor and normal tissue. The pedunculated tumor in the left main bronchus moved on respiration. Confirmation of the tumor by BF and biopsy revealed lipoma even on the distal side. Tumorectomy was performed with an HRF snare via BF under local anesthesia. The final pathological result of this tumor was sialolipoma, a benign lipomatous tumor occurring in salivary glands (10,20). Pathological findings showed a well-circumscribed mass composed of glandular tissue and mature adipose elements. The glandular components resembled normal salivary gland tissues. There has been no recurrence at 51 months.

Discussion

We set out to provide a concise overview of various benign neoplasms of the airway in a variety of possible locations and to describe the available range of approaches to diagnosis and treatment. The incidence of benign tumors in the central airway is low, and there are extremely few reports on series of such

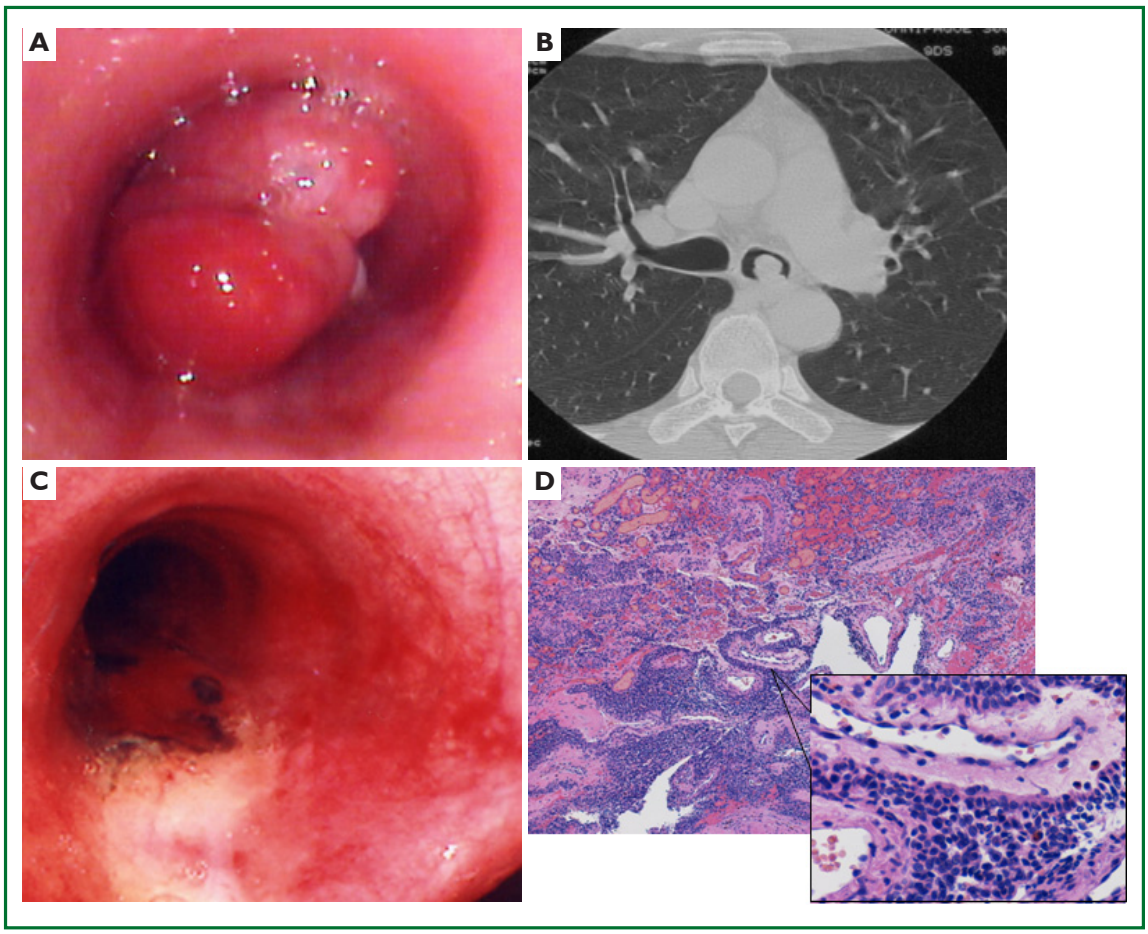

Figure 3. Case 2: BF and chest CT findings show a polypoid tumor in the left main bronchus (Figure 3 A and B). Figure 3 C shows the BF findings after tumor resection. Pathological findings show that the tumor is composed of solid sheets of cells interrupted by vessels (hematoxylin and eosin stain, 40 × and 200 × magnification).

benign tumors. In the series reported by Grillo et al. (21), most of their 198 primary tracheal tumors were malignant, and the frequency of benign tumors was 10.6%, i.e. 1.9% of all lung tumors (2). Most information on benign bronchial tumors is contained in individual case reports, which does not promote understanding of this entity. As a large referral center for pulmonary diseases, we have had the opportunity to encounter a relatively wide range of benign bronchial lesions, and here we present retrospectively selected cases that contribute to evaluation of representative management and strategies of interventional bronchology for these entities and the merits and demerits of each technique (Table 2).

