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Mucoepidermoid Carcinoma of the Lung

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Background: Mucoepidermoid carcinoma (MEC) of the lung is an uncommon tumor type, arising from minor salivary gland tissue of the tracheobronchial tree. The clinical behavior is varied. We analyzed nine cases of MEC to identify the clinical features and outcomes. Methods: The medical records of patients diagnosed with mucoepidermoid carcinomas of the lung from 1979 to 2006 were reviewed. **Results:** There were six men and three women aged 23-81 years in this series. The mean age at diagnosis was 45.9 years. Seven patients with low-grade tumors underwent surgery, with no mortality, and all were alive without evidence of recurrence at the time of this study. The other two patients with high-grade tumors received adjuvant therapy but their prognoses were poor: one died at 19.7 months after diagnosis and the other at 27 months. Conclusions: MECs of lung are more common in male patients. The prognostic factors included histological tumor grading and achievement of surgical intervention. Patients with low-grade tumors who underwent surgery had the best outcome. Adjuvant therapy was less effective for the patients with high-grade tumors.

Key words: mucoepidermoid carcinoma, lung cancer

INTRODUCTION

Mucoepidermoid carcinomas (MECs) of the tracheobronchial system were first reported in 1952 by Smetana et al.[1] and Liebow as a type of bronchial adenoma.[2] This tumor type originates in the bronchial submucosal gland. It can be divided into low-grade or high-grade variants by its growth characteristics and histological features.[3] Low-grade tumors tend to contain a higher proportion of mucous cells and high-grade tumors contain more squamous cells, mitoses and necrosis. However, low-grade MECs with high-grade biological behavior have been reported.[4] It is now defined as a malignant epithelial tumor constituting 0.1-0.2% of primary lung cancers.[5] Only a few cases of MEC of the lung have been reported from Taiwan. We analyzed the records of nine patients regarding their clinical features, treatment and outcomes.

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METHODS

From October 1979 to June 2006, nine patients were diagnosed with MEC of the lung in Tri-Service General Hospital, Taipei, Taiwan, and their records were analyzed. Data collected included age, gender, clinical presentation, radiographic, bronchoscopic and histopathology features, tumor location, staging, treatment methods and prognosis. Staging was based on the tumor, node and metastasis (TNM) classification of the revised international system for lung cancer. Each tumor was classified histologically as low-grade or high-grade by our pathology department according to mitotic activity and nuclear pleomorphism. (Fig. 1)

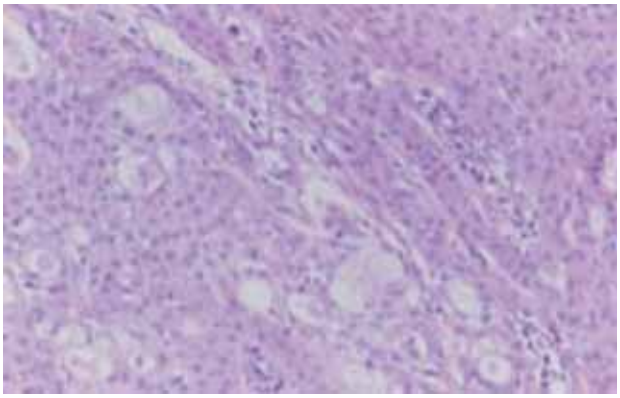

Fig. 1 Mucoepidermoid carcinoma, low grade by H&E stain with higher proportion of glandular cells.

Table 1 Patient profile

Patient	Gender	Age at diagnosis	Location	Symptoms	Operation/Treatment	Stage	Grade	Survival (months)	tumor size(cm)	Endobronchial lesion under bronchoscopy	Smoking
1	M	38	carina	cough, hemoptysis	carinal resection and reconstruction	T3N0M0	Low	352.1(alive)	1.5×1.2×1	+	N
2	F	46	RML	cough	sleeve lobectomy	T1N0M0	Low	278.9(alive)	1.5×1	+	N
3	M	57	RUL	cough	lobectomy	T2N0M0	Low	190.7(alive)	4.5×2.5×1.5	+	Y
4	F	66	LUL	cough	lobectomy	T1N0M0	Low	82.8(alive)	2×1.5×1	+	N
5	M	22	RML	cough	lobectomy	T1N0M0	Low	75.9(alive)	3×1.2×0.8	+	Y
6	M	81	RLL	abdominal fullness	target therapy	T3N2M1	High	27.1	5×2.5	+	N
7	F	56	RUL	chest pain, hemoptysis	chemotherapy	T4N3M1	High	19.7	8×5	-	N
8	M	24	RUL	hemoptysis	lobectomy	T2N0M0	Low	34(alive)	1.5×1.2×0.8	+	N
9	M	23	RLL	hemoptysis	wedge resection then lobectomy	T1N0M0	Low	27.3(alive)	2.5×1.6	-	N

