

GENERAL THORACIC SURGERY

BRONCHOSCOPIC TREATMENT OF INTRALUMINAL TYPICAL CARCINOID: A PILOT STUDY

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Objective: The curative potential of various bronchoscopic treatments such as Nd:YAG laser, photodynamic therapy, and brachytherapy for the treatment of intraluminal tumor has been reported previously. Bronchoscopic treatment can be used to treat small intraluminal tumor with curative intent, such as in patients with roentgenologically occult squamous cell cancer. In a retrospective study, we showed that bronchoscopic treatment provided excellent local control with surgical proof of cure in 6 of 11 patients with intraluminal typical bronchial carcinoid. **Methods:** In a prospective study, 19 patients (8 women and 11 men) with resectable intraluminal typical bronchial carcinoid have undergone bronchoscopic treatment under general anesthesia. Median age was 44 years (range, 20-74 years). If tumor persisted after 2 bronchoscopic treatment sessions, surgery was performed within 4 months after the treatment. **Results:** Bronchoscopic treatment was able to completely eradicate tumor in 14 of the 19 patients (complete response rate 73%, 95% CI: 49%-91%). Median follow-up of these patients is 29 months (range, 8-62 months). One patient had severe cicatricial stenosis after bronchoscopic treatment, and sleeve lobectomy was necessary. No residual carcinoid was found in the resected specimen. In the remaining 5 patients, bronchoscopic treatment did not result in a complete response and radical surgical resection was performed afterward with confirmation of residual carcinoid in the resected specimen. Median follow-up of the surgical group is 34 months (range, 12-62 months). **Conclusions:** Current data suggest that bronchoscopic treatment may be an effective alternative to surgical resection in a subgroup of patients with resectable intraluminal typical bronchial carcinoid. It alleviated the necessity of surgical resection in 68% (95% CI: 43%-87%) of the patients. (J Thorac Cardiovasc Surg 1998;116:402-6)

Many bronchoscopic techniques are currently available for the treatment of patients with tracheobronchial malignant tumors.^{1,2} In patients with roentgenologically occult intraluminal tumor, bronchoscopic therapy with curative intent, especially photodynamic therapy, may provide an alternative to surgery.³⁻⁷

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Surgical resection is the treatment of choice in patients with bronchial carcinoid and survival has been shown to be excellent. In patients with typical bronchial carcinoid, even limited surgery, such as bronchoplastic surgery, has become an accepted treatment modality.⁸⁻¹¹ Until recently, bronchoscopic treatment was considered only in patients with contraindications for surgical resection.¹² Preoperative bronchoscopic treatment enabled better assessment of tumor growth and restored airway patency to improve the preoperative pulmonary condition in patients with obstructive pneumonia.

We¹³ reported previously that bronchoscopic treatment resulted in histologically confirmed disappearance of tumor in patients with intraluminal typical bronchial carcinoid who underwent surgery after bronchoscopic treatment. Bronchoscopic treat-

Table I. Patient characteristics, tumor localization, appearance, size and visibility of distal tumor margin, data of treatment, treatment outcome, and follow-up

Patient No., sex, age (yr)	Localization	Size (cm)	Visibility of distal margin	BT	CR	Follow-up (mo)
1, M, 29	LMB-LLL	1	Yes	2 × Nd:YAG	Yes	51
2, M, 61	LB6	1	Yes	1 × BE	Yes	29
3, F, 23	RMB	1.5	Yes	1 × Nd:YAG/IXPDT	Yes	62
4, M, 46	BI	1.5	Yes	1 × Nd:YAG	Yes	38
5, F, 20	LMB-LUL	2	No	2 × BE	No	12
6, M, 65	LMB	0.5	Yes	1 × BE	Yes	21
7, M, 74	LLL	1	Yes	1 × BE	Yes	18
8, M, 31	LUL-LB4, LB5	1.5	No	2 × BE	No	23
9, M, 48	BI	2	Yes	2 × Nd:YAG	Yes	42
10, M, 38	RUL	1.5	Yes	1 × BE	Yes	33
11, M, 62	RUL-RB3	1	No	2 × BE	No	32
12, F, 41	BI	1	Yes	1 × BE	Yes	29
13, F, 60	LUL	2	No	2 × BE	No	38
14, F, 25	LUL-LLL	1.5	Yes	1 × BE	Yes	25
15, F, 40	LMB-LUL	2	No	2 × Nd:YAG	No	44
16, M, 34	LLL	0.5	Yes	1 × BE	Yes	15
17, F, 56	LUL-LLL	0.4	Yes	1 × BE	Yes	8
18, F, 47	LMB-LLL	2	Yes	2 × BE	Yes	12
19, M, 42	RLL	1	Yes	1 × BE	Yes	22

