

## Primary Lung Cancer Arising from the Wall of a Giant Bulla

Shinji Hirai, MD, Yoshiharu Hamanaka, MD, Norimasa Mitsui, MD,  
Kiyohiko Morifuji, MD, and Miwa Sutoh, MD

We report a 58-year-old man who underwent surgical treatment of primary lung cancer arising from the wall of a giant bulla. Chest roentgenography and computed tomography revealed multiple emphysematous bullae in the bilateral upper lobes, and a right upper giant bulla with a mass measuring 6 cm arising on the bulla wall. Right upper lobectomy was performed, the postoperative pathological diagnosis was large cell carcinoma arising from the wall of a giant bulla. Although the postoperative course was uneventful and he was discharged, he underwent partial resection of the jejunum for recurrence of carcinoma in the jejunum, and postoperative chemotherapy, and he was alive 20 months after that operation. In general, patients with both pulmonary bullous disease and primary lung cancer have a very poor prognosis, because they receive treatment when the tumor is at an advanced stage. On the basis of our review of the literature, we recommend that middle-age male patients with a giant bulla who smoke should have annual chest roentgenography and/or chest computed tomography to screen for lung cancer arising in or close to the bullous disease, and that a giant bulla should be resected in patients older than 50 years because of the high incidence of coexisting cancer and bulla, to improve the prognosis of this disease. (*Ann Thorac Cardiovasc Surg* 2005; 11: 109–13)

**Key words:** lung cancer, giant bulla

### Introduction

It is well known that lung cancers are often associated with emphysematous bullae, such as giant bulla. However, they are often difficult to diagnose because of their uncertain appearance, so the majority of patients receive treatment when the tumor is at an advanced stage, and hence the prognosis is very poor. We report a surgical treatment case of primary lung cancer arising from the wall of a giant bulla and discuss it based on a review of other cases in the Japanese literature.

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*From Department of Thoracic and Cardiovascular Surgery, Hiroshima Prefectural Hospital, Hiroshima, Japan*

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Address reprint requests to Shinji Hirai, MD: Department of Thoracic and Cardiovascular Surgery, Hiroshima Prefectural Hospital, 1-5-54 Ujinakanda, Minami-ku, Hiroshima 734-8530, Japan.

### Case Report

A 58-year-old man, complaining of chronic cough and slight fever elevation, was admitted to our hospital with an abnormal shadow on the chest X-ray film at his routine annual examination. He had smoked 30 cigarettes per day for 38 years. Routine blood examination showed an elevation of CRP of 13.1 mg/dl, and the tumor markers of CEA, SCC, SLX, and NSE were all within normal range. Chest roentgenography revealed a tumor lesion of the nodular opacity type with a right upper giant bulla (Fig. 1), and computed tomography revealed multiple emphysematous bullae in the bilateral upper lobes and a right upper giant bulla with a mass measuring 6 cm arising on the bulla wall (Fig. 2). Large cell carcinoma or sarcoma was suspected through transbronchial brushing cytology, but a definitive diagnosis could not be made before the surgery. Although the tumor was very large (60×55 mm), operation was selected because there were no distant