Strategy and examination

It is relatively rare for bronchial tumors to show an abnormal shadow on chest X-ray films. In some such cases, we employed conservative treatment under a diagnosis of bronchial asthma or bronchitis even though they had initially actually had had a bronchial tumor. Concerning clinical symptoms, dyspnea can show rapid exacerbation in benign lesion cases when tumor causes stenosis of the tracheal lumen of over 50% (22,23). Therefore these tumors, particularly tracheal tumors, can require much time to establish a definitive diagnosis. In this regard, patients showing respiratory symptoms continuously, unaffected by seasonal change, asthmatic patients who are minimally responsive to drugs such as bronchodilators, and patients with recurrent pneumonia must be distinguished from patients with bronchial tumors (24). It is sometimes necessary to perform chest CT, magnetic resonance image (MRI) and BF for patients suspected to have bronchial tumors. The thin-slice CT images and 3-dimensional CT (3D CT) which can display minute details are able to not only suggest tumor characteristics, but also determine whether the pedunculated mass has a narrow stalk, or is broad-based, extending across multiple cartilaginous rings, and demonstrate extramural tumor invasion, or the presence of

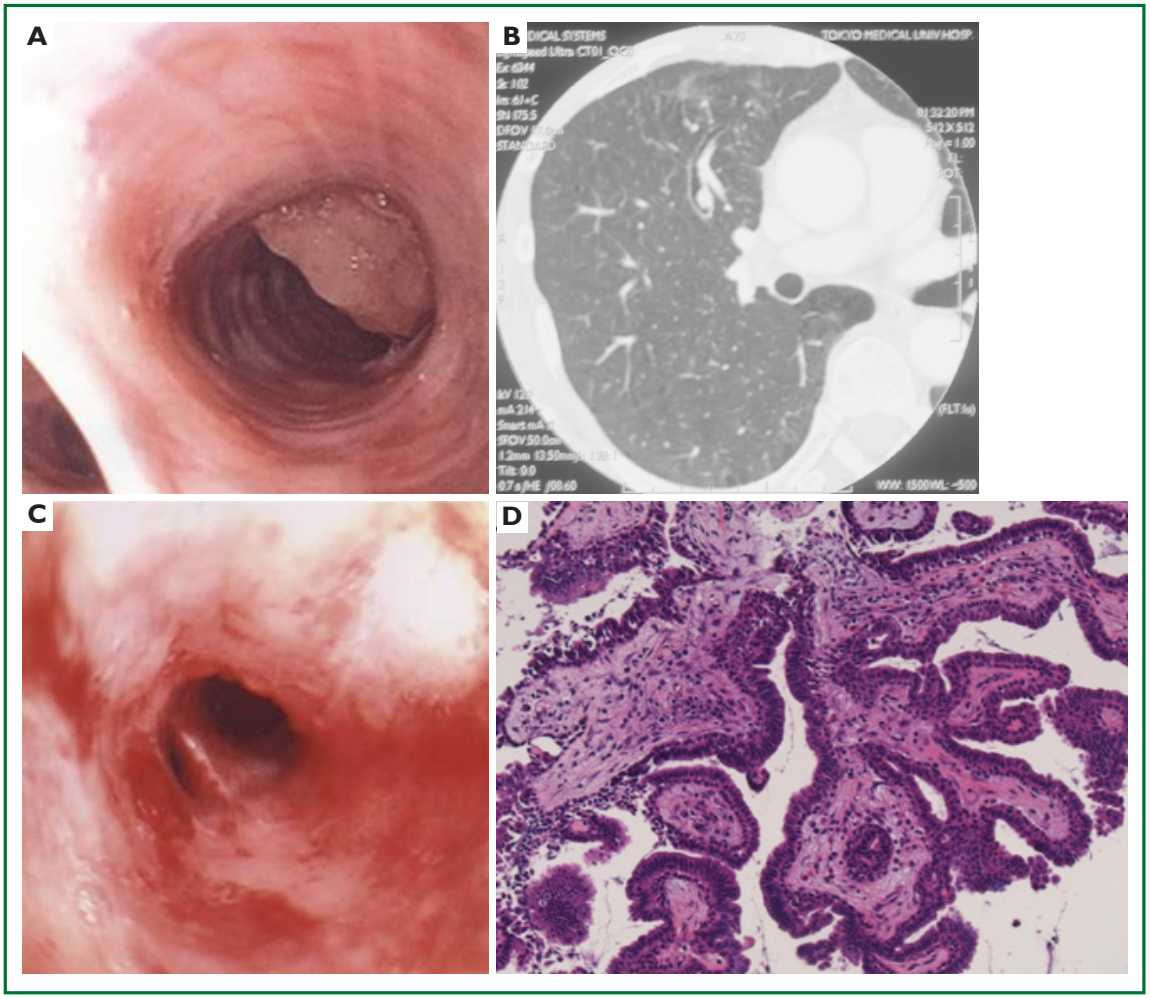

Figure 4. Case 3: BF and chest CT findings show a small polypoid tumor on the right B3b (Figure 4 A and B). Figure 4 C shows the BF findings after tumor resection. We diagnosed bronchial papilloma based on Figure 4 D pathological findings (hematoxylin and eosin stain, 100 × magnification).

distal lesions. Pretherapeutically, it is particularly necessary to accurately grasp the extramural vascular anatomy and confirm the tumor position, size, surface appearance and degree of tumor mobility.

BF (under local anesthesia) or rigid scope (under general anesthesia)?

Therapeutic strategy selection is also very important. Selection of BF with local anesthesia or a rigid scope with general anesthesia depends on conditions such as the location, size, shape, histologic type of tumor and respiratory status. However, general condition, age, cardiorespiratory state and coexistent disease are also important factors regarding choice of treatment. Usually, we use a BF under local anesthesia with the patient in an awake state if there are no problems in the overall status. Reasons for this approach include consideration of the physical burden and risk of complications for patients undergoing general anesthesia, and economic aspects such as length of hospital stay. On the other hand, if patients have a low pulmonary function, are elderly, or have a history of heart cardiac disease, treatment under general anesthesia can be desirable from the viewpoint of safety (25,26). If the tumor resection is supervised by an anesthesiologist, emergency events can be handled with maximum efficiency.

General anesthesia should be selected over awake local anesthesia if tumorectomy is anticipated to require a long time (more than 30 minutes) or if the anatomical location may be problematic, such as in the right upper lobe bronchus. Although in most cases, we use the rigid scope to deal with massive hemorrhage after resection of an inflammatory lesion or tuberculous mass; in cases with perforation of the bronchial wall with high power laser irradiation; voluminous sputum from the peripheral side after opening the site of tumor occlusion; or tumors too large to be able to be removed with conventional

