Gen Thorac Cardiovasc Surg (2010) 58:82–86
DOI 10.1007/s11748-009-0467-4

CASE REPORT

Clinicopathological study of surgically treated cases of tracheobronchial adenoid cystic carcinoma

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Received: 27 January 2009 / Accepted: 11 May 2009
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Abstract Between 1980 and 2007, five patients were pathologically diagnosed as tracheobronchial adenoid cystic carcinoma (ACC). All five patients were women aged 37–67 years. Four tumors were located in the larger airways, and one tumor was located in the peripheral lung. The following operations were done: bronchoplastic procedures in three (carinal resection with double-barreled carinoplasty in one, sleeve right pneumonectomy in one, sleeve middle lobectomy in one), left pneumonectomy in one, and left upper lobectomy in one. Three of the five patients have survived for 172, 144, and 10 months after surgery, respectively. The best local treatment for ACC of the major airway is considered to be sleeve resection of the trachea or bronchus in an area where airway reconstruction may not be disturbed and to add postoperative irradiation when there is residual carcinoma at the stump. However, it seems controversial to recommend adjuvant radiotherapy in all patients undergoing resection.

This article is based on a study first reported in Haigan (Jpn J Lung Cancer) 2008;48:261–5 (in Japanese with English abstract).

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Key words Adenoid cystic carcinoma · Tracheobronchial origin · Bronchoplastic procedure · Postoperative radiotherapy

Introduction

Adenoid cystic carcinoma (ACC), developing in the trachea/bronchi, is a relatively rare low-malignancy cancer of bronchial gland origin. Although it is a slow-growing tumor, it sometimes invades extensively inside and beyond the bronchial wall. For surgical treatment of this tumor, it is essential to determine an appropriate extent of tracheobronchial excision in individual cases. Surgery often needs to be combined with radiotherapy as an adjuvant therapy. ACC, which is unique in terms of histopathological features and the sites of onset, was analyzed clinicopathologically in the cases encountered and surgically treated at our hospital and associated institutions. The findings from this study are presented in this article.

Case reports

Of the 1909 patients with lung cancer surgically treated at our hospital and associated institutions between 1980 and 2007, five patients (0.3%) rated histopathologically as ACC were the subjects of this study. Their ages ranged from 37 to 67 years (mean 50.8 years). All five patients were women. The tumor developed in the larger airway (trachea to segmental bronchi) in four and in the periphery (subsegmental or more peripheral bronchi) in one. Lymph node metastasis was rated as N2 in one, N1 in one, and N0 in three. The final pathological stage of the

disease was IA in one, IIB in two, and IIIB in two. The operative procedure employed was pneumonectomy in two, lobectomy in two, and resection of the tracheal carina in one. Tracheobronchoplasty was additionally performed in three (Table 1)

One patient (N2 case), who underwent sleeve right pneumonectomy, died of distant metastases (skin, mammary gland, and lung) 15 months after surgery. One patient (N1 case) developed local recurrence 114 months after sleeve right middle lobectomy and underwent completion right pneumonectomy. This patient is alive at present, 58 months after the second operation. Of three patients with an N0 tumor, one died of another disease (colon cancer) 95 months after left upper lobectomy. In the other two N0 cases, the surgical stump was tumor cell-positive. One of these two patients underwent tracheal carinal resection (not accompanied by lung resection) to treat ACC of this area, followed by double-barreled carinoplasty and postoperative radiotherapy. This patient is alive at present, 144 months after surgery. In the other N0 case, with a tumor-positive surgical stump, the patient underwent left pneumonectomy to treat ACC of the left main bronchus and postoperative radiotherapy. This patient is alive at present, 10 months after surgery (Table 2). Individual cases are briefly presented below (Fig. 1).