LMB, Left main bronchus; LLL, left lower lobe; LB6, left bronchial segment number 6; RMB, right main bronchus; BI, bronchus intermedius; LUL, left upper lobe; RUL, right upper lobe; RLL, right lower lobe; BT, bronchoscopic therapy; ND:YAG, ND:YAG laser; BE, bronchoscopic electrocautery; PDT, photodynamic therapy; CR, complete response.

ment may provide a parenchyma-sparing treatment alternative for bronchoplastic surgery. This seems to be justified by the excellent survival of patients with typical carcinoid after bronchoplastic surgery, the low rate of lymph node invasion and metastasis, its central localization, its tendency for endobronchial polypoid growth, without extraluminal extension, and the feasibility of using current bronchoscopic treatment techniques to obtain tumor necrosis extending several millimeters deep. We therefore conducted a prospective study of bronchoscopic treatment, using Nd:YAG laser or bronchoscopic electrocautery, in carefully selected patients with resectable intraluminal typical bronchial carcinoid, with the purpose of complete tumor eradication, as an alternative for surgical resection.

Methods

Patients were selected from consecutive patients referred to our clinic because of intraluminal typical bronchial carcinoid. Inclusion criteria were accessibility of tumor for the fiberoptic bronchoscope and high-resolution computed tomographic (CT) scans showing no signs of bronchial wall infiltration (bronchial wall irregularities, bronchial wall thickening, peribronchial tumor invasion), or enlarged lymph nodes. Scan technique used for high-resolution CT was previously described.¹⁴ Bronchoscopic treatment was performed by means of high jet ventilation with the patient under general anesthesia. Nd:YAG laser and bronchoscopic electrocautery with both the rigid and

fiberoptic bronchoscopes were used to provide optimal management in clearing intraluminal tumor mass.¹⁵ In case of bronchoscopic electrocautery, the same technique has been used as described previously.¹⁶ Carcinoids were documented photographically before and immediately after treatment. Follow-up bronchoscopic examination was performed to assess response 4 to 6 weeks after bronchoscopic treatment. In case tumor persisted after 2 bronchoscopic treatment sessions, surgical resection was performed.

Oral informed consent was obtained from all subjects. Before bronchoscopic treatment, there was always a consensus about treatment strategy between the surgical oncologist and the pulmonologist. This study was approved by the scientific and ethical board of our hospital.

Results

So far, 19 patients (8 women and 11 men), median age 44 years, range 20 to 74 years, have been treated. Bronchoscopic findings before bronchoscopic treatment with regard to localization, estimated tumor size, and visibility of distal tumor margin are shown in Table I. Technique used and result of bronchoscopic treatment are also shown in Table I. No complications occurred during bronchoscopic treatment, and no significant bleeding occurred. The use of Nd:YAG laser or bronchoscopic electrocautery under general anesthesia provided an optimal treatment setting to control hemorrhage. Follow-up data including treatment management of

those not obtaining a complete response despite 2 bronchoscopic treatment sessions are also shown in Table I.

Bronchoscopic treatment was unable to provide a complete response in 5 of the 19 patients and radical surgery was performed afterward. In all these patients distal tumor margin was invisible for the bronchoscopist. In patient 5, radical lobectomy was feasible, whereas before bronchoscopic treatment a pneumonectomy was considered necessary. Thus bronchoscopic treatment allowed a less extensive surgical resection. Patient 3 underwent sleeve lobectomy because photodynamic therapy resulted in nonselective necrosis and caused complete cicatricial stenosis of the right main stem bronchus. No residual carcinoid was found in the resected specimen. In patient 11, the definite diagnosis after surgery proved to be atypical carcinoid with positive hilar node in contrast to the diagnosis before resection.

Overall, the complete response rate after bronchoscopic treatment was 74% (95% CI: 49%-91%), and 68% (95% CI: 43%-87%) of the patients were spared surgery. During follow-up, bronchoscopic examination was performed at a 3- to 4-month interval. Median follow-up of patients after bronchoscopic treatment has been 29 months (range, 8-62 months). Surgical patients had a median follow-up of 34 months (range, 12-62). These patients did not undergo regular bronchoscopic examination except once after resection, because surgical resection was radical.