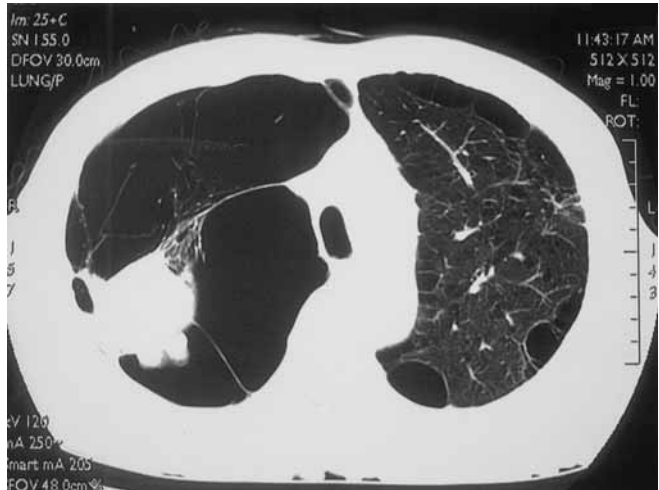


**Fig. 1.** Chest roentgenography revealed a tumor lesion of the nodular opacity type, with a right upper giant bulla.

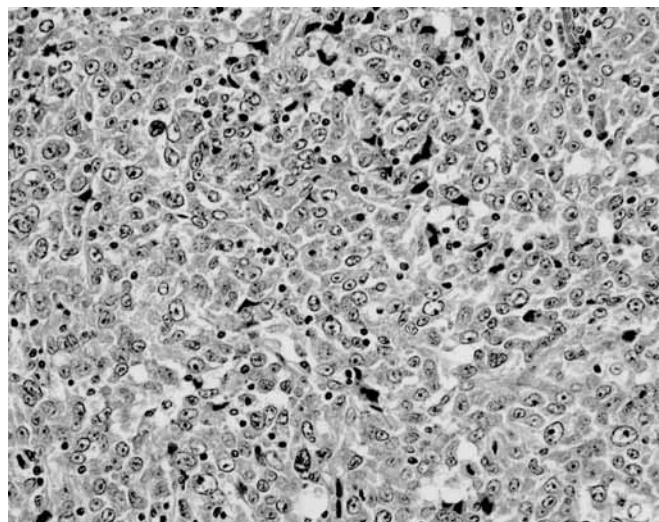
metastases in the preoperative findings. Right upper lobectomy was performed based on the intraoperative histological diagnosis. The postoperative pathological diagnosis was large cell carcinoma arising from the wall of a giant bulla (Fig. 3), and the tumor stage proved to be pT4N0M0 (stage IIIB) due to multiple metastasis lesions in the same upper lobe. The postoperative course was uneventful and the patient was discharged. However, he developed a recurrence of carcinoma in the jejunum with ileus at 37 days after the operation. He underwent partial resection of the jejunum and received carboplatin (600 mg), docetaxel hydrate (100 mg × 3 times), gemcitabine hydrochloride (1400 mg), and vinorelbine ditartrate (30 mg) administration as postoperative chemotherapy at our hospital, and he was alive 20 months after that operation.

## Discussion

It is well known that the incident of lung carcinoma in association with bullous disease is high. The first report of lung cancer associated with bullous disease was in



**Fig. 2.** Computed tomography revealed multiple emphysematous bullae in the bilateral upper lobes and a right upper giant bulla with a mass measuring 6 cm arising on the bulla wall.



**Fig. 3.** The histological examination showed large cell carcinoma.

1951.<sup>1)</sup> Goldstein MJ et al.<sup>2)</sup> reported that 18 (3.8%) of 411 patients with bronchogenic carcinoma had associated bullous disease, and all cases were male smokers. Stoloff IL et al.<sup>3)</sup> also reported that the relative risk of lung cancer in patients with bullous disease was 32 times that of patients without bullous disease.

To our knowledge, 34 cases of lung cancer associated with giant bullae have been reported in Japan since 1980 including our case, as shown in Table 1.<sup>4-21)</sup> The mean age of the patients was 52.7±9.9 yr, with an age range of 35 to 79 yr. All patients were males (100%), and most patients were heavy smokers with a smoking index range