Table 1 Characteristics of patients with adenoid cystic carcinoma ($n = 5$)

Parameter	No. of patients[a]
Age	37–67 years (average 50.8 years)
Sex	
Male	0
Female	5
Location	
Large airways	4
Carina	1
Right main bronchus	1
Left main bronchus	1
Middle lobe bronchus	1
Periphery	1
Pathological stage	
IA	1
IIB	2
IIIB	2
Operative procedure	
Bronchoplasty	3
Double-barreled carinoplasty	1
Sleeve right pneumonectomy	1
Sleeve right middle lobectomy	1
Pneumonectomy	1
Lobectomy	1

[a]Except for the patients' age

Case 1 was a 54-year-old woman. She underwent sleeve right middle lobectomy to treat an ACC arising from the right middle lobe bronchus. She developed tumor recurrence in the residual right lung 114 months later. She underwent reoperation because no distant metastasis was noted. Tumor recurrence was identified in right S6. The tumor metastases to the hilar lymph nodes had invaded the pulmonary artery. Thus, a completion right pneumonectomy was carried out. This patient is alive at present, 172 months after the initial operation (58 months after the reoperation).

Case 2 was a 67-year-old woman. This was the only case of peripheral-type ACC among the five cases studied. Left upper lobectomy was performed to treat the coin lesion of the left upper lobe. The resected tumor was pathologically diagnosed as ACC. Macroscopically, no evident relation was noted between the tumor and the central bronchi. However, because cartilage-deficient bronchioles were histologically detected in the periphery of the tumor-affected area, it seemed likely that the tumor had developed from the fifth- or sixth-order bronchiole. This patient died of colon cancer 95 months after surgery.

Case 3 was a 42-year-old woman referred to our department with a chief complaint of cough. Bronchoscopy and computed tomography (CT) scans revealed ACC (10×10 mm) at the tracheal carina (Fig. 2). She underwent carinal resection (without lung resection) and subsequent double-barreled carinoplasty (Fig. 3). Because the surgical stump of the right main bronchus

Table 2 Clinical course and prognosis of five female patients with adenoid cystic carcinoma

Case no.	Age (years)	Location of the tumor	pTNM	Operative procedure	Result (months)
1	54	Rt. middle bronchus	T2N1M0	Sleeve rt. middle lob.	Alive (114)
		Local recurrence		Completion pneumo.	Alive (58)
2	67	Lt. S4b	T1N0M0	Lt. upper lob.	Died from colon cancer (95)
3	42	Carina	T4N0M0	Double-barreled carinoplasty	Alive (144)
4	37	Rt. main bronchus	T4N2M0	Sleeve rt. pneumo.	Died of disease (15)
5	54	Lt. main bronchus	T3N0M0	Lt. pneumo.	Alive (10)

