Asia-Pacific Journal of Clinical Oncology

Asia-Pacific Journal of Clinical Oncology 2016; 12: e105–e112 doi: 10.1111/ajco.12126

ORIGINAL ARTICLE

Lung cancer presenting as thin-walled cysts: An analysis of 15 cases and review of literature

Juntang GUO, Chaoyang LIANG, Yu'e SUN, Naikang ZHOU, Yang LIU and Xiangyang CHU

Department of Thoracic Surgery, Chinese PLA General Hospital, Beijing, China

Abstract

***Aim*:** Lung cancer presenting as cysts is a rare entity in clinical practice. Differential diagnosis is difficult in the benign-like cyst.

***Methods*:** We conducted a retrospective analysis of the clinical records of 15 patients who underwent surgery for primary lung cancer presenting as cysts (wall thickness <5 mm) in our department between 2007 and 2012. The whole group underwent postoperative follow-up.

***Results*:** The subjects' age ranged from 18 to 80 years with a median age of 58.3 years. Eight cases presented with respiratory symptoms while seven showed abnormal shadows on a chest computed tomography without symptoms. Histological analysis showed that 10 cases were of adenocarcinoma, two of squamous cell carcinoma and one of large cell carcinoma. Two patients died at 13 and 26 months and the remaining 13 patients are alive and disease free at 3–38 months.

***Conclusion*:** Cystic lung cancer should be considered in the differential diagnosis of focal benign cyst. Cystic lung cancer could achieve a good outcome if early diagnosis can be obtained.

Key words: Computed tomography, cystic, cyst, lung cancer.

INTRODUCTION

Cysts are commonly detected lesions in the lung on chest radiography and chest computed tomography (CT). Traditionally, the term "cyst" is used to describe an air-containing space surrounded by a relatively thin wall (less than 4 mm), and the term "cavity" is used to describe an air-containing space within a pulmonary consolidation with a relatively thick wall (more than 4 mm) or within a surrounding infiltrate or mass identified upon radiological examination.[1,2] In general, solitary cyst found on the lung have been considered as benign disease. Lung cancer presenting as cystic lesions was first described by Anderson and Pierce in 1954.[3] As an unusual type of lung cancer, lung cancer presenting as cyst was often misdiagnosed in clinical practice. We describe 15 patients with proven lung cancer showing as cysts. In this paper, we named this special type of lung cancer as cystic lung cancer.

METHODS

From March 2007 to December 2012, 3268 patients with primary lung cancer were admitted in the Department of Thoracic Surgery of the Chinese People's Liberation Army General Hospital. Of these, 15 patients with lung cancer presenting as cysts underwent surgical treatment. Their clinical data were selected and formed the basis for this review. Chest X-ray and CT scans were performed in every patient, and in four patients, ^{18}F-fluorodeoxyglucose positron emission tomography-CT scans were performed.

We defined a "pulmonary cyst" as a cavitary lesion with a wall thickness of 4 mm or less along at least 75%

Correspondence: Mr Xiangyang Chu MD, Department of thoracic surgery, Chinese PLA General Hospital, 28# Fuxing Street, Beijing, China. Email: drchu301@sohu.com

Conflict of interest: none

Accepted for publication 4 July 2013.

of the circumference of the lesion. Each patient's clinical course, pathological findings and surgical results were investigated.

Tumor-nodes-metastasis classification was based on the International Union Against Cancer 7th edition. The survival time was measured from the date of surgery to the date of the most recent follow-up examination.

RESULTS

The incidence of cystic lung cancer was 0.46% (15 of the 3268) of surgical cases. At same period, 306 patients with benign solitary pulmonary cysts underwent surgical operation in our department. "Malignant cyst" incidence was 4.6% (15 of the 321) of surgical cases. Our series included 12 males and three females with a mean age of 58.3 years (Table 1). Seven cases were asymptomatic and were discovered by chance, whereas eight had respiratory symptoms. Of these eight patients, six presented with a cough, four with hemoptysis and one with a fever. Additionally, only five of the patients had a history of being a heavy smoker. Only one patient in all had a history of bullae. Eight of 15 cases had a routine examination every year and no abnormal sign was found in past X-ray or CT except for the case with bullae.

Chest CT revealed solitary cysts with a diameter of 2 to 6 cm in 15 cases. A gradually growing cyst was observed on a CT scan in three cases before operation (Fig. 1). No abnormal increase in metabolism was detected on a PET-CT scan in the four patients. All 15 lesions were found on the periphery of the lung. There were four patients with emphysema coexistence in CT scans. The location of the tumor was in the right upper lobe in four patients, left upper lobe in three patients, right lower lobe in three, left lower lobe in four and right middle lobe in one patient respectively.