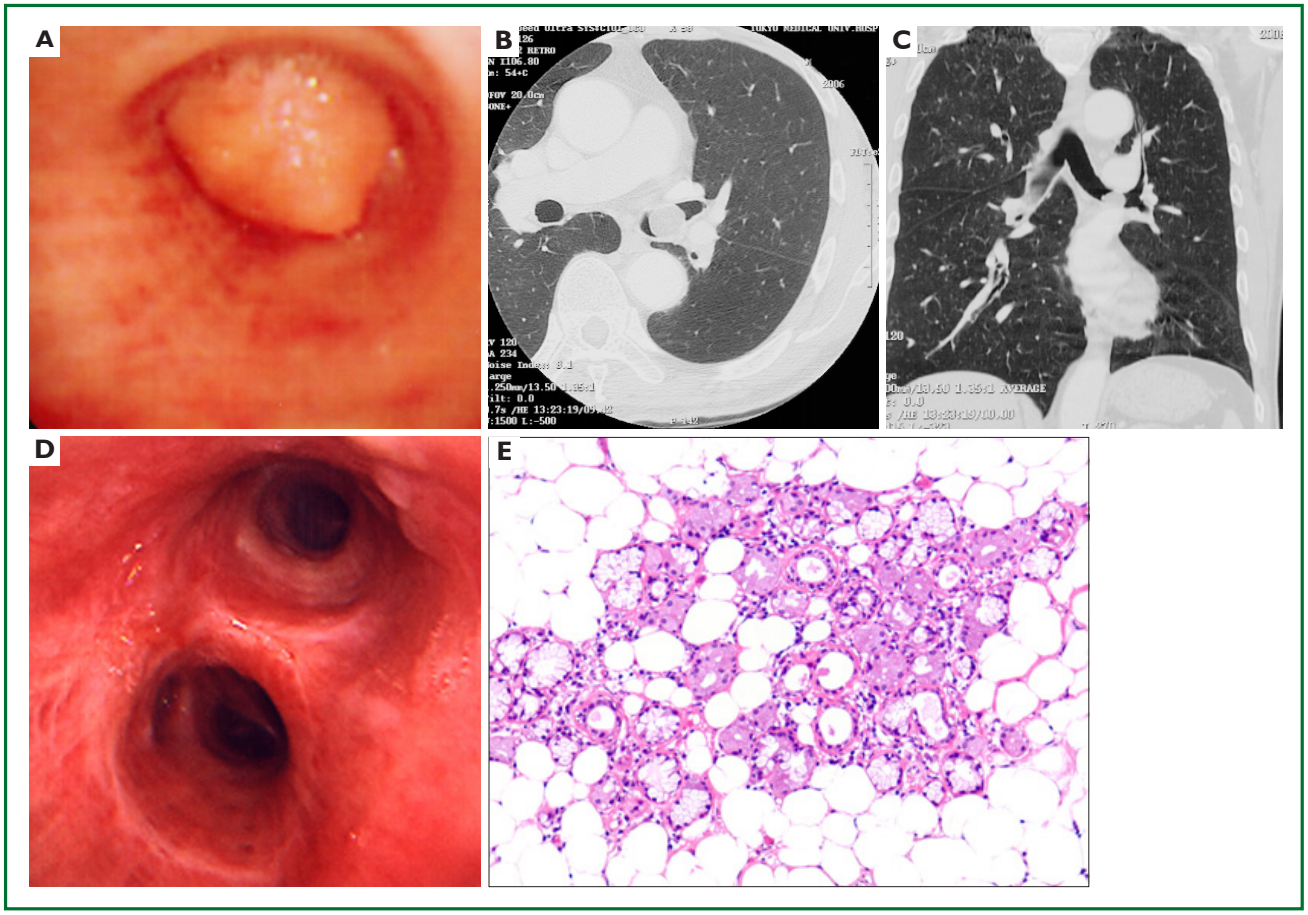

Figure 5. Case 4: BF and chest CT, MR shows a round mass in the left main bronchus with the same density level as fat (Figure 5A, B and C). Figure 5D shows the BF findings after tumor resection. The tumor was diagnosed as bronchial sialo-lipoma based on the pathological findings Figure 5E (hematoxylin and eosin stain, 40 × magnification). Pathological findings show benign lipomatous tumor occurring in the salivary gland.

forceps (24,26). Use of the rigid scope is also recommended if large blood vessels are recognized near the tumor.

Intervention or surgical treatment?

While endoscopic treatment is frequently the best choice, careful consideration about the choice and application of therapeutic implements is essential before treatment. When the possibility of malignancy cannot be denied, or when there are indications for surgical resection because of peripheral pulmonary organizing pneumonia or bronchiectasis due to repeated infection, surgical resection of the lung together with the bronchial tumor, is frequently performed (2). The following conditions are considered as indications for surgical resection, rather than endoscopic treatment: when malignancy cannot be denied histologically, cases accompanied with organizing pneumonia or remarkable bronchodilation of the peripheral side beyond the tumor (2), tumors with extensive infiltration of the bronchial wall across more than 3 bronchial cartilage rings or appearing to invade beyond the tracheal wall (2). Furthermore, endoscopic therapy is not indicated in cases in which it is not possible to confirm the status of the peripheral bronchus beyond the point of tumor obstruction, or cases in which fatal hemorrhage might be caused by bronchial wall perforation. In such cases, the possibility