Abstract

Objective: To compare the identifiable pulmonary abnormalities during thoracoscopy with the histological findings in patients requiring surgical intervention for recurrent or persistent primary spontaneous pneumothorax (PSP) and correlate these with the postoperative events.

Methods: From January 1999 to December 2002, 94 consecutive patients underwent video-assisted thoracoscopic wedge excision and apical pleurectomy for PSP. Vanderschueren's classification was used for macroscopic staging and histological observation for microscopic features. Clinical data of these patients and the outcome of surgery were described. Results: All patients were successfully treated using video-assisted thoracoscopic technique. Recurrent pneumothorax was the most frequent indication for surgery, occurring in 60 cases. The method of management was stapling of an identified bleb or apex of the upper lobe and apical pleurectomy. In 67 cases (71%), clear bullae were found in types III and IV. In 15 cases (16%), type II pleuropulmonary adhesions were identified and in 12 (13%) cases thoracoscopy failed to reveal any abnormality (type I). The actual site of air leakage could be located during thoracoscopy in 24 (26%) patients. Histologically, 74 patients had subpleural bullae/blebs formation and 20 had emphysema without bullae. Fifty-three patients had cellular infiltration and 82 had pleural fibrosis. In the microscopic examination, the actual site of air leakage could be located at the site of subpleural blebs or bullae in 15 patients and elsewhere at the lung surface in five other patients. Postoperative prolonged air leak occurred in 4 out of 12 patients in type I and in two of the remaining patients, \( p = 0.001 \). Mean follow-up is 48 months (range, 30—60 months) for all patients. Pneumothorax recurred in three patients (3.1%). Two patients from type I (16.6%) and one patient from the other types (1.2%) had recurrence (\( p = 0.01 \)).

Conclusions: Video-assisted thoracoscopic stapling of an identified bleb or apex of the upper lobe and apical pleurectomy represents the standard treatment for the majority of recurrent or persistent PSP. Most patients with surgically treated PSP have subpleural blebs or bullae or isolated emphysema. In type I cases, simple apical excision and apical pleurectomy are not sufficient and perhaps additional talc poudrage might be indicated.

Keywords: Blebs; Bullae; Pneumothorax; Video-assisted thoracoscopy; Pleurectomy

1. Introduction

Primary spontaneous pneumothorax (PSP) is a relatively common disease defined as the accumulation of air in the pleural space with secondary lung collapse. The cause of PSP is unknown although it is mostly attributed to the rupture of a subpleural bleb or bulla [1]. The etiology of bulla and bleb formation is obscure. Numerous therapeutic options are available for the treatment of PSP, including simple observation, chest tube thoracostomy, thoracotomy, and video-assisted thoracoscopic surgery (VATS) [1—3]. The indications for surgical treatment include persistent air leak, recurrent PSP, contralateral PSP, and PSP in high-risk occupations such as being a pilot or a diver [4]. Recently, VATS has been used as an alternative to thoracotomy in the treatment of recurrent or persistent PSP to avoid morbidity associated with thoracotomy approach [2,3]. However, there are still some issues remaining regarding the type of operation and technique in relation to the absence or presence of blebs or bullae. Very few studies have dealt with the correlation between the type of bullae and the risk of postoperative events [5—8]. No studies have dealt with the correlation between pathology and postoperative events. In this study, therefore, we prospectively compared the macroscopic findings with the histological findings in patients who underwent VATS treatment for persistent or recurrent PSP.

2. Materials and methods

The study was conducted at Chest Diseases Hospital in Kuwait, which is the only center for the surgical treatment of chest diseases in Kuwait. Patients with PSP were considered eligible for inclusion in the study. Patients with secondary or
iatrogenic SP were excluded from the study. From January 1999 to December 2002, 94 consecutive patients with persistent or recurrent PSP treated by VATS were included in the study. No patients with PSP and VATS indication which were not included in the study during the study period. Investigations included a chest radiograph, complete blood count, serum electrolytes, and renal function test. All patients with PSP were also tested negative for any other lung disorder besides PSP before they were included.