Rt., right; Lt., left; lob., lobectomy; pneumo., pneumonectomy

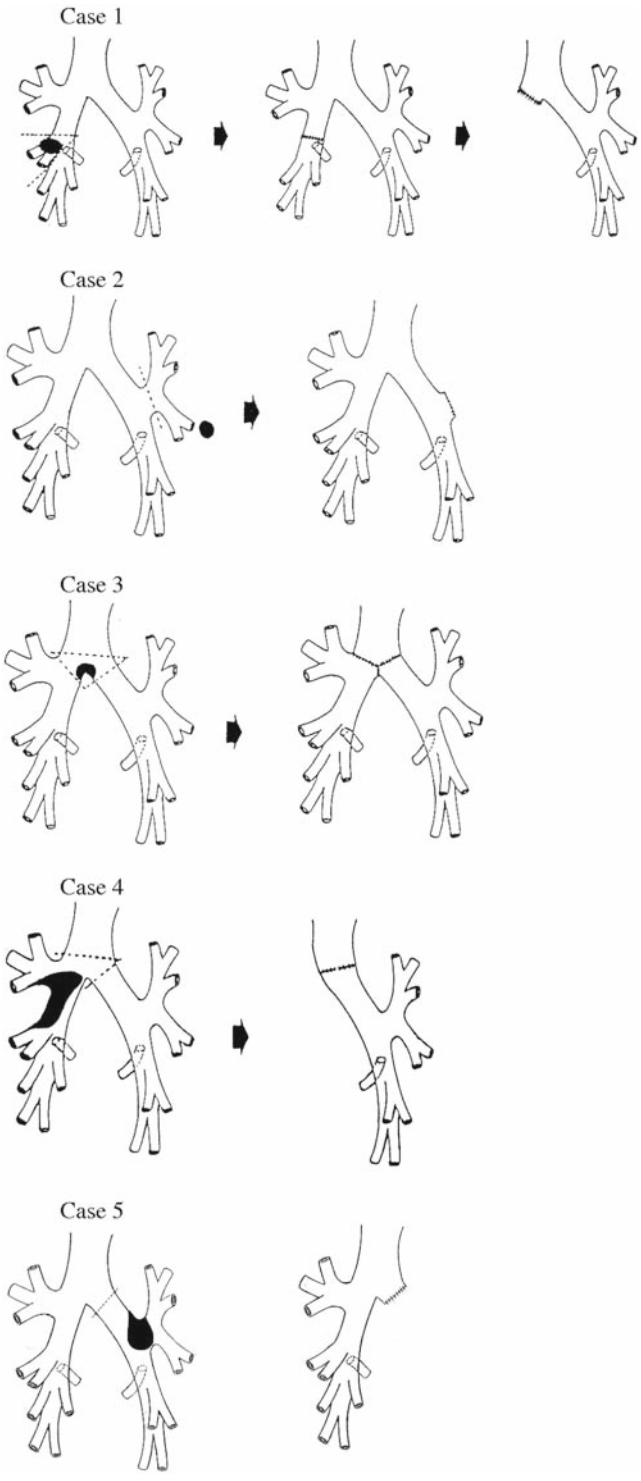

Fig. 1 Operative procedures for five patients with tracheobronchial adenoid cystic carcinoma

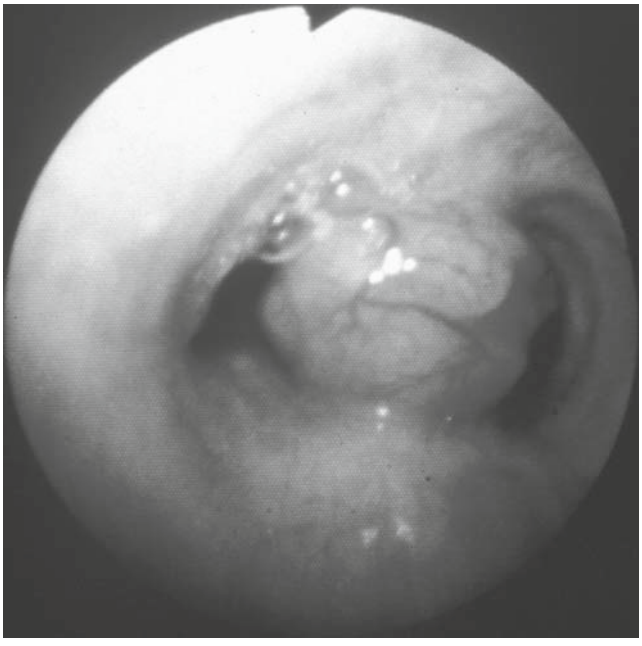

Fig. 2 Bronchoscopy on admission revealed the presence of a tumor at the carina measuring 10 × 10 mm (case 3)

