

Pleurodesis as a Palliative Treatment of Advanced Lung Cancer with Malignant Pleural Effusion

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ABSTRACT

Purpose: This study was conducted to evaluate the success rate of management of advanced. Lung cancer patients with malignant pleural effusion comparing talc powder with tetracycline for pleurodesis.

Patients and Methods: We report 60 patients with lung cancer associated with malignant pleural effusion treated in the department of surgery NCI, Cairo University, between January, 1998 and February, 2003.

Patients were Divided Into Three Groups:

- Group I: Pleurodesis using tetracycline (20 patients).
- Group II: Pleurodesis using talc slurry (20 patients).
- Group III: Pleurodesis using talc insufflation (20 patients).

Good response to pleurodesis is defined as no pleural fluid re-accumulation or minimal pleural fluid re accumulation not causing symptoms or requiring further aspiration for one month.

Results: There were 34 males and 26 females, mean age was 54 years with range of 42-66 years, right sided effusion was present in 32 patients (53%) and left sided in 28 patients (47%).

Pathological subtypes were adenocarcinoma in 32 patients, squamous cell carcinoma in 18 and undifferentiated carcinoma in 10 patients. In group I, 12 patients (60%) showed good response to intra pleural tetracycline, 15 patients (75%) responded in group II, while 17 patients (85%) showed good response in group III. Post pleurodesis complications included, fever, chest pain and empyema.

Conclusion: It is concluded from this study that thoracoscopic talc insufflation was an effective, easy and low cost method for producing pleurodesis in patients with recurrent malignant pleural effusion and proved to be better than talc slurry and tetracycline.

Key Words: Lung - Malignant - Effusion - Pleurodesis.

INTRODUCTION

Malignant pleural effusion represents the majority of effusions in patients over 60 years, accounting for nearly 50% of the newly diag-

nosed exudative pleural effusion in adults and for 28-61% of pleural effusion in hospitalized patients [1]. Pleural effusion is a common complication in patients with malignancy occurring in 50-70% in the course of their illness [2].

Carcinoma of any organ can metastasize to the pleura, however, carcinoma of the lung is the commonest malignancy to invade the pleura and produce malignant and paramalignant pleural effusion [3].

Lung cancer accounts for nearly 36% of all cases with malignant pleural effusion, when carcinoma of the lung metastasize to the pleura, both visceral and parietal surfaces tend to be involved. The mechanisms involved in the formation of the malignant pleural effusion are:

Impaired lymphatic drainage, altered microvascular permeability of the pleural vessels and actual invasion of the pleura by malignant cells [4].

Adenocarcinoma is the most common cell type to involve the pleura because of its peripheral location and spread by contiguity, followed by anaplastic and undifferentiated types, while squamous cell carcinoma rarely produce effusion [5].

The diagnosis of malignant pleural effusion is usually straight forward, the only difficulty exists when a patient without a known primary cancer present with an exudate [6].

On plain chest roentgenogram, evidence of underlying lung cancer is often seen, but may be obscured by effusion [7].

Thoracentesis is a simple and essential step in the diagnosis of malignant pleural effusion, cytological examination of aspirated pleural fluid is the gold standard for diagnosis [6]. At least 250ml of the pleural fluid should be obtained, small amount often contains too few cells for adequate study and more than one thoracentesis may be required to prove that this effusion is malignant [8]. Chromosomal analysis of the cells found in pleural space is sometimes useful in suspicious cases, but it doesn't provide histopathological diagnosis [8]. Closed pleural biopsy using Abram's needle is indicated when first thoracentesis failed to yield positive results [8].

When two or more studies of the pleural fluid including pleural biopsy do not provide a diagnosis, pleuroscopy and biopsy under direct vision is probably the last choice with a diagnostic yield of 93-96% [9].