2.1. Operative technique of VATS

The patient was kept under general anesthesia using a double-lumen endotracheal tube and one-lung ventilation and was placed in a posterolateral thoracotomy position. A 10-mm trocar was introduced through a 1.5-cm skin incision in the eighth intercostal space at the midaxillary line for insertion of a 0° videothoracoscope (Karl Storz, Tuttlingen, Germany). Two additional ports were then inserted under direct vision: a 12-mm trocar through the fifth intercostal space on the anterior axillary line and a 12-mm posterior trocar through the fifth intercostal space near the tip of the scapula. An air leak was identified by instilling Ringer’s solution into the pleural cavity and ventilating the collapsed lung. Bullae or blebs were identified and grasped with an empty sponge stick. When no blebs were visible, a small portion of the apical upper lobe was resected. The excision was done by using an ENDO-GIA stapling device (Auto-Suture Company, United State Surgical Corp., Norwalk, CT, USA). Then, apical pleurectomy was performed. A 28-F chest tube was inserted through the inferior incision in the eighth intercostal space and connected to underwater seal.

All surgical specimens were obtained from hemithorax with the visualized pneumothorax, identified parenchymal or pleural abnormality, or hemithorax in which the patient had experienced previous pneumothoraces. A total of 94 lung wedge specimens and parietal pleura specimens were obtained. All histological specimens were reviewed by the same pulmonary pathologist who was instructed about the purpose of the study and also to look for ruptured blebs/bullae or site of air leakage. The specimens were infused with formalin and leak was detected if there was ruptured bleb/bulla or air leak in the resected specimen. Then, for microscopic examination, the pathologist did serial sectioning of the specimen that had leak.

A bulla and bleb were defined, respectively, as a sharply demarcated region of emphysema >1 cm in diameter and as a focal air-containing space contiguous to or within the visceral pleura. The diagnosis of emphysema was based on the presence of abnormally expanded airspaces distal to the terminal bronchiole with destruction of the walls of the involved airspaces. Irregular emphysema was defined by random destruction and enlargement of any portion of the pulmonary acinus with associated scarring and fibrosis.

2.2. Postoperative care

All patients were extubated in the operating room and transferred to the thoracic surgery ward. An analgesic, Pethidine, was administered i.m. every 4–6 h according to the patient request, and an oral analgesic (acetaminophen) was given as needed. The intercostal drain was removed when the underlying lung was fully expanded with no air leakage and <100 mL pleural fluid drained through the tube for 24 h. All patients were discharged one day after removing the chest tube.

2.3. Statistical analysis

Data were expressed as mean ± SD; data analyses were made using SPSS software windows version 10 package (SPSS, Chicago, IL, USA). The cut-off level of statistical significance was P < 0.05. The unpaired Student’s test was used to assess the significance between the means of variables in the two groups. The Pearson χ² test was used to ascertain the significance of association between two categorical variables. The χ² test was replaced by Fisher’s exact test if the cell frequency of any of the 2 × 2 contingency table went below 5.

2.4. Postoperative assessment

Data recorded for all patients included the number of episodes of pneumothorax, thoracoscopic findings, and the operative time. The duration of pleural drainage after operation, length of hospital stay, postoperative air leak, pathologic findings, and recurrences were also recorded. The follow-up chest radiograph was done at intervals of 1 week, 1 month, and 3 months, and then patients were followed up with a telephone communication. The recurrence was proved by chest radiography during the follow-up period.

3. Results

This series included 81 male and 13 female patients (age, 24.6 ± 5.8 years; range, 16–40 years). Sixty patients (64%) were operated on after a recurrent episode of PSP. There had been second, third, and fourth actual recurrences in patients who were operated for recurrent episodes of PSP in 52, 6 and 2 patients, respectively. In 34 patients (36%) VATS was done because of persistent air leak for more than 7 days. VATS was unilateral in all cases, and all procedures were performed by the same surgeon, on the right side in 48 cases (51%) and on the left side in 46 cases (49%). All patients were successfully treated using the VATS technique. The mean operative time was 46 ± 7.9 min (range, 30–69 min).

3.1. Thoracoscopic findings

Macroscopic findings according to the classification of Vanderschueren [9] were 12 (13%) type I cases (normal finding), 15 (16%) type II cases (pleuropulmonary adhesions), 53 (56%) type III cases (blebs, bullae < 2 cm diameter), and 14 (15%) type IV cases (bullae > 2 cm diameter). Subpleural blebs or bullae were present in 67 cases (71%) and an endoscopic stapler resected them. We identified blebs or bullae in 26 out of 34 patients (76%) with first time PSP and 41 out of 60 (68%) with recurrent PSP. In the absence of an identifiable lesion, the apex of the upper lobe was excised; this was done in 27 cases (29%). The actual site of air leakage could be located in 24 patients (26%): 18/34 patients (53%)


with first time PSP and 6/60 patients (10%) with recurrent PSP, \(p < 0.0001\). Apical pleurectomy was done in all cases. The postoperative hospital stay for VATS patients ranged from 2 to 13 days (mean, 3.3 ± 2 days). There were no deaths in this series, and no patient required monitoring in the ICU.

