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ABSTRACT

Background: Post pneumonectomy bronchopleural fistula represents the most serious complication in thoracic surgery. Delayed fistula following tri modality treatment for mesothelioma is a serious problem regarding diagnosis and treatment. Surgical repair of the bronchial stump through a lateral thoracotomy is a dangerous attempt due to mediastinal fibrothorax and the risk of pulmonary artery stump damage.

Patients and Methods: Between 2002 and 2007, 85 extra pleural pneumonectomies for mesothelioma were performed. Only 58 patients completed the assigned tri modality treatment, five of them developed delayed bronchial stump dehiscence. The interval between primary surgery and stump dehiscence ranged from 6 months to 2 years.

Results: There were 4 right and one left sided fistulae. We had 4 males and one female, the mean age was 41 years. Bronchial stump was stapled in 3 patients and hand sewn closure was used in the remaining 2. By bronchoscopy, no stump recurrence was observed, but all patients with stapled bronchus had longer remaining stump. Empyema was present in all patients. All complicated patients received 2 field post operative radiotherapy with mediastinal dose of 40-45 Grays. The initial treatment consisted of tube thoracostomy followed by exploration through the previous thoracotomy incision with thorough curettage and wash of the infected space and removal of any exposed infected mesh. Bronchial stump was identified and re sutured. Re enforcement of the bronchial stump was done. Three patients required mechanical ventilation and 2 of them died. Surgery was successful in the remaining 3 patients.

Conclusion: Delayed bronchial stump dehiscence is liable to develop especially for right sided lesions. Prophylactic augmentation of right sided stumps during radiotherapy and improvement of radiation techniques may improve the dose distribution.

Key Words: Delayed – Bronchial – Stump – Fistula – Tri modality – Mesothelioma.

INTRODUCTION

Post pneumonectomy bronchopleural fistula represents the most serious complication in thoracic surgery. Its incidence ranges from 1 to 4% and most of cases occur after right pneumonectomy [1]. Studies have shown that diagnosis and therapeutic management remain as major problems with a high mortality rates ranging from 20-70% [2].

Algar and colleagues [3] reported that bronchopleural fistula is divided into early and late according to the time of occurrence. Early bronchopleural fistula happens within a month after an operation, whereas late bronchopleural fistula happens after this period. Varoli and colleagues [4] reported that early fistula was associated with perioperative technical error, while late fistula was linked to impaired healing of the bronchial stump. Delayed bronchial stump fistula following tri modality treatment for malignant pleural mesothelioma is more complicated regarding diagnosis and treatment due to extensive fibrosis following surgery and hemi thoracic irradiation that increases with time. Surgical repair of the bronchial stump through a lateral thoracotomy is a dangerous attempt due to mediastinal fibrothorax and the risk of pulmonary artery stump damage.

Diagnosis of early fistula is much easier than delayed ones due to long period between
primary surgery and the fistula development. Also, absence of pleural sac following extra pleural pneumonectomy leads to spreads of the infection deeply into the chest wall making infection control very difficult. Mesh repair of the previously excised diaphragm and/or pericardium makes things more complicated. For all these reasons trans thoracic repair of the fistula is a must in our opinion. Improperly curetted hemi thorax and incompletely removed mesh are the causes of persistent infection following surgery.

In this study, we retrospectively reviewed our incidence of delayed bronchial stump fistula following extrapleural pneumonectomy for patients with malignant pleural mesothelioma that had received tri modality treatment protocols. Aiming at finding the optimal treatment options for the management of this serious problem.

PATIENTS AND METHODS

We retrospectively reviewed the data of 85 consecutive patients with malignant pleural mesothelioma who underwent extrapleural pneumonectomy with systematic hilar and ipsilateral mediastinal lymph node sampling or dissection done at the department of Surgery, National Cancer Institute, Cairo University between January 2002 and June 2007. We routinely performed bronchial stump coverage for all right sided lesions using intercostal muscle, azygos vein for safe pulmonary resection.

This study was approved by our Institutional ethical committee and informed patient consent was taken.

The data retrieved included age, sex, medical comorbidities, smoking history, history of asbestos exposure, preoperative pulmonary function tests, echocardiograms and routine laboratory investigations. Chemotherapy or radiotherapy given were reported. The final pathologic stage was classified according to the International Mesothelioma Interest Group (IMIG) staging system. Hand-sewn versus stapled closure (the principal surgical stapler used was a Premium Multifire TA 30-4.8 stapler manufactured by United States Surgical Company [Norwalk, CT]).