In all cases, nine patients underwent lobectomy and five patients underwent wedge resection. Pleural biopsy was performed in one patient with pleural metastasis. Nine patients had node-negative, stage I disease, but two patients had N1 disease, and two patients (13%) had N2 disease. N3 and M1a disease was confirmed in one patient each (Table 1).

In our series, adenocarcinoma ($n = 11$) including six invasive adenocarcinoma, three adenocarcinoma *in situ* (AIS) and two minimally invasive adenocarcinoma (MIA) was the major type of histology (Fig. 2). There were two squamous-cell carcinoma cases, one adenosquamous cell carcinoma and one large cell carcinoma in other four cases. There were two patients with synchronous multiple primary lung cancer. One have a large cell carcinoma in the right middle lobe displaying as a solid pattern and adenocarcinoma in the lower lobe presenting as a cyst. The other one have a cystic lesion in upper lobe and a solid one in lower lobe in left lung. In

Table 1 Clinical characteristics of the 15 patients with thin-walled cystic lung cancer

No.	Gender	Age	Location	Procedure	Stage	Histology	Diagnosis period (weeks)	SI	Survival (months)
1	M	51	RUL	lobectomy	IIA	LC	20	600	38 alive
2	F	34	RLL	biopsy	IIIB	ADC	24	0	13 dead
3	M	58	RLL	lobectomy	IIA	SCC	8	1200	29 alive
4	M	39	LLL	WR	IV	MIA	4	0	26 dead
5	M	70	RML	lobectomy	IA	AIS	1	0	26 alive
6	F	65	RUL	WR	IA	ADC	32	0	24 alive
7	M	60	LLL	lobectomy	IA	MIA	4	150	23 alive
8	M	77	RUL	lobectomy	IA	AIS	4	0	23 alive
9	M	69	LLL	WR	IIIA	AIS	8	0	22 alive
10	M	57	LUL	WR	IIIA	SCC	16	900	20 alive
11	M	69	RUL	WR	IA	ADC	2	0	20 alive
12	M	45	RML	lobectomy	IA	ADC	8	0	16 alive
13	M	51	LLL	lobectomy	IA	ADC	2	0	12 alive
14	F	58	LUL	lobectomy	IA	ADC	3	0	6 alive
15	M	72	LUL	lobectomy	IB	ASC	2	500	3 alive

ADC, adenocarcinoma; AIS, adenocarcinoma in situ; ASC, adenosquamous cell carcinoma; F, female; LC, large cell carcinoma; LLL, left lower lobe; LUL, left upper lobe; M, male; MIA, minimally invasive adenocarcinoma; RLL, right lower lobe; RML, right middle lobe; RUL, right upper lobe; SCC, squamous cell carcinoma; SI, smoking index; WR, wedge resection.
International Union Against Cancer (UICC) 7th edition was used for TNM classification.

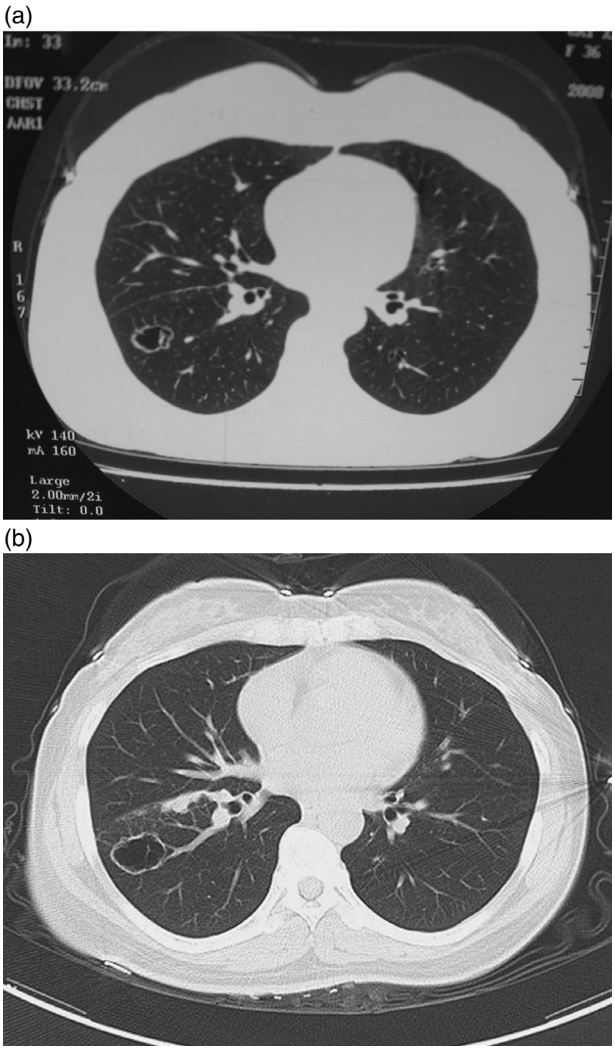

Figure 1 A 34-year-old woman, anti-TB therapy for 6 months. (a) Computed tomography (CT) revealed a thin-walled cystic lesion in right lower lobe. (b) CT was taken 6 months later. An enlarged thin-walled cystic lesion associated with interlobar pleural metastasis.