Discussion

This prospective study was started after our retrospective data showed that bronchoscopic treatment may provide complete tumor eradication in a subgroup of patients with intraluminal typical bronchial carcinoid. Their carcinoid seemed not to be the tip of an iceberg.¹⁶ Currently, several bronchoscopic treatment alternatives are available for palliation in patients with obstructive tracheobronchial malignant tumors.^{1,2} These techniques have been used to completely eradicate intraluminal tumor, and their curative potential for multiple, occult cancers and carcinoma in situ has been established.^{3,7,17,18} The indication and limitation of bronchoscopic therapy has been addressed recently.¹⁹ The success rate of bronchoscopic treatment with curative intent depends on the malignant behavior of the tumor. Patients with occult cancer 3 mm thick or less and with a longitudinal axis of 20 mm or less have been shown not to have lymph node metastasis.^{20,21}

Therefore photodynamic therapy has been proposed as a "normal tissue-sparing" treatment alternative for surgical resection, partly on the basis of the issue of photodynamic therapy selectivity.^{5,22} However, data to support this drug selectivity are lacking, and skin photosensitivity remains a problem.^{23,24} Randomized trials comparing the different bronchoscopic treatment techniques are not available. It is, however, fair to ask whether the technique per se is the most important determinant for cure.¹⁹ Early stage cancers several millimeters thick require necrosis of several millimeters regardless of the technique of choice.

We presumed that the same may apply for the selected patients with intraluminal typical bronchial carcinoid in whom the relatively benign nature of the disease justified bronchoplastic surgery. Previous surgical series have shown that bronchoplastic surgery is indeed an acceptable treatment strategy in patients with intraluminal or mural, pedunculated or sessile typical carcinoid of limited size.⁹⁻¹¹

As shown in our present series, tumors were intraluminal and never exceeded 2 cm in diameter. High-resolution CT scan did not show gross peribronchial tumor involvement.¹⁴ In depth necrosis of several millimeters is sufficient to completely eradicate these tumors. We used both ND:YAG laser and electrocautery to achieve this. In our clinical experience no difference was found between these techniques with regard to tumor clearance.¹⁶ Intraluminal typical bronchial carcinoid localizations may be such that surgical bronchoplasty is not always feasible, resulting in a relatively wasteful parenchymal surgical resection, while the "preservation of as much normal lung tissue as possible is one of the primary goals of therapy."²⁵ Previous series also show that parenchyma-sparing resection yields excellent survival.^{9-11,26} Typical carcinoid behaves differently from the atypical variant, with excellent survival after complete surgical resection despite the presence of metastasis in lymph nodes.^{8,27} It is therefore understandable that patients suitable for bronchoplastic surgery might be excellent candidates for bronchoscopic treatment. Our series shows that mural type carcinoid was not necessarily the tip of an iceberg and that indeed the findings of high-resolution CT are correlated to complete response. We have more difficulties, however, in treating intraluminal typical bronchial carcinoid extending to the segmental bronchi, where the distal tumor margin was invisible for the bronchoscopist. In patients 5, 8, 11, 13, and 15, tumor was located in a segmental

bronchus of the left or right upper lobe, and the distal involvement of carcinoid was difficult to assess during and after bronchoscopic treatment. In retrospect, it was therefore not surprising that bronchoscopic treatment did not result in complete tumor eradication and that salvage surgery was necessary. Therefore it seems that patients with intraluminal typical bronchial carcinoid in whom distal tumor margin is less clear are not candidates for bronchoscopic treatment. This is a problem similar to treatment of occult squamous cell lung cancer and shows the limitation of bronchoscopic treatment in general.^{1-4, 19} It is of interest that in patient 8, repeated thin-section CT scans revealed an enlarged hilar node after the first bronchoscopic treatment had resolved the atelectasis. Transbronchial needle aspiration showed carcinoid cells in the hilar node, and the patient underwent surgical resection. In patient 11, complete response could not be obtained despite repeated bronchoscopic treatment, and in the resected specimen atypical carcinoid was found with a diseased hilar node. This particular case is a warning that bronchoscopic treatment as the initial therapy for patients with resectable intraluminal typical bronchial carcinoid may have a certain risk. However, the use of general anesthesia in combination with techniques that provide excellent coagulation enables the bronchoscopists to collect representative biopsy specimens for histologic examination. Still, definite histologic classification is sometimes possible only after a complete surgical resection.

In conclusion, bronchoscopic treatment seems to be an effective initial treatment alternative for patients with resectable intraluminal typical carcinoid. This prospective study supports our earlier experience¹³ that patients with intraluminal typical bronchial carcinoid may be given bronchoscopic treatment after a careful selection has been made. These selection criteria are good bronchoscopic tumor accessibility with clearly visible distal tumor margin and high-resolution CT scans showing no extraluminal tumor extension. Bronchoscopic treatment may optimize the parenchyma-conserving treatment strategy in patients with intraluminal typical bronchial carcinoid.⁹⁻¹¹ A less extensive surgical resection may also be possible after preoperative bronchoscopic treatment. Surgery can be performed afterward in case of persistent or residual tumor. Longer follow-up will reveal whether bronchoscopic treatment is as effective as bronchoplastic surgery in a subgroup of patients with resectable intraluminal typical bronchial carcinoid.

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