A comparison of macroscopic findings of patients with PSP with clinical data is summarized in Table 1. There were no differences concerning the age, body mass index (BMI), sex, and smoking status between the macroscopic types. Type IV bullae were more frequently found in patients with persistent PSP (10 out of 14 patients; 71%); type II were found more frequently in patients with recurrent PSP (14 out of 15 patients; 93%); \(p = 0.001\). Air leak occurred in 4 out of 12 patients in type I in whom no blebs were identified and in two of the remaining patients. The difference is statistically significant \((P = 0.001)\). Furthermore, type I cases required longer pleural drainage and postoperative hospital stay 4.5 and 5.5 days, respectively, than other types. The difference is statistically significant \((P = 0.001)\). During a follow-up period ranging from 30 to 60 months (mean, 48 months), 2 patients (16.6%) in type I cases developed recurrences. This rate was higher than that of the other types (1.2%; \(P = 0.01\)).

### 3.2. Pathologic findings

The resected lung apices demonstrated subpleural emphysematous changes with bullae/blebs formation in 74 out of 94 patients (79%) (Fig. 1) and emphysema without bullae in 20 out of 94 patients (21%) (Fig. 2). Irregular emphysema was the most common pattern of emphysema identified \((n = 14)\). Other types of emphysema identified included distal acinar (paraseptal) emphysema \((n = 5)\) and mixed irregular and distal acinar \((n = 1)\). In the microscopic examination, the actual site of air leakage could be located at the site of subpleural blebs or bullae that ruptured in 15 patients and elsewhere at the lung surface in five other patients.

Inflammatory changes in the lung of the patients with PSP were observed. In 53 patients, lung specimens showed either lymphocytic infiltration \((n = 42)\) or mixed lymphocytic and
plasma cell infiltration ($n = 11$). The remaining lung apices showed no cellular infiltration.

Parietal pleural specimens showed either pleural fibrosis alone ($n = 71$) (Fig. 3), pleural fibrosis with mesothelial thickening and hyperplasia ($n = 11$), or normal pleura ($n = 9$). Inflammatory changes in the parietal pleura were invariably observed. The hematoxylin–eosin staining clearly showed presence of lymphocytes, eosinophils, mesothelial thickening, and proliferation of the pleura.

### 3.3. Thoracoscopic–Pathologic correlation

All patients with blebs/bullae identified on thoracoscopy ($n = 67$) had bullae identified histologically. Fifty-three patients in this group had only isolated emphysematous blebs or bullae. Irregular emphysema with bulla formation was confirmed in 12 other patients and two patients had distal acinar emphysema with bulla formation. Pleural fibrosis was evident in 60 patients in this group.

Of the 27 patients with no parenchymal abnormality seen on thoracoscopy, 19 had emphysematous bullae and eight had irregular emphysema without bulla formation. Twenty-five patients in this group had evidence of pleural fibrosis with or without mesothelial proliferation.

Of patients with bullae identified on thoracoscopy, 38 patients had cellular infiltration of lymphocytes with or without plasma cell infiltration while cellular infiltration was evident in 15/27 patients with no parenchymal abnormality seen on thoracoscopy.

At thoracoscopy, air leaks were identified in 24 patients. The pathologist found the site of air leaks in 20 patients. Fourteen of the 20 patients were included in the group of the 24, in whom air leakage was identified intraoperatively. Therefore, the total number of patients in whom a pleural defect was found, either intraoperatively or in the resected specimen, was 30.

### 3.4. Follow-up

All patients in this study were followed up regularly (mean follow-up time, 48 months; range, 30–60 months). Recurrent ipsilateral pneumothorax occurred in 3 of the 94 procedures (3.1%). These occurred at 10, 20, and 28 weeks after the original VATS procedure. Two of these recurrences occurred in patients in whom no blebs were identified (2 out of 12 patients; 16.6%), and one occurred in the other groups (1 out of 82 patients; 1.2%). The difference is statistically significant ($P = 0.01$). Two recurrences occurred in patients in whom postoperative air leak developed (2 out of 6 patients; 33%) and 1 out of 88 patients (1.1%) had no postoperative air leak ($P = 0.01$). Two patients who had recurrences after the original procedure were from type I cases and managed by rest and without drainage. One patient from type IV case underwent a reoperation by thoracotomy and excision of blebs that were inadequately excised in the first procedure and partial pleurectomy.

