

Primary Bronchogenic Carcinoma Associated with Emphysematous Giant Bulla^{*)}

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ABSTRACT

Operations for emphysematous giant bulla have been performed on 17 patients. Complications of primary lung cancer were observed in four of the 17 patients. All the patients who had such lung cancer were male and heavy smokers. As to histological type, squamous cell carcinoma were found in three patients and undifferentiated cancer of large cell type in one patient. The three had squamous cell carcinoma generated from the bronchus on the central side of the giant bulla, while the large cell carcinoma observed in one patient was generated from the bronchus close to the bulla. In two patients, cancer was generated while bulla was under observation. In one patient, the generation of cancer was found simultaneously with the bulla discovery. In the other patient, cancer was generated after bullectomy. These findings suggest that physicians should always pay careful attention to generation and complication of cancer while treating giant bulla

INTRODUCTION

Giant bulla is thought to include cases called emphysematous bulla, giant cyst, lung cyst and vanishing lung. However, it was treated as a giant type of emphysematous bulla in this paper. Since many patients of such a disease basically have emphysematous change of lung tissue, their surgical operability should be carefully determined. In general, there are measures to indicate the need for operation such cases with a giant bulla which occupies more than 25% of the lung or enlarges progressively, that is, showing the vanishing lung syndrome⁹⁾, and cases in which the normal lung is compressed aside and post-surgical recovery of pulmonary function is expected²⁰⁾. Operation is also needed in cases of combined by infection, pneumothorax and lung cancer, etc. The operation has been performed mainly by the bullectomy preserving the pulmonary parenchyma as much as possible and by the Naclerio-Langer's method¹²⁾ that includes bullectomy and pneumorrhaphy. Re-

cently, some reports have stated that cancer association may also occur in cases of giant bulla⁶⁾, lung cyst^{7,8,21)}, and sarcoidosis associated with vanishing lung¹⁰⁾, which have been treated as benign diseases. These findings suggest that bullous disease should always be observed, examined and operated with great caution against the generation of malignant tumor. Of the giant bulla patients in our clinic, the cases which had cancer association are reported in this paper.

MATERIALS AND METHODS

1. Case of giant bulla

Seventeen operations for giant emphysematous bulla have been performed in our clinic since 1970 as shown in Table 1. All the patients were male at an average age of 46.3 ranging from 29 to 61. Sixteen patients (94%) had smoking history and were all chronic heavy smokers with a Brinkman Index (number of years x number of cigarettes smoked a day) of more than 400. Four had a bulla generated

*¹⁾ 西亀正之, 奥道恒夫, 吉岡伸吉郎, 山根 基, 江崎治夫: 気腫性巨大肺嚢胞に合併した原発性肺癌の検討

Table 1. Summary of Clinical and Roentgenographic Data of Giant Bulla Cases

Patient	Age (Years)	Sex	Smoking History (Brinkman Index)	Roentgenographic Location of Giant Bulla	Operation Method and Site	Remarks
1	49	M	840		R-Lower Lobectomy (R-S ⁶)	Died of postop. 1st day due to opposite pneumothorax
2	48	M	420		Bullectomy, Pneumorrhaphy (R-S ¹)	
3	29	M	0		Bullectomy, Pneumorrhaphy (R-S ³ , S ⁶)	Postoperative pneumonia
4	44	M	430		R-Upper Lobectomy (R-S ^{1,2})	
5	41	M	400		Bullectomy, Pneumorrhaphy (R-S ^{1,2})	
6	39	M	460		Bullectomy, Pneumorrhaphy (R-S ¹ , S ⁶)	
7	40	M	800		Bullectomy, Pneumorrhaphy (L-S ¹⁺² , S ³)	Postoperative collapse Reoperation
8	40	M	600		Bullectomy, Pneumorrhaphy (R-S ^{1,2} , S ⁶)	
9	50	M	1,200		R-Upper Lobectomy (R-S ^{1,2})	
10	44	M	1,040		Bullectomy, Pneumorrhaphy (L-S ¹⁺²)	
11	61	M	1,125		Bullectomy, Pneumorrhaphy (L-S ¹⁺² , S ⁶)	Cancer association
12	49	M	960		L-Upper Lobectomy (L-S ¹⁺²)	Postoperative atelectasis, Cancer association
13	54	M	600		Bullectomy, Pneumorrhaphy (L-S ¹⁺²)	
14	60	M	1,000		Bullectomy, Pneumorrhaphy (R-S ¹)	
15	38	M	420		Bullectomy, Pneumorrhaphy (R-S ¹)	
16	49	M	600		R-Upper Lobectomy R-S ¹	Cancer association
17	52	M	2,220		R-S ⁴ Segmentectomy, Bullectomy, Pneumorrhaphy (R-S ¹)	Cancer association