Thoracoscopy and biopsy may be necessary to confirm the diagnosis with high diagnostic yield approaching 100%, while the yield of pleural fluid cytology alone is 25% and that of combined pleural fluid cytology and closed pleural biopsy is 40% [10]. Patients with malignant pleural effusion have significantly short survival and the treatment is usually palliative [11], it should be remembered that not all malignant pleural effusion require treatment, the criteria for instituting therapy for malignant effusion are based on the frequency and pattern of reaccumulation in addition to the degree of symptomatic compromise.

Pleurodesis is the process by which fibrosis is induced between the visceral and parietal pleurae in order to obliterate the pleural space. It is the most commonly used method for palliation of malignant pleural effusion [12].

A variety of agents could be used to induce pleurodesis and are classified into two broad categories according to their modes of action, cytostatic agents (that control the effusion by reducing the tumor volume) and sclerosants (which produce a chemical pleurisy that lead to formation of adhesions and subsequent obliteration of the pleural space) [13].

Among these substances, tetracycline, a broad spectrum antibiotic can be used with a dose of one gram in 50ml of normal saline

injected through the chest tube [6]. Its mechanism of action is not well known, the main side effects of tetracycline pleurodesis are fever (33%) and pain (31%) [14]. Unfortunately, the commercial unavailability of tetracycline has prompted consideration of alternative agents for induction of pleurodesis, of those, talc powder is the commonest used agent. The mechanism by which it causes pleural fibrosis is not well understood, it's often assumed that adhesion caused by talc powder is caused by an inflammatory reaction. The dose of talc powder required for effective pleurodesis is between 5-10gms [15]. The methods of administration of talc powder are: At the time of thoracotomy, through thoracoscopy (Powderage) and through the chest tube (Slurry).

Talc related complications are, pain, fever, surgical emphysema, pleural thickening and acute pneumonitis [12].

Other methods of pleurodesis are intrapleural chemotherapy, blood pleurodesis, Nd: YAG Laser pleurodesis and pleural abrasions.

The aim of this work is to evaluate the palliative effect of management of malignant pleural effusion comparing talc powder (either through thoracoscopic insufflation or injection through chest tube) versus tetracycline for pleurodesis.

PATIENTS AND METHODS

Sixty patients with malignant pleural effusion from lung primaries underwent pleurodesis using thoracoscopic talc insufflation, talc slurry and tetracycline as a palliative treatment for recurrent malignant pleural effusion between (Jan. 1998 - Feb. 2003).

All Patients were Subjected to:

- Full history taking and full clinical examination.
- Chest radiographs, posteroanterior and lateral views.
- CT scan of the chest.
- Documented malignant pleural effusion of lung primary.
- Full laboratory investigations.

Patients were Divided Into 3 Groups:

Group I: Included 20 patients subjected to pleurodesis using tetracycline.

Group II: Included 20 patients in whom talc powder slurry was the method used for pleurodesis.

Group III: Included 20 patients, in whom thoracoscopic talc powderage was used for pleurodesis.

Technique:

Group I:

- Premedication with atropine sulphate (0.02mg/kg body weight) and 5-10mg diazepam.

- Chest tube insertion to drain the pleural effusion and after complete evacuation, 20-25mg/kg of tetracycline is diluted in 50ml normal saline and instilled in the chest tube.

Group II:

The patients were premedicated with atropine sulphate and diazepam.

After insertion of the chest tube and the output is less than 50ml/24hrs, 5-10gm of purified talc powder was mixed with 100ml normal saline and 10ml of 2% lidocaine to form suspension which was instilled into the chest tube, clamped for 2hrs and then removed.

Group III:

Ten cc of 2% xylocain is injected locally at the site of port introduction, General anaesthesia used in incooperative patients.

Zero angled telescope was used, suctioning the pleural effusion, a powder blower was filled with 5-10gm of purified talc powder and insufflated into the pleural cavity followed by removal of the chest tube when daily output was less than 50ml.

Chi-square test was used to compare independent proportions.

After discharge all patients were followed-up every 2 weeks in the 1st month by chest radiograph and then monthly interval till death.