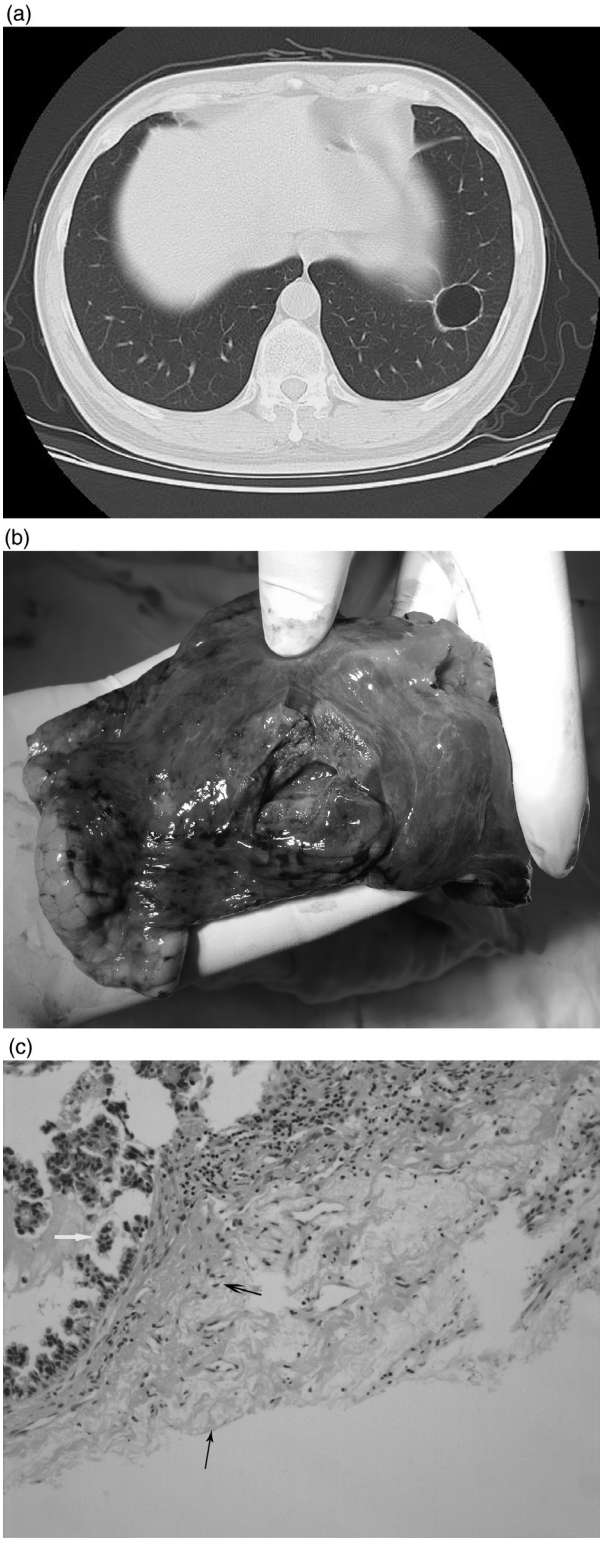

Figure 2 A 69-year-old male. (a) Computed tomography revealed a thin-walled cystic lesion in left lower lobe. (b) Gross specimen of cystic lesion. The inner surface of cyst was totally lined with thin tumor issue. (c) Cyst wall (small arrow) together with hyperplastic mucinous epithelium (large arrow) adjacent to the well differentiated mucinous bronchioloalveolar carcinoma (open arrow). (Hematoxylin and eosin, ×100.)

pathology, cystic lesion was invasive adenocarcinoma and solid one was AIS.