**Table 1. Reported cases of primary lung cancer arising from a bulla wall in Japan since 1980**

Reporter	(year)	Age/Sex	Detection of bulla (Interval)	Diagnosis	Histology	Therapy	Stage	Outcome
1) Shirakusa	(1980)	57/M	RUL (0)	surgery	La	Seg	–	11m death
2) Urayama	(1981)	48/M	LUL (0)	MS	SCC	Lob+C+R	IIIB	8m death
3) Urayama	(1981)	39/M	RUL (0)	surgery	Ad-SCC	Lob+C+R	IIIA	2m death
4) Urayama	(1981)	53/M	RUL (1y3m)	surgery	Ad	Lob+C+R	IIIA	2m death
5) Miyata	(1981)	44/M	LUL (0)	surgery	SCC	Bul→Lob+C	IIIA	4m alive
6) Harada	(1982)	53/M	RUL (1y9m)	surgery	Ad	Lob+C	–	3m alive
7) Nishiki	(1984)	61/M	LUL+LLL+RUL (2y)	TBB	SCC	C+R	–	1y8m alive
8) Nishiki	(1984)	49/M	LUL (0)	TBB	SCC	Lob	I	3y8m alive
9) Nishiki	(1984)	49/M	RUL (3y)	TBB	SCC	Lob with CW	IIIA	4m death
10) Nishiki	(1984)	52/M	RML (1y8m)	TBB	La	Bul→Seg	–	4m death
11) Aoki	(1987)	44/M	RUL (0)	surgery	La	Lob	I	6.5m death
12) Nagai	(1989)	36/M	RUL (0)	NB	Sm	C	–	11m death
13) Nakahara	(1989)	60/M	RUL (1y)	surgery	La	Bul→Lob+C	IB	5m death
14) Yamamoto	(1990)	45/M	RUL (0)	NB	Ad	Lob with CW	IIIA	8m alive
15) Nakamura	(1994)	65/M	LUL (0)	TBB	Sm	C	IIIB	6m alive
16) Nakamura	(1994)	79/M	RLL (0)	TBB	Ad	C	IV	3m death
17) Nakamura	(1994)	69/M	RUL (0)	TBB	SCC	Lob	II	3m alive
18) Nakamura	(1994)	56/M	RUL (0)	TBB	La	Lob	IIIB	4m death
19) Nakamura	(1994)	69/M	RUL (0)	unknown	Ad	C	IV	1m death
20) Nakamura	(1994)	35/M	RUL (0)	unknown	La	Lob	I	1y death
21) Sakamaki	(1995)	64/M	RUL (7m)	surgery	La	Lob	IA	2y alive
22) Tetsuka	(1997)	57/M	RUL (1y5m)	surgery	Ad	Lob+C	IIIA	4m alive
23) Sato	(1998)	55/M	RUL (unknown)	surgery	La	Lob	I	6y6m death
24) Sato	(1998)	59/M	RUL (6y)	surgery	La	Lob	I	8y10m alive
25) Sato	(1998)	39/M	RUL (0)	TBB	La	Lob	IV	1y10m death
26) Sato	(1998)	44/M	RUL (9y)	TBB	La	Lob	I	6y11m alive
27) Sato	(1998)	53/M	LUL (3y)	TBB	Ad	Lob	IIIA	3y3m death
28) Hiranuma	(2000)	54/M	RUL (0)	surgery	Ad	Seg with P	–	1m alive
29) Okada	(2002)	53/M	LUL (0)	surgery	Ad	Bul→Lob+C	IA	11m alive
30) Okada	(2002)	40/M	RUL (5y)	surgery	Ad	Bul→Lob+C	IA	1y8m alive
31) Tanigawa	(2003)	47/M	LUL (0)	surgery	Cs	Par+C+R	–	3m death
32) Nakamura	(2003)	57/M	RUL (0)	surgery	Ad	pneumo	–	2.5m death
33) Mizuguchi	(2004)	51/M	BUL (1y)	surgery	La (rt) Ad (Lt)	Lob with CW (rt) Bul→Seg+R (lt)	IIIB IB	3y alive
34) Hirai	(2004)	57/M	LUL (0)	surgery	La	Lob+C	IIIB	1y8m alive

y: year, rt: right, m: month, Lt: left, RUL: right upper lobe, LUL: left upper lobe, RML: right middle lobe, LLL: light lower lobe, BUL: bilateral upper lobe, MS: mediascopic lung biopsy, TBB: transbrochial biopsy, NB: transpercutaneous needle aspiration biopsy, La: large cell carcinoma, Sm: small cell carcinoma, Par: partial resection, SCC: squamous cell carcinoma, Ad: adenocarcinoma, pneumo: pneumonectomy, C: chemotherapy, P: pleural resection, CW: chest wall resection, Ad-SCC: adenosquamous cell carcinoma, Lob: lobectomy, Bul: bullectomy, Seg: segmentectomy, CS: carcinosarcoma

of 440 to 1600. This suggests that middle-age male patients with bullous disease who smoke have an increased risk of lung cancer. The location of the tumor was in the right upper lobe in 23 patients (68%), in the left upper lobe in seven patients (21%), in the bilateral upper lobes in two patients, in the right middle lobe in one patient, and in the right lower lobe in one patient. This distribution is considered dependent on the finding that most patients have bullous disease in the upper lobe. The method of diagnosis was surgery in 18 cases (53%), transbrochial biopsy (TBB) in 11 cases, transpercutaneous needle as-