on the right side, two on the left side and eleven on both sides. The indications for surgery were: dyspnea in 8 patient, vanishing lung syndrome in 8 patients, cancer association in 4 patients, traumatic pneumothorax in 1 patient, etc. The operating procedure were, as follows: bullectomy and suture ligation of bronchial orifice and pneumorrhaphy were conducted on 11 patients based on the Naclerio-Langer's method. Five patients underwent lobectomy, since two had cancer association and the other 3 a giant bulla of almost an entire lobe with little normal lung tissue remaining. In Case 1 of postoperative complications died of contralateral pneumothorax on the first postoperative day after resection of the right lower lobe. Case 7 suffered from inflation insufficiency due to air leakage from the sutured site and thoracotomy and suturing of pulmonary fistula were reperformed. One case each of mild pneumonia (Case 3) and atelectasis (Case 12) was also observed. As to prognosis, excepting the patients having cancer association, one of the other 13 patients died but the remaining 12 resumed activities similar to those they had engaged in before surgery.

2. Case of cancer association

Cancer was associated in 4 patients, as shown in Table 2 and as described below.

Case 1

The patient was a 61-year-old man, a farmer. He had Lt-spontaneous pneumothorax in June 1976 and was healed after one month's rest. Since then he has had similar attacks five times. Giant bullae were discovered on both sides in 1980 and he was admitted to our department for operation (Case 11). His lung function were depressed showing, VC 1.7L, %VC 52%, %FEV_{1.0} 49% and %RV/LC 66%. The left posterolateral thorax was opened and an infant's head-sized bulla each was found at L-S¹ and S⁶⁻⁸. Bullectomy and pneumorrhaphy were performed. The postoperative course was uneventful and he was being followed up satisfactorily in the outpatient department. On June 19, 1982, he came to our hospital complaining of exertional dyspnea. His chest X-ray film revealed an abnormal shadow in the region of the hilum hilus (Fig. 1, 2). After he was admitted to hospital, bronchofiberscopy and biopsy were carried out. Squamous cell carcinoma was found in the L-B⁶ region and the left lower lobectomy was scheduled. However, the second bronchofiberscopy revealed the presence of two more carcinoma: one in the site of the R-B^{1,2} bifurcation and the other in the site of the bifurcation of L-B⁶ and B¹⁻³. As a result, a diagnosis of multiple squamous cell carcinoma

Table 2. Cases of Bronchogenic Carcinoma Associated with Giant Bulla

Patient	Sex Age (Years)	Roentgenographic Location of Giant Bulla and Cancer	Location of Cancer in the Lung	Histology of Cancer	Relationship of Cancer Appearance with Bulla	Treatment	Follow up
1 (11)*	M 61		1. R-B ^{1,2} 2. L-B ⁶ 3. L-B ^{1+2,3}	Squamous cell carcinoma	Followed of Bulla opera- tion	Postop. for Bulla, non-sur- gical for cancer	Alive 2 years later
2 (12)*	M 49		L-B ^{1+2,3} , B ^{4,5}	Squamous cell carcinoma	Same time	L-Upper Lobectomy	Alive 3 years later
3 (16)*	M 49		R-B ¹	Squamous cell carcinoma	Followed of Bulla	R-Upper Lobectomy	Died 4 months later
4 (17)*	M 52		R-B ⁴	Large cell carcinoma	Followed of Bulla	Bullect- omy and R-S ⁴ Segment- ectomy	Alive 1 month later

*Case number in total giant bulla cases in Table 1.