Epidermal growth factor receptor (EGFR) and Kirsten rat sarcoma viral oncogene homolog (KRAS) mutation

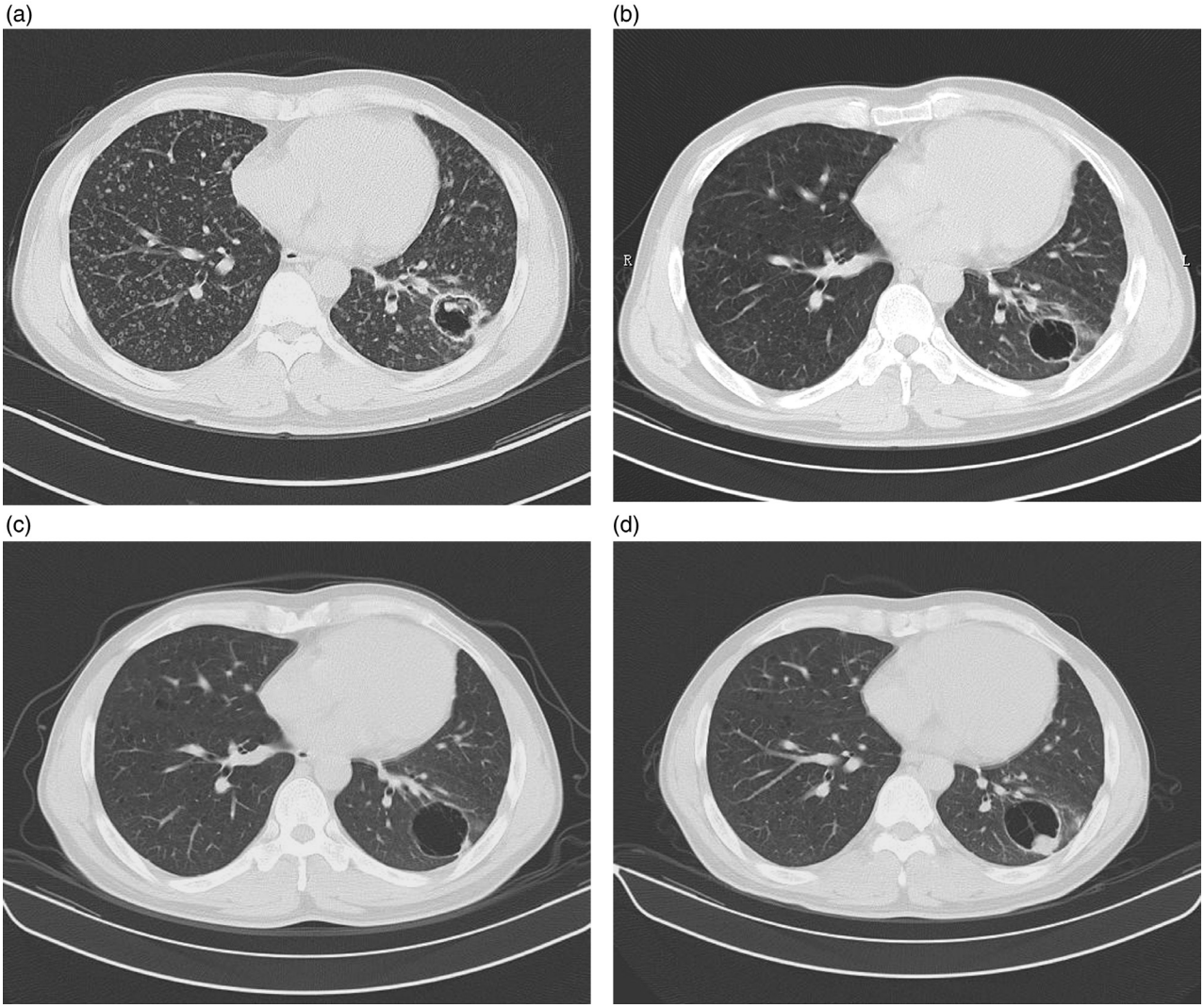

Figure 3 The four computed tomography (CT) pictures showed a variation of a thin-walled cystic lung cancer of left lower lobe. (a) CT revealed a thin-walled cystic lesion in left lower lobe with intrapulmonary metastasis in bilateral lung. (b) After taking EGFR-TKI treatment for 2 months, intrapulmonary metastasis disappeared and wall of cyst became smooth and regular. (c) CT scan after EGFR-TKI treatment was administered for 6 months. (d) Tumor progressing after target therapy was stopped for 7 months.

were detected in eight cases. The outcome showed three patients have an EGFR mutation affecting exons 19($n = 2$ deletion) and 21($n = 1$ L858R) mutation. There was no KRAS mutation in all eight patients. One patient was detected with exons 19 deletion initially, and after 18 months, administered EGFR-TKI treatment T790M mutation in 20 exons developed.