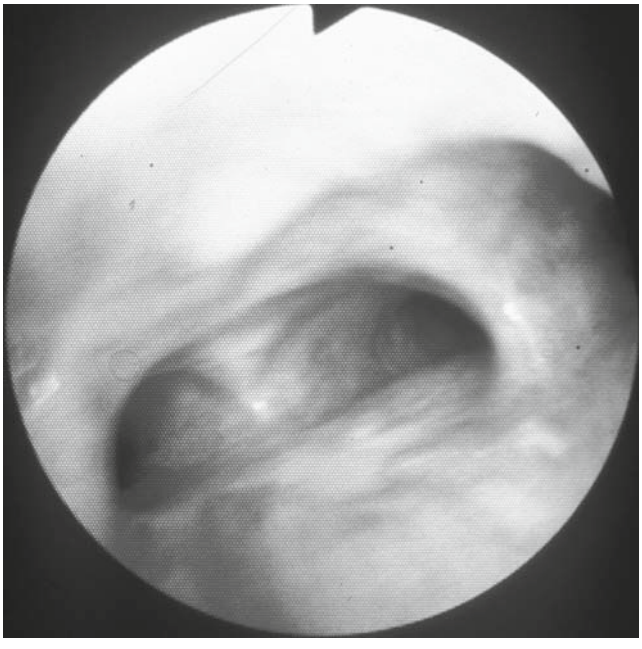

Fig. 3 Bronchoscopy 24 months after surgery showed double-barreled carinoplasty with smooth, patent bilateral orifices (case 3)

was found to be tumor cell-positive by pathological examination of the permanent specimen, 50 Gy radiotherapy was administered postoperatively. This patient is now alive, 144 months after surgery.

Case 4 was a 37-year-old woman with an ACC arising from the right main bronchus. In this case, the tumor primarily affected the right main bronchus, obstructing its lumen almost completely. The hilar lymph nodes around the main bronchus and the subcarinal lymph nodes had become markedly swollen, indicating that the

tumor was the intraluminal and extraluminal invasion type. To resect the tumor en bloc, sleeve right pneumonectomy was carried out. The patient died of cancer (metastases to skin, mammary gland, and left lung) 15 months after surgery.

Case 5 was a 54-year-old woman with an ACC arising from the left main bronchus. The tumor had obstructed the left main bronchial lumen almost completely, making it impossible to advance the bronchoscope toward the periphery beyond the tumor-affected area. Left pneumonectomy was carried out. The tumor was found to have invaded the outside from inside the bronchial wall. When the permanent specimen was examined pathologically, tumor cells were detected in a part of the dissected area around the bronchus and at the surgical stump of the left main bronchus. Radiotherapy (50 Gy) was administered after surgery. The patient is alive at present, 10 months after surgery.

Discussion

Primary tumor of the upper airway is relatively rare. Its annual incidence is as low as ≤0.2 per 100 000 population. This tumor was detected in only one of 15 000 autopsied cases.[1] Squamous cell carcinoma is the most frequent type of tracheal tumor, and ACC is the second most frequent histological type of tracheal tumor. Regarding the sex-related difference in the incidence of this tumor, Clough and Clark[2] reported four males and nine females with ACC; Albers et al.[3] reported five males and nine females with ACC; and Prommegger et al.[4] reported nine males and seven females with ACC. Thus, there was no predominance of males in the incidence of ACC, unlike the other histological types of lung cancer. Also in the present study, all of the five patients with ACC were female.

It has been reported that because of its manner of progression ACC requires surgical resection more frequently than any other type of tracheal tumor.[5] Thus, ACC often develops in a relatively major airway between the trachea and the lobular bronchi. Because of this feature, combined with the recent advances in techniques of tracheobronchoplasty, surgical treatment has often been used when dealing with ACC, and the number of reports on surgically resected cases of ACC has been increasing.[1] However, there are limitations with extensive resection and subsequent reconstruction of the trachea. It is not rare that radical resection of the trachea and its reconstruction are difficult because the tumor has already spread extensively along the major axis of trachea at the time of diagnosis. A characteristic of ACC arising from the trachea is that even when the trachea is resected with upper and lower margins of 1 cm from the macroscopic or palpable tumor the surgical stump is sometimes tumor cell-positive. In such cases, postoperative radiotherapy seems indispensable. The report from the Toronto group[1] also showed that postoperative adjuvant radiotherapy favorably affected the survival rate. Because of such high radiosensitivity of ACCs, which can be deemed a biological characteristic of ACCs, Sayar et al.[6] thought that so far as ACC is concerned detection of tumor cells in the pathological examination of the surgical stump is not a significant issue clinically.