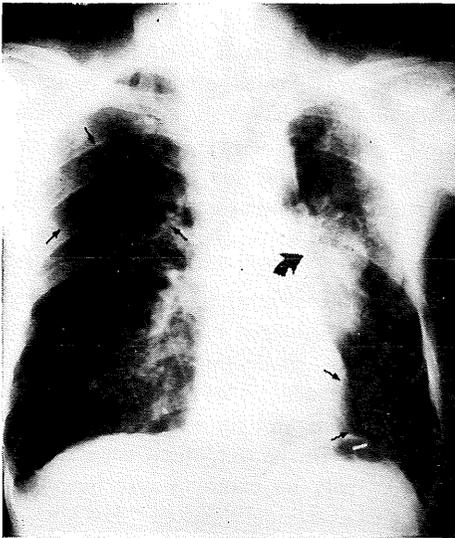


Fig. 1. Case 1 (11) Postero-Anterior Chest Film

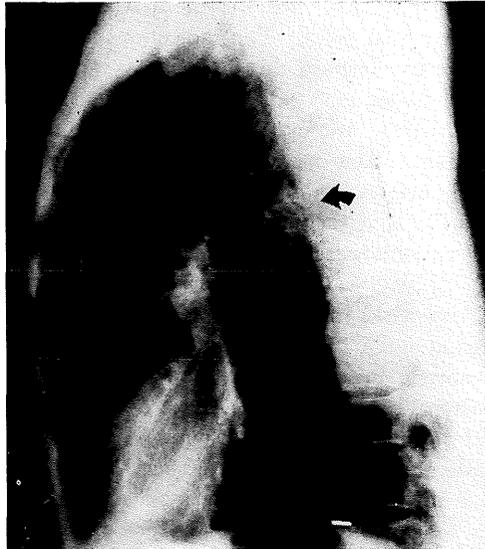


Fig. 2. Case 1 (11) Lateral Chest Film

Shadow of tumor was detected in a follow-up study approximately 2 years after bullectomy and pneumorrhaphy in Case 1 (11). Postero-anterior chest film (Fig. 1) shows bullous shadows in the right upper and left lower lung fields (small arrow) and tumor associated by notching in left hilum hilus (large arrow). Lateral chest film (Fig. 2) shows irregularly edged tumor shadow (large arrow) in the middle lung on anterior of thoracic vertebrae.

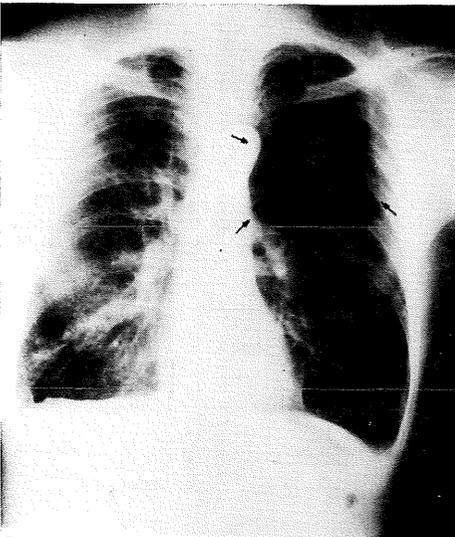


Fig. 3. Case 2 (12) Postero-Anterior Chest Film

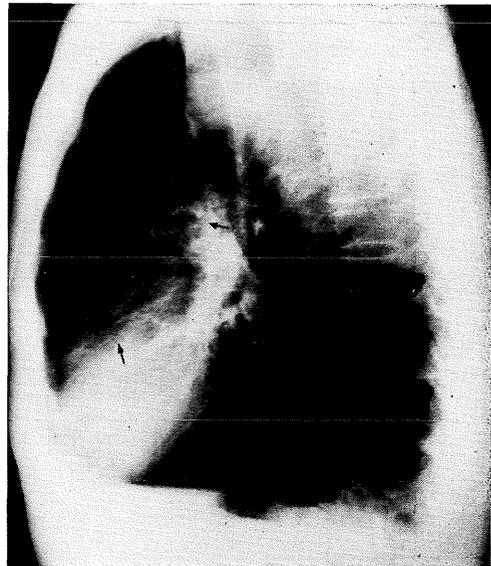


Fig. 4. Case 2 (12) Lateral Chest Film

Preoperative chest X-ray film of Case 2 (12) are shown. Both P-A and lateral films indicate shadows of giant bulla in the upper lung field (arrow). There is no tumor shadow on either film. Shadows suggesting bronchitis and fibrosis are found in the right middle and lower lung fields.

at three sites was made. The patient was given irradiation of 5,000 rads over the main tumor at L-S⁶ and 20 mg of Mitomycin C[®] by bronchial arterial infusion. One year after the discovery of his cancer, he is treated with Crestin[®], 3.0 g/day in the outpatient department and is leading an ordinary life.