The observation period before diagnosis of lung cancer was from 1 week to 32 weeks (median period of 9 weeks). Four patients were misdiagnosed as tuberculosis and one as fungus before operation. Of the six patients with advanced stage tumor, four patients underwent chemotherapy and one was treated with chemotherapy combined with radiotherapy. The other patient of IV stage opted for take EGFR-TKI treatment. He received six cycles chemotherapy when acquired drug resistance happened after taking EGFR-TKI for 18 months (Fig. 3).

The median follow-up period was 19.8 months. Except for one with IIIB stage and one with IV stage, 13 patients were alive and there were no evidence of recurrence. The patient with adenocarcinoma of IIIB stage

Table 2 Summary of literature about thin-walled cystic lung cancer

NO	Author	Year	Number of cases	Age	Sex	Histology	Therapy	Stage
1	Singh[6]	2012	1	45	M	SCC	Chem	cIIIB
2	Goto[7]	2011	1	60	M	ADC	Lob	pT2aN0M0
3	Lan[8]	2010	1	27	F	ADC	Chem+RT	pT2N3M0
4	Kondo[9]	2010	1	60	F	ADC	Chem	cIV
5	Matsuoka[10]	2010	1	79	F	ADC	Lob	pT1N0M0
6	Iwata[11]	2009	1	68	M	SCC	Lob	pT2N2M0
7	Sugimoto[12]	2007	8					
8	Tanaka[13]	2006	1	45	M	ADC	Chem	cT4N3M1
				62	M	ADC	Lob	pT2N2M1
				84	M	ADC	WR	cT3N2M0
				78	M	ADC	WR	cT3N2M0
				78	F	ADC	Lob	pT1N0M0
				81	M	SCC	Lob	pT1N0M0
				72	M	SCC	Lob	pT1N0M0
				79	M	ASC	Lob	pT2N0M0
				71	M	LC	Lob	pT1N0M0
9	Jakopovic[14]	2005	1	40	F	LC	Lob	pT2N0M0
10	Kobashi[15]	2005	1			ASC	Lob	pT2N2M0
11	Prichard[16]	1984	2					
				30	F	BAC	Lob;	IB
						BAC	pneumonectomy	IIB

ADC, adenocarcinoma; ASC, adenoaquamous cell carcinoma; BAC, bronchoalveolar carcinoma; Chem, chemotherapy; LC, large cell carcinoma; Lob, lobectomy; RT, radiotherapy; SCC, squamous cell carcinoma; WR, wedge resection.

cannot tolerant the side effect after taken Erlotinib for 1 month. She underwent eight cycles chemotherapy. But the cancer progressed and she succumbed to brain metastasis within 13 months of operation. The patient with adenocarcinoma of IV stage mentioned above who underwent EGFR-TKI treatment, chemotherapy and brain radiotherapy died with intrapulmonary and brain metastasis at 26 months after surgery.

DISCUSSION

The terms *cyst*, *cystic airspace* and *cavity* have overlapping meanings and are sometimes used interchangeably. In this paper, the term *cyst* is used to mean a clearly defined air-containing space surrounded by a relatively thin (≤4 mm) wall. In contrast, the term *cavity* is used to refer to an air-containing lesion with a relatively thick (>4 mm) wall or within an area of a surrounding infiltrate or mass.

Generally, a solitary cystic lesion in the lung was considered benign. Malignant disease shows a significantly higher incidence rate of thick cavitary walls compared with benign lesions.[4] Woodring *et al*. reported that the thickness of the thickest part of the cavity wall could be used to differentiate between benign and malignancy of pulmonary cavitary lesions among their 65 patients.[5] In their study, all of the cavities with a wall thickness of 1 mm or less in the thickest part were benign; among lesions whose thickest measurement was 2–4 mm, 14% were malignant; among lesions whose thickest measurement was 5–15 mm, 49% were malignant; and among lesions whose thickest measurement was more than 15 mm, 95% were malignant neoplasms. Our study revealed the malignant incidence of 4.6% among the surgical cases of focal pulmonary cysts, which include bulla, congenital cystic lesions, tuberculosis and pulmonary fungi disease. Except for lung cancer, mucinous adenocarcinoma, cystic metastasis of sarcoma and some pulmonary metastatic tumors also have appearance of cysts in lung.[1] Our report does not include these diseases.

Lung cancer presenting as cysts was first reported by Anderson and Pierce in 1954.[3] Several cases of malignant neoplasms with pulmonary thin-walled cavity have been reported in past two decades[6–16] (Table 2), most of which came from Asian countries. The mean age of 19 cases reported in these literatures was 62.3 years, including 13 males and six females, which is similar with our

series. Sugimoto reported eight cases of primary lung cancer which showed a thin-walled cavity on a chest X-ray and CT in 2007 in Japanese, which is the largest group of a resembling report so far.[12] In this study, we collected 15 cases with lung cancer presenting as cysts. We defined lung cancer of this type as cystic lung cancer.