piration biopsy in two cases, mediascopic lung biopsy in one case, and unknown in two cases. Bullous disease was diagnosed prior to lung cancer in 13 cases and simultaneously in 21 cases. The observation period before the diagnosis of lung cancer was from seven months to nine years (mean period: 36.7±31.2 months), including unknown in one case. This suggests the difficulty of diagnosis using cytological or histological methods before surgery, because fiberoptic bronchoscopy and percutaneous CT-guided needle biopsy, with the risk of pneumothorax and hemothorax, can not always reach a small

tumor on the wall of a bulla at an early stage. Pathological examination revealed large cell carcinoma in 12 cases, adenocarcinoma in 11 cases, squamous cell carcinoma in six cases, small cell carcinoma in two cases, adenosquamous cell carcinoma in one case, carcinosarcoma in one case, and both large cell carcinoma on the wall of the right bulla and adenocarcinoma on the wall of the left bulla in one case. Surgical treatment (with chemotherapy in seven patients, and with chemotherapy and radiotherapy in five patients) was undertaken in 29 patients, chemotherapy only in four patients, and chemotherapy combined with radiotherapy in one patient. The method of the surgical procedure was lobectomy in 20 cases (with chest wall resection in three patients), segmentectomy in two cases (with pleural resection in one patient), partial resection in one case, pneumonectomy in one case, and bullectomy in six cases, including lobectomy in the right side and bullectomy in the left side in one case. In the bullectomy cases, four patients were transferred to lobectomy with chemotherapy, and two patients were transferred to segmentectomy (with radiotherapy in one patient), because of existing occult lung cancer without evidence of parenchymal lesions. Eighteen patients (53%) died after the first operation and 10 (56%) of those patients died within six months. There was no clear relationship between the surgical procedure and the prognosis of the patients. Tsutsui M et al.<sup>22)</sup> reported that tumor in the advanced stage was seen in 58.3% of the patients, and that a large bulla in patients older than 50 years should be resected because of the higher incidence of coexisting cancer and bulla (51.6%), and interfering respiratory function.

In general, patients with both pulmonary bullous disease and primary lung cancer have a very poor prognosis, because they receive treatment when the tumor is at an advanced stage.<sup>6,9,13-18)</sup> Hanaoka et al.<sup>23)</sup> reported that the prognosis of bronchogenic carcinoma with emphysematous bullae disease was similar to that of primary bronchogenic carcinoma in non-small cell lung cancer, if resected at an early stage. Therefore, careful follow-up must be done to discover lung cancer at an earlier stage, when emphysematous bullae disease, including a giant bulla, is recognized. Annual chest roentgenograph and/or chest computed tomography can enable the comprehension of the existence of minimal cancer only by comparison of current and previous radiographic pictures, before the tumor has reached a considerable size. As characteristic radiographic features, three major patterns have been reported: nodular opacity within or adjacent to the

bulla, partial or diffuse thickening of the bulla wall, and secondary signs of the bulla (changed diameter, fluid retention, and pneumothorax).<sup>22)</sup> It is easy to suspect a malignant lesion of the nodular opacity type. However, it is difficult to suspect the other types, because it can not be determined whether a lesion is due to cancer when it is revealed as growing along the bulla wall or developing multifocally in the wall (i.e., a giant bulla has a thickened wall due to compressed lung tissue and inflammatory reactions of the adjacent lung tissue) and few patients have secondary signs. This might also cause difficulty in detecting early stages of lung cancer.

Hence, on the basis of our review of the literature, we recommend that middle-age male patients with a giant bulla who smoke should have annual chest roentgenography and/or chest computed tomography to screen for lung cancer arising in or close to the bullous disease, and that a giant bulla should be resected in patients older than 50 years because of the higher incidence of coexisting cancer and bulla, and interfering respiratory function. Furthermore, even in bullectomy cases without evidence of parenchymal lesions, surgical resection of the bulla should be as complete as possible and accurate pathological examination of all resected material should be performed because of suspected existing occult or small lung cancer.

## Conclusion

We reported a 58-year-old man who underwent surgical treatment of primary lung cancer arising from the wall of a giant bulla, and recommend that middle-age male patients with a giant bulla who smoke should have annual chest roentgenography and/or chest computed tomography, and that a giant bulla should be resected in patients older than 50 years, to improve the prognosis of this disease.

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