of malignant tumor cannot be denied preoperatively and therefore surgical resection is indicated. When carcinoma remains at the resected stump, sleeve lobectomy and cylindrical tracheal resection with end-to-end anastomosis should be considered. These therapeutic methods can also help maintain respiratory function. However, if surgery or combined surgery and other methods are contraindicated due to low pulmonary function or poor general status, the following endoscopic techniques may be used.

High power laser (wavelength 1020~1064 nm): Diode / Nd -YAG laser

High power laser irradiation is often considered to be the first treatment of choice for emergency airway maintenance. The effective depth of laser power is several mm to several cm, depending on the laser power output. If the length of tracheal cartilage destruction is 4 cm or less (27), tangentially applied high power laser up to 40 W is indicated. Care is needed to avoid too much power per shot, and for irradiation of surrounding normal tissue the setting should be lower than 40 W. Dividing laser irradiation into several shots, while continuously confirming the results is the safest method. Careful examination is necessary to prevent bronchial wall perforation and massive bleeding from surrounding blood vessels. Massive bleeding during treatment may be controlled by epinephrine saline spray in the airway or compression by the cuff of the tracheal tube. However, in the few cases of pulmonary artery bleeding from the carina, main bronchus or truncus intermedius, the hemorrhage is often massive, control is difficult, and the results can be catastrophic, therefore it is essential to perform contralateral intubation to maintain the airway, and high power laser cauterization while periodically checking the condition of the tumor.