Like solid tumor, cystic lung cancer presents bronchopulmonary symptoms. Some patients are asymptomatic and cysts were observed by chest X-ray or CT by chance. The average observation period before diagnosis was 9.2 weeks in this series. Anti-tuberculosis drugs were often taken several months before obtaining definite diagnosis. This suggests that the diagnosis of cystic lung cancer is difficult on the account of their atypical features. Therefore, more attention should be paid to this unusual type of lung cancer in daily clinical practice.

It is difficult to differentiate a malignant cyst from a benign lesion. High-resolution CT still is the mainstay of diagnosis in cystic lung cancer. When encountering with a new cystic lesion in lung without an emphysema and bullae history, we should raise the suspicion of malignancy. Close follow-up should be proposed for patient. Farooqi indicated that the finding of an isolated cystic airspace with increased wall thickness suggest the possibility of lung cancer at annual repeat CT screening.[17] If a cyst shows malignant features on an image, such as wall irregularity, notching, inhomogeneous thickening of the wall and an enlargement, it is necessary to perform surgical intervention. PET seems having no help for diagnosis in cystic lung cancer.

Ordinary percutaneous needle biopsy and transbronchial biopsy rarely get sufficient diagnostic specimen in cystic lung cancer because of the thin walls. Moreover, puncture might result in rupture of tumor and pneumothorax. Sputum cytology examination has a poor sensitivity because most cystic lung cancers are peripheral. Nakahara *et al*. performed a CT-guided percutaneous needle washing (PNW) technique in 27 pulmonary thin-walled cavitary lesions.[18] The diagnostic sensitivity of PNW for malignant diseases was 91%. PNW may be a good alternative diagnostic technique for pulmonary thin-walled cavitary lesions when a diagnosis cannot be established by other techniques.

Traditionally, squamous cell carcinoma was believed to have a tendency to form thin-walled cavities.[19] All five cases in the Anderson and Pierce series were squamous cell carcinoma in histology.[3] However, an increasing number of such cavities have recently been reported among patients with pulmonary adenocarcinoma, especially with bronchoalveolar carcinoma (BAC, named as AIS in new classification). In our group, adenocarcinoma including AIS (formerly named as BAC) and MIA was the major histology type. Eleven cases were proved to be adenocarcinoma among 19 patients reported in last two decades including Sugimoto's group.[6–16] The other were four cases of squamous cell carcinoma, two of large cell carcinoma and two of adenosquamous cell carcinoma in histology. Cavitation has been reported in up to 7% of patients with AIS, but cysts are rare in AIS.[20,21]

Several mechanisms of pulmonary cavity formation have been proposed:[6,11,16,19,22] (i) A check valve mechanism induced by the narrowed airway; (ii) central breakdown of solid lesions due to necrosis, detachment, abscess formation, enzymatic digestion or thrombus followed by expectoration of the debris into the bronchial tree; (iii) extending cavitation and thinning of the wall by elastic extraction of surrounding pulmonary tissue; or (iv) invasion of the disease on the wall of a preexisting cystic structure such as a bronchogenic cyst or bulla. Check valve mechanisms are believed to be the possible causes in most cyst formation.[6,11,23] But no sufficient evidence in pathological changes supported this hypothesis in our data.

Lung cancer arising from bronchogenic cysts or bullae has been reported in several literatures.[24–26] Incidence of bulla associated lung carcinoma was about 3.5%. But Sabloff *et al*. reported that the relative risk of lung cancer in subjects with bullous disease was approximately 32 times higher than in those without bullous disease.[27] The possible carcinogenic mechanism remains uncertain, but scar cancers have been proposed by several authors.[28] In this series, only one case had an identified history of bullae. Heavy smoking might cause emphysematous changes and reduce the strength of surrounding tissues which might promote cyst formation.[19] The three cases in this study with a history of heavy smoking were shown to be non-adenocarcinoma. Patients with pulmonary bullae should have annual chest radiographs or CT to screen for the potential development of lung cancer in or close to the bullous disease.

There are also a few reports on congenital cystic adenomatoid malformation (CCAM) complicated by lung cancer.[29–33] By our knowledge, there are 12 cases of CCAM associated with lung cancer in English literatures. Most of them are young except for 1-year-old patient. The mechanism of lung carcinogenesis in CCAM has not been defined clearly. Cass *et al*.[34] reported increased cell proliferation and decreased apoptosis in the lungs of CCAM patients. Thoracic surgeons have to keep this rare combination of CCAM and malignancy in mind.