### 4. Discussion

Subpleural blebs or bullae, which are designated as emphysema-like changes (ELCs), are seen in 75–100% of patients with PSP even in non-smoking PSP patients [10–12]. In a large study of 432 patients treated with VATS, Cordillo et al. [7], showed no pathomorphologic changes in only 6.9% of cases. Inderbitzi et al. [8] reported no pathomorphologic changes in only 5.1% of cases. In 67 out of 94 (71%) patients described in the present report, clear bullae were found in types III and IV. In 15 (16%) cases (type II) pleuropulmonary adhesions were identified. In only 12 (13%) patients (type I) did thoracoscopy fail to reveal abnormality.

The actual site of air leakage, however, can be located at the ELCs which may be ruptured in some cases or elsewhere at the lung surface (“pleural porosity”). True visible air leaks at the site of the ELCs have been observed in a highly variable percentage of PSP patients undergoing thoracoscopy or thoracotomy [13,14]. Hatz et al. [14] observed 109 spontaneous pneumothorax patients who underwent VATS; leaking or ruptured blebs were seen in 72 patients (76% of PSP). The actual site of air leakage in this series was seen in 24 patients (26%) at thoracoscopy. The relatively high recurrence rate of PSP after bullectomy alone (up to 20%) may also reflect the fact that the actual site of air leakage may not always be at the ELCs but elsewhere at the lung [11,14,15].

Light microscopy studies have shown that only about 25% of ELCs in PSP are truly ruptured, whereas in the rest of the cases other lesions were present, referred to as “pleural porosity” [11,16]. This porosity consisting of mesothelial cell proliferation disruption and elastofibrosis. In the present study, light microscopy has shown the actual site of air leakage at the site of ELCs in 15 patients (16%) and elsewhere at the lung surface in 5 other patients (5%).

A variety of pathologic changes are seen at the lung apices. These changes include ELCs, airway inflammation, and emphysema. In our study, 74 out of 94 patients (79%) who required surgical intervention for persistent or recurrent PSP had a diagnosis of ELCs. Irregular emphysema, which was the most common type of emphysema identified, was seen in 14 patients. Jordan et al. [17] identified in resected specimens emphysema with or without bulla formation in 106/116 (91%) patients. The diagnosis was emphysema with bulla formation.
in 93 patients (80%) and emphysema without bulla in 13 (11%). This study shows a pleural inflammatory reaction in patients with PSP, which is characterized by increases in parietal pleural tissue eosinophils and neutrophils and associated with pleural fibrosis. Previous reports on pleural cell counts in patients with PSP have been published showing increases in total and differential cell counts that were associated with the duration of pneumothorax [18,19]. Our results also confirm the previously demonstrated mesothelial thickening and proliferation of the pleural in patients with PSP.

Another interesting observation in our study is that all patients had microscopic evidence of underlying lung disease in the excised apex of the lung. These results suggest that these lesions are the result of a degenerative process of the lung as has been suggested by Janssen et al. [6]. It seems sound to care for the apex of the lung because spontaneous pneumothorax originates from dystrophic areas located in the apexes of the lung, and not from any kind of pleural disease. These observations support the presence of underlying lung disease in the etiology of PSP. In the study by Lichter and Gwynne [20], chronic inflammation was found in most of the resected specimens of their patients with a pneumothorax. Janssen et al. [6] reported high incidence of adhesions in 25% (15 out of 61) of patients with first spontaneous pneumothorax, suggesting that an inflammatory reaction has preceded the event of pneumothorax.

Understanding the exact pathophysiology of PSP in an individual is important because recurrence prevention treatment may differ accordingly. The recurrence prevention technique focuses on the treatment of lung abnormalities such as ELCs or treatment of pleura. In type III and IV cases, VATS bleb-/bullectomy plus apical pleurectomy or pleurod-esis is effective. Persistent air leak and recurrence rates of PSP were higher in type I cases after the excision of the apex and apical pleurectomy. This may represent that the lung apices are not the actual site of the air leak or air leakage occurs elsewhere at the visceral pleura. Therefore, simple apical excision and apical pleurectomy in these cases are not sufficient and perhaps additional talc poudrage to induce more pleural symphysis might be indicated.

5. Conclusions

In all cases of PSP, pathomorphologic changes were observed. Even when no apical blebs are identified, pathology of the resected apex virtually always identifies paraseptal emphysema on such specimens. The actual site of air leakage was seen in 26% of patients at thoracoscopy and in 21% at microscopic examination. VATS stapling of identified blebs or apex of the upper lobe and apical pleurectomy represent the standard treatment for recurrent and persistent PSP. In the absence of blebs or bullae, additional talc poudrage might be indicated.

References