Case 2

The patient was a 49-year-old man, farmer. He had been complaining of cough and sputum for six years and dyspnea which began about one year ago. Giant bulla was diagnosed by the chest X-ray examination (Case 12) (Figs. 3, 4). He was admitted to our hospital. During examination, an irregular bosselation in the bifurcation of L-B¹⁻³ and B⁴⁻⁵ was discovered on bronchofiberscopy. Blushing cytology was carried out and the diagnosis was Class V, squamous cell carcinoma. Lung function was depressed: VC 2.08L; %VC 67.7%; %FEV_{1.0} 45.2%; %RL/LC 71%. A L-upper lobectomy, including bulla located at L-S¹⁺², was performed. The cancer was an early lung cancer at the T₁N₀M₀ stage I and a case of clinical occult cancer.

Now, three years after operation, he leads a normal daily life. The extirpated sample in-

cluded a fist-sized bulla with other lung tissue showing enhanced anthracosis and serious emphysematous change (Fig. 5).

Case 3

The patient was a 49-year-old male office worker. His chest X-ray film revealed a giant bulla in 1979 (Case 16). However, since there were no symptoms, he had been followed up in the outpatient department. About 3 years

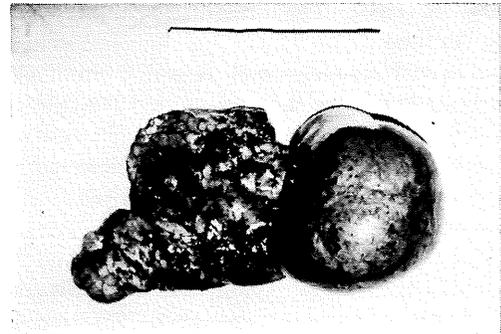


Fig. 5. Case 2 (12) Extirpated Sample

The extirpated sample of Case 2 (12) is shown. Mann's fist-sized giant bulla is on the right and resected upper lobe lung tissue is on the left. Serious anthracosis and emphysematous changes are observed on the lung tissue.

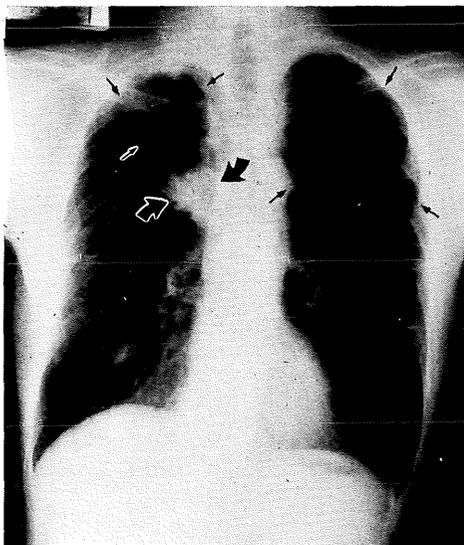


Fig. 6. Case 3 (16)

These are chest X-ray films of giant bullae (small arrows) in both upper lung fields, taken approximately 3 years after commencement of follow-up.

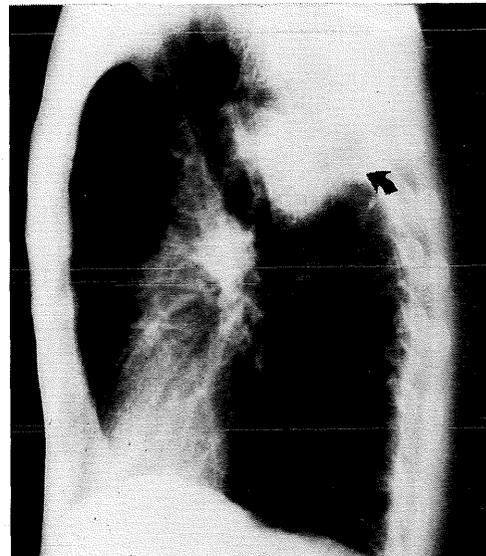


Fig. 7. Case 3 (16)

Postero-Anterior view (Fig. 6) indicates an abnormal triangular shadow ranging from the hilum hilus to the upper lung field. Lateral view (Fig. 7) shows tumor shadow accompanied by notching of relatively smooth edge in the posterior portion of the upper lung field.

later, in August, 1982, stiffness in the right shoulder began, and in October, a pain began to be felt from the right thorax to the back. In November, about 3 months after manifestation, an abnormal shadow was found in the region of the right hilum hilus (Figs. 6, 7). After admission to hospital, bronchofiberscopy was carried out and brushing cytology revealed the presence of malignant cells of adeno-type at R-B². An operation was performed on January 18, 1983. The tumor had infiltrated to the 7th thoracic vertebra. Left upper lobectomy and partial thoracic wall resection were performed, but were not curative. The patient died of progressed primary lesion and systemic metastasis five months later. The resected tumor was found to be squamous cancer.