Chemotherapy was started pre operatively in 3 patients using: Gemcitabine 1250mg/m2 day 1, day 8 and cisplatin 80mg/m2 day 1 with hydration every 3 weeks for 3 cycles.

Adjuvant chemotherapy was started within 6 weeks after surgery for every 3 weeks for 6 cycles in the form of: Holoxan 1500mg/m2 day 1, 2, 3 and carboplatin (area under curve = 5) in day 1.

Radiation therapy was given with 2 parallel opposing fields using linear accelerator, including the entire hemithorax, the ipsilateral mediastinal pleura, the ipsilateral pericardial surface, ipsilateral bronchial stump and the full thickness of the thorax at the site of the thoracotomy incisions and sites of chest drains, a margin of 1cm was used, with an added separate electron beam field for the operative scar or drain sites.

Only 58 patients completed the assigned tri modality treatment, five (8.6%) of them developed delayed bronchial stump dehiscence. The remaining 27 patients were excluded because they did not complete the planned tri modality treatment protocol. The interval between extra pleural pneumonectomy and stump dehiscence ranged from 6 months to 2 years.

The stump dehiscence was suspected clinically by severe breathlessness, irritating cough and expectoration of large amounts of infected sputum when lying down or on healthy side. A chest roentgenogram showed a hydropneumothorax occupying the pneumonectomy space.

Fiber optic bronchoscopy was done for all patients and proved the presence of a fistula. In patients with stapled bronchus, remnants of staple clips were identified. During bronchoscopy, multiple biopsies were taken to exclude tumor recurrence and biopsies were negative in all patients. Empyema was present in all patients. Tube thoracostomy (36 French gauge) was inserted for all patients with difficulty as a first step procedure with systemic antibiotics according to the culture and sensitivity from the chest tube.

RESULTS

There were 4 right and one left sided fistulae. We had 4 males and one female, the mean age was 41 years. During extra pleural pneumonectomy, bronchial stump was stapled in 3 patients and handsewn closure was used in the remaining 2. All patients complicated with disruption of
the bronchial stump received 2 field post operative radiotherapy with mediastinal dose 40-45 Grays (3 of them received a dose of 45Gy while the other 2 patients received 40Gy). Aspiration pneumonia was found pre operatively in all patients.

The surgery was started with double lumen endo tracheal tube to avoid contra lateral aspiration, the previous thoracotomy incision was reopened, and the cavity was debrided with thorough curettage of the cavity due to deep spread of infection into the chest wall. Any remnants of mesh reconstruction of the pericardium or the diaphragm was totally removed. The cavity was copiously washed out with povidone-iodine and hydrogen peroxide. The bronchial stump was carefully dissected, and positive-pressure ventilation help to identify a small fistulae.

Dissection of the bronchial stump was started posteriorly in all patients except one to avoid injury of the pulmonary artery stump that lie directly anterior to the bronchial stump, that is liable to be injured if the stump dissection started from anterior.

After complete exposure of the bronchial stump, refashioning of the edges was done, then interrupted 3-O vicryl was used to close the fistula. The bronchial stump was then checked for air leakage with 30-40cm H$_2$O sustained airway pressure. Re enforcement of the bronchial stump was done by using serratus anterior muscle flap in 3 patients and latissimus dorsi muscle in the remaining 2. A chest tube was placed near the bronchial stump to water seal drainage in the first 2 patients and open window drainage was used in the remaining 3.

Intra operative hemorrhage due to pulmonary artery injury occurred in the first patient in whom we started to dissect the bronchus anterior, the bleeding was successfully controlled.

All patients developed post operative pneumonia, 3 of them required mechanical ventilation and died 5, 8 and 12 days post operatively.

Surgery was successful in the remaining 2 patients both were discharged 15 days and 20 days respectively after surgery.

One patient developed peritoneal recurrence and died one year after fistula repair. The remaining patient was alive and disease free.
DISCUSSION

Risk factors for bronchial stump fistula are male sex, right-sided pneumonectomy, pneumonia leading to ARDS and prolonged postoperative mechanical ventilation [5,6]. Preoperative radio-chemotherapy is an important risk factor because it damages bronchial circulation and interferes with the healing process due to radiation-induced vascular obliterations [7].