On the other hand, the Toronto group[1] and the Boston group[7] strongly insisted that when dealing with tracheobronchial ACC postoperative radiotherapy should be routinely performed irrespective of the presence/absence of tumor cells in the stump. This view is based on the experience with cases encountered by Grillo (one of the surgeons belonging to the Boston group)—patients in whom a local recurrence developed 18 years (at maximum) after surgery among the patients who had received no postoperative radiotherapy because of tumor cell-negative stumps. Following experience with these cases, Grillo and his colleagues began in 1984 to apply postoperative radiotherapy to all cases, with the goal of elevating the local control rate. To date, however, no concrete data showing the extent of elevation in local control rate following adoption of postoperative radiotherapy have yet been reported. Meanwhile, Regnard et al.[8] reported that analysis of 64 cases of ACC resulted in no significant difference in the long-term survival rate even when postoperative radiotherapy was applied to patients with a tumor cell-negative stump. Thus, it seems controversial to recommend postoperative radiotherapy for all patients with ACC undergoing resection.

The first choice of treatment for ACC is complete surgical resection of the tumor. However, we cannot ignore the fact that ACC is likely to grow along the major axis of the trachea and that tumor invasion beyond the resectable limit (more extensive than the preoperatively assessed extent of invasion) is often found intraoperatively. For these reasons, tracheobronchoplasty is often needed during surgical treatment of this tumor. Also among the cases presented in this article, operative procedures requiring high skill—e.g., resection of the tracheal carina and reconstruction with double-barreled carinoplasty (case 3) and sleeve right pneumonectomy (case 4)—were needed. This indicates that surgery for ACC should be performed by experienced chest surgeons.

Adenoid cystic carcinoma sometimes develops in the peripheral lung.[9] The relatively low incidence of ACC arising in peripheral lung is probably associated closely

with the distribution of glandular cells. Regarding the structure of bronchial glands, it is known that the fifth-order and subsequent bronchi assume the form of peripheral type, and their density of gland distribution decreases, with the density of the sixth-order bronchus being only 11.3% that of the proximal bronchi and the density of the seventh-order and subsequent bronchi being close to zero. This structural feature probably explains why ACC rarely develops in the peripheral lung. Complete resection can be often done easily for ACCs developing in the peripheral lung, without necessitating bronchoplasty. A good prognosis is therefore expected for this type of ACC. However, because some ACCs developing in the peripheral lung are large, have rapid tumor growth, or have a high potential for local invasion, careful follow-up is advisable.

Regarding chemotherapy for ACC, no particularly effective drug has been reported. However, because our case 4 patient showed distant metastases, we judged that chemotherapy is indispensable when dealing with advanced ACC and have been applying CDDP-based multidrug chemotherapy after surgery for ACC. Recently, Suemitsu et al.[10] reported cases of ACC of tracheal origin where postoperative tumor recurrence in mediastinal and hilar lymph nodes and tumor metastasis to lung were successfully treated with a combination of chemotherapy using uracil-tegafur (UFT) and cisplatin (CDDP) plus radiotherapy, resulting in long-term survival. This treatment regimen deserves to be tried from now on.

The ACCs of tracheobronchial origin are likely to result in a local recurrence or distant metastasis some time after the onset.[4] Therefore, evaluation as to the radicality of a given treatment for ACC should be based on long-term follow-up, and it seems rational to use the10-year survival rate rather than the 5-year survival rate for its evaluation. In other words, we may say that ACC is usually slow-growing, metastasizes rarely, and often grows extensively along the bronchial wall.

Conclusion

The ACC deserves to be called a "slow-growing tumor." Long-term survival can be often achieved by adding postoperative radiotherapy for patients with a tumor-positive stump. Many of these tumors require tracheobronchoplasty, and high-risk surgery (e.g., resection of the tracheal carina) is sometimes needed. Thus, a high level of skill is required for surgical treatment of ACC.

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