Case 4

The patient, a 52-year-old man, worked for a building concern. Giant bulla was detected at another hospital in September, 1981, and the patient had been followed up there (Case 17).

An abnormal shadow was discovered in the right middle field on chest X-ray examination in May 1983 (Figs. 8, 9). After admission to hospital, a tumor was detected at R-B^{4b} by bronchofiberscopy and a diagnosis of squamous cell cancer was confirmed by biopsy. The patient was admitted to our department for surgery. The lung function was depressed: VC 2.91 L; %FVC 55.2%; %FEV_{1.0} 69.4%; %RC/LC 49.2%. An operation was performed on August 2. Lymph node metastasia was detected on the mediastinum. Considering the impaired lung function, a resection of S⁴ including the tumor and a fist-sized bullectomy on the upper lobe with pneumorrhaphy were conducted. The stage was T₂N₂M₀ at stage III. The operation was not curative. Now, approximately two months after the operation, the impaired lung function is not improved and assisted respiration, using a respirator, is being continued, thus making weaning difficult.

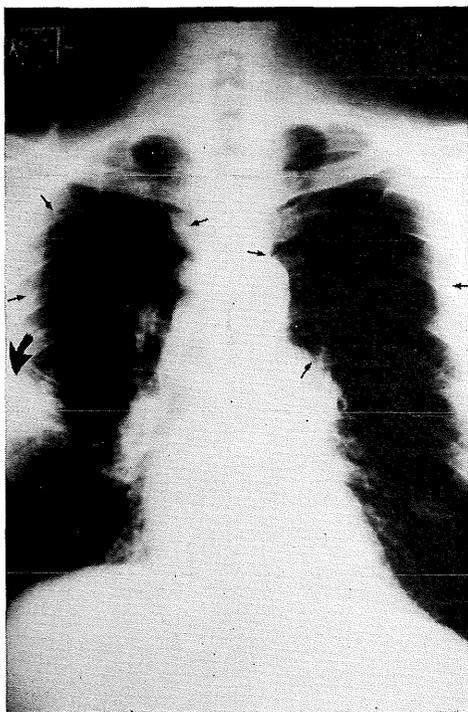


Fig. 8. Case 4 (17)

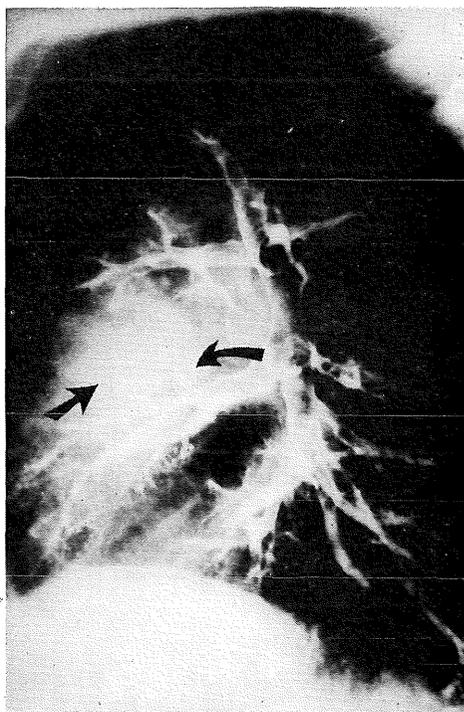


Fig. 9. Case 4 (17)

Chest X-ray films of Case 4 (17), taken approximately 2 years after commencement of follow-up of giant bulla. There are giant bullae in both upper lung fields (small arrows). Postero-anterior view shows irregularly edged tumor shadow in the lateral portion of the middle lung field. Lateral broncogram (Fig. 9) indicates obstruction of B^{4b} and a circular tumor shadow coincident with S⁴.