M: male; F: female; RUL: right upper lobe; LUL: left upper lobe; RML: right middle lobe; RLL: right lower lobe; Y: yes; N: no

RESULTS

Clinical features

There were six men and three women in the series (Table 1). The mean age at diagnosis was 45.9 years (range 22-81). The presenting symptoms included productive cough, hemoptysis and fever. The chest radiographs were all abnormal. Masses and nodular lesions were recognized accompanied by atelectasis. One case of obstructive pneumonitis was seen. The tumor sizes ranged from 1.5 to 8.0 cm. Flexible bronchoscopic examinations were done for all patients. There were negative findings in two patients and five had endobronchial tumors. One patient had a mass lesion located in the right main bronchus and one other had a carinal lesion.

Treatment

Tumor staging was evaluated for each patient before planning any treatment. Three tumors were noted in the right upper lobe of the lung; two in the right lower lobe; two in the right middle lobe; one in the left lower lobe; and one in the carina. Two patients diagnosed with high-grade tumors had distant metastases (stage IV). Target therapy with gefitinib, shifting to erlotinib, was administered to one patient after a liver biopsy showed a metastatic mucoepidermoid carcinoma. The other patient with advanced disease had liver, brain and cervical lymph node metastases and received systemic chemotherapy with gemcitabine and pemetrexed. The other six patients with low-grade tumor underwent surgical intervention with lobectomy and dissection of mediastinal lymph nodes including one sleeve lobectomy (Fig. 2). The patient with a carinal tumor underwent carinal resection and reconstruction. All cut bronchial ends were negative for tumor tissues histologically. There were four cases of stage IA tumor, two cases of stage IB and one case of stage IIB among the patients with low-grade tumors.

Survival and prognosis

All patients with low-grade tumors were still alive without any disease recurrence when checked by regular clinical visits at the time of this study. One patient who received oral target therapy and hospice palliative care died 27 months after diagnosis. The other survived only 19.7 months despite multiple regimen chemotherapy.

DISCUSSION

The submucosa of the tracheobronchial tree contains mucous glands resembling salivary glands. MECs are the most common malignancy in salivary glands, and were first described by Stewart et al. in 1945.[6] On the other hand, MEC of the trachea and bronchi is quite rare, accounting for 1-5% of bronchial gland tumors and 0.1-0.2% of all lung tumors. It is seen in a broad age range including childhood but mostly in the fifth decades.[7] Yousem et al. reported a mean age of 34.8 years in 45 patients with low-grade MECs and a mean age of 44.5 years in 13 patients with high-grade MECs.[8] Yang et al. reported a mean age of 58.9 years in 11 patients.[9] The mean age in our study was 45.3 years, which could be related to the predominance of low-grade tumors.

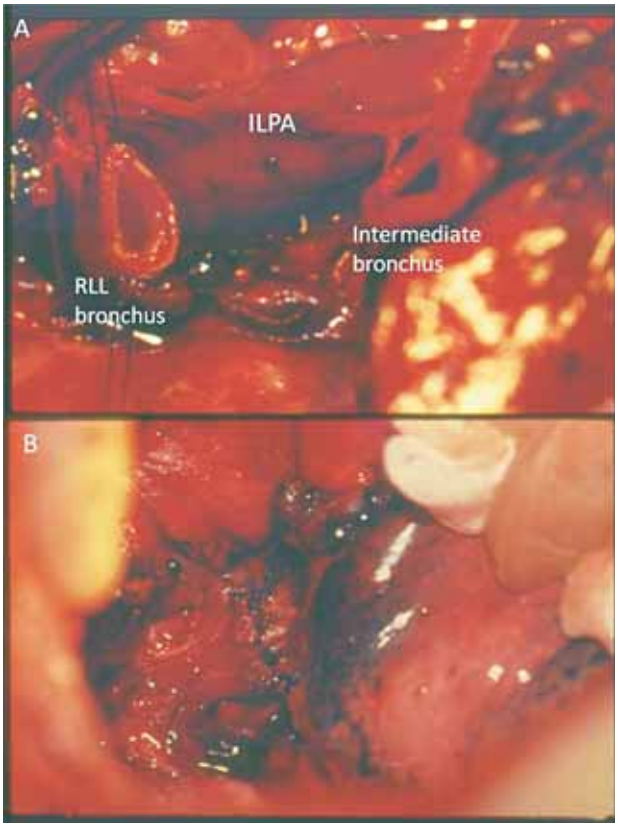

Fig. 2 (A): Demonstration of relationship of interlobar pulmonary artery (ILPA), intermediate bronchus and right lower lobe (RLL) bronchus after sleeve lobectomy of right middle lobe. (B): Anastomosis of intermediate bronchus and right lower lobe bronchus.