Most asymptomatic cysts in the lung do not need surgical treatment. Surgical removal of lung cysts has been recommended in some "potential hazard cysts" because of the high incidence of complications in the form of infection, hemorrhage and rupture producing pneumothorax. The potential hazard cysts should concern the presentation of cystic bronchogenic carcinomas, apparently innocuous cysts. We believe that the cases presented here offer further evidence of the need for early surgery for lung cysts because of the risk of associated carcinoma. The surgery procedure of cystic lung cancer is similar as common lung cancer.

Unlike cavitary lung cancer, patients with cystic lung cancer in this group had a relatively good prognosis. The principal explanation for this is that the mechanism of formation for these two types of cancer is different. Vascular invasion and metastases are more common in cavitary carcinomas than in non-necrotic, non-cavitating or necrotic, non-cavitating primary bronchial carcinomas.[19] However, most cystic lung cancers develop by a check valve mechanism. Secondly, stage of TNM in this group is relative early and eight cases were stage IA. Thirdly, five tumors in 15 cases proved to be AIS and MIA by new classification of lung adenocarcinoma by International Association for the Study of Lung Cancer/American Thoracic Society/European Respiratory Society,[35] which commonly has a good outcome. Another possible reason is that we are cautious when patients present with new cystic lesions in the lung without emphysema and follow-up CT scans are taken every 3 months. For patients that are less than 60 years of age with growing cysts or newly arising cysts, surgical treatment is recommended as soon as possible.

Cystic lung cancer is a rare entity. This atypical presentation of lung cancer should be kept in mind during differential diagnosis. Cystic lung cancer could achieve a good outcome if early diagnosis can be obtained.

REFERENCES

1 Ryu JH, Swensen SJ. Cystic and cavitary lung diseases: focal and diffuse. *Mayo Clin Proc* 2003; **78**: 744–52.
2 Vourtsi A, Gouliamos A, Moulopoulos L *et al*. CT appearance of solitary and multiple cystic and cavitary lung lesions. *Eur Radiol* 2001; **11**: 612–22.
3 Anderson HJ, Pierce JW. Carcinoma of the bronchus presenting as thin-walled cysts. *Thorax* 1954; **9**: 100–5.
4 Wigh R, Gilmore FR. Solitary pulmonary necrosis: a comparison of neoplastic and inflammatory conditions. *Radiology* 1951; **56**: 708–17.
5 Woodring JH, Fried AM, Chuang VP. Solitary cavities of the lung: diagnostic implications of cavity wall thickness. *AJR Am J Roentgenol* 1980; **135**: 1269–171.
6 Singh N, Bal A. Lung cyst caused by centrally located bronchogenic carcinoma. *Arch Bronconeumol* 2012; **48**: 99–101.
7 Goto T, Maeshima A, Oyamada Y, Kato R. Cavitary lung cancer lined with normal bronchial epithelium and cancer cells. *J Cancer* 2011; **2**: 503–6.
8 Lan CC, Wu HC, Lee CH, Wu YK. Lung cancer with unusual presentation as a thin-walled cyst in a young nonsmoker. *J Thorac Oncol* 2010; **5**: 1481–82.
9 Kondo T. Lung adenocarcinoma with giant cyst formation showing a variety of histologic patterns: a case report. *J Med Case Rep* 2010; **4**: 377.
10 Matsuoka T, Fukamitsu G, Onoda M, Uesugi N, Kawano K, Katou T. Synchronous multiple lung cancer including a lesion with a thin-walled cavity; report of a case. *Jap J Thorac Surg* 2010; **63**: 164–67.
11 Iwata T, Nishiyama N, Nagano K *et al*. Squamous cell carcinoma presenting as a solitary growing cyst in lung: a diagnostic pitfall in daily clinical practice. *Ann Thorac Cardiovasc Surg* 2009; **15**: 174–77.
12 Sugimoto Y, Semba H, Fujii S, Furukawa E, Kurano R. [Clinical analysis of primary lung cancer with a thin-walled cavity to explain the mechanism of thin-walled cavity formation.] *Nihon Kokyuki Gakkai Zasshi* 2007; **45**: 460–64. (In Japanese.)
13 Tanaka K, Tsuboi M, Kato H. Large cell neuroendocrine carcinoma of the lung with a cystic appearance on computed tomography. *Jpn J Thorac Cardiovasc Surg* 2006; **54**: 174–77.
14 Jakopovic M, Slobodnjak Z, Krizanac S, Samarzija M. Large cell carcinoma arising in bronchogenic cyst. *J Thorac Cardiovasc Surg* 2005; **130**: 610–12.
15 Kobashi Y, Mouri K, Fukuda M *et al*. [A case of pulmonary adenosquamous cell carcinoma with thin-wall cavities.] *Nihon Kokyuki Gakkai Zasshi* 2005; **43** (1): 59–62. (In Japanese.)
16 Prichard MG, Brown PJ, Sterrett GF. Bronchioloalveolar carcinoma arising in longstanding lung cysts. *Thorax* 1984; **39**: 545–49.
17 Farooqi AO, Cham M, Zhang L *et al*. Lung cancer associated with cystic airspaces. *AJR Am J Roentgenol* 2012; **199**: 781–6.
18 Nakahara Y, Mochiduki Y, Miyamoto Y. Percutaneous needle washing for the diagnosis of pulmonary thin-walled cavitary lesions filled with air. *Intern Med* 2007; **46**: 1089–94.
19 Chaudhuri MR. Primary pulmonary cavitating carcinomas. *Thorax* 1973; **28**: 354–66.
20 Strollo DC, Rosado-de-Christenson ML, Franks TJ. Reclassification of cystic bronchioloalveolar carcinomas to adenocarcinomas based on the revised World Health