DISCUSSION

Many patients of giant bulla have associations of basic emphysematous change in their lung tissue and also have chronic obstructive lung dysfunction. Consequently, indications for surgery require careful examination. As to indications for surgery, many reporters attach importance to: the presence of lung tissue which is compressed by bulla but can be reinflated, not having serious underlying obstructive lung disease, and not having lung infection. The measures in our clinic are, as follows: (1) More than one third of the hemithorax is occupied by the bulla. (2) The size of the bulla increases progressively. (3) There are some subjective symptoms. (4) The bulla compresses the parenchyma around it and results in lung dysfunction. (5) Bulla causes infection or is associated with other diseases such as cancer.

Plication and bullectomy are suitable operative procedures for giant bulla. It has been made a principle to preserve as much lung tissue as possible and not to perform lobectomy.

Fain stated that bullectomy was performed on 20 patients of emphysematous giant bulla and that the result of operation was favorable in all patients⁵. Potgieter reported two deaths out of 21 operations, with a mortality rate of 9.5% Cor pulmonare in one patient and postoperative complication of spontaneous pneumothorax on contralateral lung in the other patient¹⁵. In our investigation, a single death was also found due to spontaneous pneumothorax on contralateral lung just after operation and the mortality rate was 5.8%.

It is reported by Nakamura et al. that lobectomy was performed in 19 patients and that preoperative $\%FEV_{1.0}$ and regional \dot{V}/V dynamics were available to estimate postoperative lung function, and that when $\%FEV_{1.0}$ was greater than 40% and regional \dot{V}/V dynamics was greater than 0.5 before operation, there were no problems in the postoperative course¹⁸.

Kuwabara reported that operative procedures were decided depending upon patient condition. However, according to the report, trans-thoracal bullectomy and drainage, a method modifying Monaldi's drainage, were carried out as treatment and preoperative procedure and led to good results⁹.

Recently, it has been noted that diseases

which had been regarded and treated as benign can be complicated with malignant tumor.

It is well known that cancer generates from scars of peripheral lung tissue²⁸. There are many reports that bullae or blebs associated with subpleural scars were complicated by malignant tumor, discovered as spontaneous pneumothorax^{2,4}. Lung cyst complicated by malignant tumor is also reported. Huntington found complication of epidermoid cancer⁷ and Svennevig reported it of adenocarcinoma¹⁹.

As to emphysematous giant bulla, reported in this paper, cancer association has become an important problem. Scannel reported 4 cases of cancer association. Two patients of the four had spontaneous pneumothorax. He stated that in elderly patients, thorough attention to the presence of occult cancer was required¹⁶. Stoloff et al. analyzed chest X-ray films of 75,000 subjects and reported that cancer association was found in 6.1% of the subjects having bullous disease and in 0.16% of the subjects without bullous disease. The frequency in the subjects having bullous disease was approximately 32 times higher¹⁸. Further, it is reported by Goldstein et al. that when chest X-ray films of 411 patients with primary lung cancer were analyzed, giant bullae were detected in 3.9% of the patients. The tissue types of those patients having complications were anaplastic cancer in twelve, squamous cancer in four, and adenocarcinoma in two⁶. In our investigation, squamous cancer was found in 3 patients and giant cell carcinoma in one. Shirakusa also reported the occurrence of giant cell carcinoma association¹⁷.

Smoking has been discussed as a cause of the occurrence of cancer in the patient having giant bullae. Sixteen of the 17 patients in our analysis were heavy smokers. Similar findings were also reported in other reports. However, Aronberg noted that cancer association was found even in a young patient with giant bulla who smoked few cigarettes¹.

Ohata et al. observed the structure of giant bulla in detail using scanning electron microscope. Compared with other bullous diseases, the internal of the giant was disintegrated most seriously while there were normal pleural epithelial cells on its surface¹⁴.

Investigating these reports, the following things were speculated. Smoking induces blood

stream failure in alveoli pulmonis, which results in destruction of alveoli pulmonis and formation of bulla. The presence of bulla over a long period of time causes regional ventilation failure. Then metaplasia of the epithelial cells of the draining bronchus occurs and cancer is generated. Womack et al. also stated that metaplasia of epithelial cells results in cancer²²⁾. These speculation will be clarified through histologic investigation on resected bronchi with giant bulla.

For patients having giant bulla, even without symptoms, continuous attention to the generation of cancer is required during both the observation period of non-operated patients and the postoperation follow-up period. When abnormal shadows are detected, a detailed examination should be immediately carried out. This effectively serves to detect occult cancer, as shown in our patient of Case 2 (12). As to surgical procedure, though there are many patients with depressed lung function, lobectomy is necessary in some cases. It is desirable to confirm the absence of cancer association before bullectomy and plication.

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