Inhalation of cauterization fumes can aggravate respiratory status through airway damage. We therefore have to remove tissue cauterization fumes in synchrony with patient exhalation, thereby minimizing absorption of fumes.

High power laser therapy usually induces reactive hyperplasia of granulation immediately, even if there is temporary regression of inflammatory granular tissue, which is the reason why it is considered unsuitable for tuberculosis lesions. Cauterization of excessively large areas of tumor at a single time can induce temporary edema and exacerbate airway stenosis. Several pulmonologists reported (23,27,28) that laser therapy using high concentrations of oxygen of more than 40% fraction inspired oxygen concentration (FiO_2) might cause airway fire. Operators must continuously monitor oxygen concentration in the airway, and refrain from high-power laser therapy in cases requiring persistent high-concentration oxygen administration.

MW solidification (3-5)

Tissue irradiated with MW solidifies, and compared with high power laser, MW solidification has the advantages of less bleeding and minimal smoke inhalation. MW solidification has a low risk of bronchial wall bleeding or perforation. This method also permits the use of high concentration oxygen inhalation. Although the cauterization power of MW solidification is weak and therefore safer (the power of normal MW for tissue solidification generally needs 20 W output), it is suitable for a wide range of tissue solidification procedures. High-power laser is monodirectional and can be irradiated only in a straight line directly toward the target. However, MW has the advantage of irradiation not only in a straight line but also from any approach angle, even tangential to the target. If the tumor is located at a bifurcation with an acute angle such as in the bilateral upper lobe bronchi, it would probably be best to perform MW initially.

APC solidification (6-8)

APC involves solidification with a non-contact type monopolar electrode. The high-frequency current reaches the target tissue along with the flow of ionization argon. In argon plasma, the electric current flows toward tissue with least resistance and solidifies tissue surface equally so that it spreads to the non-solidified part and bleeding parts of tissue. The depth of solidified tissue is controlled automatically. Only the tissue surface shows APC solidification effect and its cauterization range is limited. Therefore while this therapy has a low risk of perforation of the bronchial wall, it is not optimal for large pedunculated tumor resection.

HRF snare (9, 10)

As its name implies, the HRF snare enables delivery of alternating current into tissue at a high frequency (105-107 Hz). The strong heating action of this device enables both tissue solidification and tumor resection. This can be effective in initial treatment, especially for polypoid-type tumors occluding central airways, particularly for poorly vascularized pedunculated polyps. While the HRF snare has a low risk of complications due to fumes or aggravation of respiratory status during cauterization and burn edema of the airway after treatment, this technique can be difficult for wide-based tumors. One merit of the HRF snare is that it can resect a tumor mass in a short time, and with little histological change of the resected specimen, unlike when laser or MW irradiation are used.

Dehydrated ethanol injection therapy (11)

Dehydrated ethanol injection therapy can be effective in cases of possible hemorrhage or at high risk for bleeding. Usually the injection dosage is about 0.2 - 0.3 ml dehydrated ethanol per site until the surrounding mucosa turns white. This method is particularly useful preventing hemorrhage before cauterization of the base of a tumor. This treatment is not only effective with tumor tissue but also with inflammatory granulation tissue.

Risk management

When performing interventional bronchology, many considerations must be kept in mind; during treatment

patients must be attached to a pulse oxygen monitor and an electrocardiogram monitor to grasp the cardiopulmonary status, and preparations for emergency airway maintenance are necessary at all times. If interventional techniques under local anesthesia are insufficient, it may be necessary to convert to rigid endoscope under general anesthesia.

The most important point in airway cauterization is oxygen concentration control. In cauterizing during tracheal intubation, we must maintain oxygen concentration below 30%. Post treatment management, such as steroid administration, is essential for the prevention of airway mucosal edema. Removal of tumors greater than 2 cm in diameter may require tracheostomy (29). Furthermore, since some tumors show recurrence and malignant transformation even after resection, careful periodical BF observation of the resection stump is necessary.

Limitations

The main limitation of this study is the small number of cases. However we believe that this is a good reference manuscript for the description and characteristics of the various therapeutic options available with both rigid and flexible broncoscopes in the treatment of benign airway tumors.

Conclusions

Interventional bronchology techniques for benign bronchial tumor are simple and usually safe, and can be immediately effective, even in patients in whom surgery is contraindicated due to insufficient cardiopulmonary reserve or poor general status.

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