Some authors practice bronchial stump protection and give great importance to bronchial artery preservation during lymphadenectomy. The bronchial stump closure technique is very important to prevent fistula formation. One of the most used techniques is the Sweet suture, performed by simple interrupted stitches introduced from the pars membranacea to the cartilaginous rings.

Delayed bronchial stump fistula following tri modality treatment for malignant pleural mesothelioma is a very rare and serious complication that is not discussed thoroughly in the literature.

The exact mechanism for this delayed dehiscence is not well known, but post operative mediastinal irradiation is considered the leading cause for this fatal complication.

This complication is difficult to diagnose and very hard to treat for many reasons:

First, long duration between definitive surgery and fistula development (6 or more months) that leads to extensive chest wall and mediastinal fibrosis. Second, absence of parietal pleura makes infection spreads deeply in the chest wall resulting in deep necrosis resistant to treatment. Third, presence of foreign material (mesh repair of surgically removed pericardium and/or diaphragm) that makes infection more resistant to treatment. Fourth the use of post operative radiation therapy increases the fibrosis and makes trans thoracic surgery more difficult, ischemic tissues are also have poor healing power.

Probably due to the smaller number of stapled bronchial closures in this study (13 patients out of 58), only a statistical trend could be found towards a higher rate of stump dehiscence in the stapled group compared with hand sewn group. What was observed in our patients was that stapled bronchi were longer than hand sewn ones which is considered a risk factor for stump dehiscence. The literature review is undecided regarding this discussion [8,9].

Multiple techniques have been developed to address this difficult problem including re-suturing and re-stapling techniques by redo
thoracotomy or sternotomy and the Claggett procedure \[10,11,12\]. Recent interest has been focused on minimally invasive procedures such as fibrin glue application and placement of endobronchial stent valves, or the use of a porcine collagen plug \[13\].

For all reasons mentioned before, the only surgical approach applicable to this specific group of patients is by redo thoracotomy to debride all necrotic tissues and to remove any mesh remnants before fistula closure.

Anterior dissection of the bronchial stump was tried in the first patient, that led to bronchial artery injury, this technique was aborted in the following 4 patients in whom dissection was started posterior.

After fistula repair, bulky muscle should be used to protect the bronchus and to close the infected cavity. Serratus anterior muscle flap was used in 3 patients in whom serratus sparing thoracotomy was done, and latissimus dorsi muscle flap in the remaining 2 patients, in spite of previous cutting of this muscle, revascularization of distal part of this muscle is observed after this long period allowing its successful use. However serratus anterior muscle is better to be used if serratus sparing thoracotomy was done in primary surgery as this muscle will be more bulky than the previously incised latissimus dorsi muscle.

Large chest tube was used for drainage at the end of the procedure, but this technique was followed by persistent infection. In the remaining 3 patients, Claggett procedure was used for better drainage and better outcome after surgery.

Our mortality rate of this serious complication was 60%, this coincide with the international mortality rates of 20%-70% \[2,5,9,14\]. The use of Claggett procedure in the last 3 patients was associated with reduced post operative mortality in one out of 3 patients, compared with 2 of 2 patients when large chest tube was used.

**Conclusion:**

Post pleuro pneumonectomy bronchial stump dehiscence is a very rare complication with high mortality rate. These very special type of fistulae are due to mediastinal radiation as there is long latency between the primary surgery and the onset of the fistula. It is well known to thoracic surgeons that radiation-induced vascular obliterations are likely to cause delayed healing of the bronchial anastomosis and consequently bronchial stump fistula and leakage. Improvement of radiation techniques using conformal radiotherapy or more complex planning using intense modulated radiotherapy may improve the dose distribution but it is highly complex and time consuming.

Marking of the bronchial stump during surgery with surgical clip helps marking and shielding of the stump during radiation therapy.

Proper surgical techniques during primary surgery, preservation of bronchial blood supply, short bronchial stump and proper covering of all right sided stump aiming at avoiding some co factors for stump dehiscence.

This fatal complication should be diagnosed and treated early before infection spreads deeply in the chest wall, preferably using the same thoracotomy incision with Claggett procedure to be done at the end of surgery.

**REFERENCES**


Delayed Bronchial Stump Dehiscence Following Trimodality Treatment