There were six male and three female patients in our series. Although some studies have reported a male predominance for this tumor type, most studies have failed to confirm this. All three patients with low-grade tumors younger than 30 years were female in the study of Yang et al.[9] On the contrary, all patients with low-grade tumor younger than 30 years were male in our study. The relationship between the age of the patient and gender is not clear for this tumor type and further larger studies are necessary. Only two patients smoked: as reported previously, a smoking habit is not associated closely with the risk of developing this tumor.[8,10]

The symptoms were mainly bronchial irritation and obstruction, which were identical in both low-grade and high-grade groups. In this series, coughing and hemoptysis were the most common symptoms, followed by recurrent pneumonia and fever. One patient who complained of a sensation of abdominal fullness was diagnosed as having a high-grade mucoepidermoid carcinoma with liver metastasis after ultrasound and computed tomography (CT) scans. This was confirmed by histopathology of a liver biopsy. The other patient with a high-grade tumor sustained chest pains, which may have been related to the bulky tumor and suspected chest wall invasion.

Radiographically, MECs usually present as a central mass with postobstructive pneumonia or peripheral atelectasis, or as a solitary pulmonary nodule or nodules in the tracheobronchial tree. The tumors are usually smoothly oval or lobulated on CT scans.[11] Mild to moderate enhancement after administration of contrast is typical, and punctate calcifications might be noted. Ishizumin et al. highly recommended high resolution CT with contrast enhancement. However, it could be difficult to distinct pulmonary carcinoids from MECs as they give similar findings in CT scans.[12]

Bronchoscopy is necessary for all patients with MECs of the lung because endobronchial lesions and symptoms of airway irritation or obstruction are common. Heitmiller et al. reported a 100% positive rate of bronchoscopy in 18 patients.[10] In our study, all patients underwent bronchoscopy: two were normal; four showed endobronchial lesions; one had a mass over the right main bronchus; and one had a carinal tumor. Near total occlusion of the right upper lobe bronchus with repeated obstructive pneumonitis was seen in one patient.

MECs of the trachea and bronchi are classified as low-grade or high-grade based on nuclear pleomorphism, mitotic activity and the presence or absence of necrosis. These tumors are composed of squamous, mucous and intermediate cell types with varying of proportions. Necrosis and mitoses with atypical activity are restricted to high-grade MECs. In this series, the histological grading was clearly associated with tumor staging and prognosis. All seven patients with low-grade MECs are still alive whereas the two patients with high-grade MECs died of multiple distant metastases with a mean survival of 23.4 months.

Surgical intervention is the treatment of choice for patients with MECs if they have no distant metastases or unresectable lesions. Low-grade tumors should be removed completely for the best therapeutic effect. Anatomical resection with lobectomy and mediastinal lymph node dissection is efficient and simple. Patients with central lesions might require more aggressive approaches, such as sleeve resection or pneumonectomy. In the report of Heitmiller,[10] only five out of 16 patients underwent lobectomies and the other 11 patients were treated with tracheal resection and reconstruction, bilobectomies, sleeve resections or pneumonectomy. Breyer et al. suggested

that to preserve pulmonary function better the surgeon should plan a conservative resection with bronchoplasty or sleeve resection for a localized tumor diagnosed as MEC.[13] Santambrogio et al. reported the first video-assisted sleeve lobectomy for MEC of the left lower lobar bronchus.[14] Sometimes the tumor originates at the carina and a complicated carinal resection with reconstruction might be needed.[15,16] Endoscopic resection is not recommended because of difficulty in control of hemorrhage and incomplete resection. Li et al. successfully managed two cases of MECs with bronchoscopic neodymium yttrium aluminum garnet (Nd-YAG) laser surgery.[17] Although such laser surgery is less invasive than surgical resection and preserves lung function, further long-term follow-up is needed for possible tumor recurrence.

Postoperative chemotherapy is not suggested for patients with low-grade MECs. Adjuvant chemotherapy or radiotherapy can be considered for patients with incomplete resection or advanced disease but there is no strong evidence about their roles. In the present study, two patients with distant metastases did not have surgery and underwent palliative target therapy or chemotherapy. They died at 19.7 and 27 months after diagnosis.

In conclusion, MEC of the lung is a rare type of malignancy that usually presents with obstructive symptoms. Early diagnosis can be accomplished if the clinician is alert to persistent pneumonia, coughing and tumor obstruction on image studies. Bronchoscopy is necessary for evaluating endobronchial lesions and confirming the diagnosis. Surgical removal is the treatment of choice for all low-grade tumors without distant metastases. A planned conservative resection is preferred if the diagnosis can be made before surgery. The roles of chemotherapy, radiotherapy and minimal invasive laser surgery are not yet clear. Histological grade, tumor staging and complete tumor resection are important prognostic indicators.

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