Organization Classification of Lung and Pleural Tumours. *J Thorac Imaging* 2003; **2**: 59–66.
21 Greco RJ, Steiner RM, Goldman S, Cotler H, Patchefsky A, Cohn HE. Bronchoalveolar cell carcinoma of the lung. *Ann Thorac Surg* 1986; **41**: 652–56.
22 Kim TS, Koh WJ, Han J *et al*. Hypothesis on the evolution of cavitary lesions in nontuberculous mycobacterial pulmonary infection: thin-section CT and histopathologic correlation. *AJR Am J Roentgenol* 2005; **184**: 1247–52.
23 Ohi S, Matsushita K, Tanioka F, Neyatani H, Suzuki K, Kazui T. Lung cancer with a cystic lesion formed by the check-valve mechanism. *Kyobu Geka* 2006; **59**: 1099–102.
24 Hirai S, Hamanaka Y, Mitsui N, Morifuji K, Sutoh M. Primary lung cancer arising from the wall of a giant bulla. *Ann Thorac Cardiovasc Surg* 2005; **11**: 109–13.
25 Kaneda M, Tarukawa T, Watanabe F, Adachi K, Sakai T, Nakabayashi H. Clinical features of primary lung cancer adjoining pulmonary bulla. *Interact Cardiovasc Thorac Surg* 2010; **10**: 940–44.
26 Endo C, Imai T, Nakagawa H, Ebina A, Kaimori M. Bronchioloalveolar carcinoma arising in a bronchogenic cyst. *Ann Thorac Surg* 2000; **69**: 933–35.
27 Stoloff IL, Kanofsky P, Magilner L. The risk of lung cancer in males with bullous disease of the lung. *Arch Environ Health* 1971; **22**: 163–67.
28 Ogawa D, Shiota Y, Marukawa M *et al*. Lung cancer associated with pulmonary bulla. Case report and review of literature. *Respiration* 1999; **66**: 555–58.
29 Benouaich V, Marcheix B, Begueret H, Brouchet L, Velly JF, Jougon J. Malignancy of congenital cystic adenomatoid malformation of lung in aged. *Asian Cardiovasc Thorac Ann* 2009; **17**: 634–36.
30 West D, Nicholson AG, Colquhoun I, Polluck J. Bronchioloalveolar carcinoma in congenital cystic adenomatoid malformation of lung. *Ann Thorac Surg* 2007; **83**: 687–89.
31 Sudou M, Sugi K, Murakami T. Bronchioloalveolar carcinoma arising from a congenital cystic adenomatoid malformation in an adolescent: the first case report from the Orient. *J Thorac Cardiovasc Surg* 2003; **126**: 902–3.
32 Papagiannopoulos K, Hughes S, Nicholson AG, Goldstraw P. Cystic lung lesions in the pediatric and adult population: surgical experience at the Brompton Hospital. *Ann Thorac Surg* 2002; **73**: 1594–98.
33 de Perrot M, Pache JC, Spiliopoulos A. Carcinoma arising in congenital lung cysts. *Thorac Cardiovasc Surg* 2001; **49**: 184–85.
34 Cass DL, Quinn TM, Yang EY *et al*. Increased cell proliferation and decreased apoptosis characterize congenital cystic adenomatoid malformation of the lung. *J Pediatr Surg* 1998; **33**: 1043–47.
35 William DT, Elisabeth B, Masayuki N *et al*. International Association for the Study of Lung Cancer/American Thoracic Society/European Respiratory Society international multidisciplinary classification of lung adenocarcinoma. *J Thorac Oncol* 2011; **6**: 244–85.