Good response was defined as no pleural fluid reaccumulation during the follow-up period or pleural fluid reaccumulation not causing symptoms or requiring further aspiration for one month.

RESULTS

Sixty patients with malignant pleural effusion were included in this study. There were Thirty-four males and twenty six females, the mean age was 54 years with range between 42-66 years, right sided effusion was present in 32 patients (53%) and left sided effusion in 28 patients (47%).

Pathological subtypes were, metastatic adenocarcinoma in 32 patients, squamous cell in 18 and undifferentiated carcinoma in 10 patients (Fig. 1).

Group I:

Table (1) shows the success rate of different types of pleurodesis. In group I twelve patients (60%) showed good response to intrapleural tetracycline. Eight patients (40%) showed treatment failure i.e. there were rapid reaccumulation of the pleural fluid. Treatment related complications developed in 6 patients (30%).

Group II:

Good response was evident in 15 patients (75%) and treatment failure developed in 5. Complications were observed in 3 patients. Figs. (2,3) show massive right sided pleural effusion before and one month following talc powder slurry.

Group III:

In this group, 17 patients (85%) showed good response to intrapleural talc insufflation, the remaining 3 patients failed to respond to treatment. Figs. (4,5) show massive left sided pleural effusion before and one month after thoracoscopic talc powder insufflation. Four patients developed postoperative complications. Table (2) presents the complication rate of different types of pleurodesis.

Although the success rate of talc insufflation is higher than that of talc slurry (85% versus 75%), and the success rate of talc slurry is better than tetracycline pleurodesis (75% versus 60%), but these differences is not statistically significant (p value = 0.2).

Also the complication rate of tetracycline pleurodesis was higher than that of talc powder pleurodesis, yet this difference is not statistically significant (p value = 0.5).

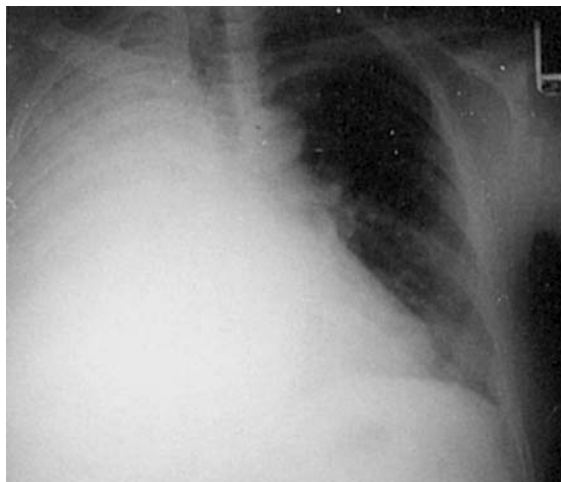
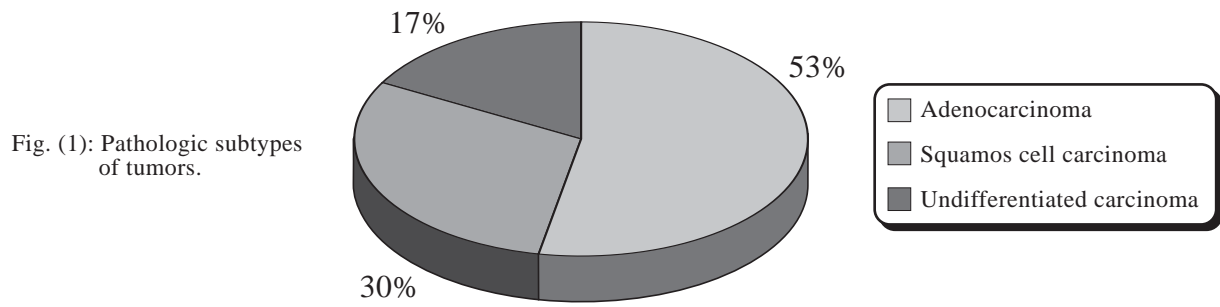


Fig. (2): Massive right sided effusion.



Fig. (3): One month following talc slurry.

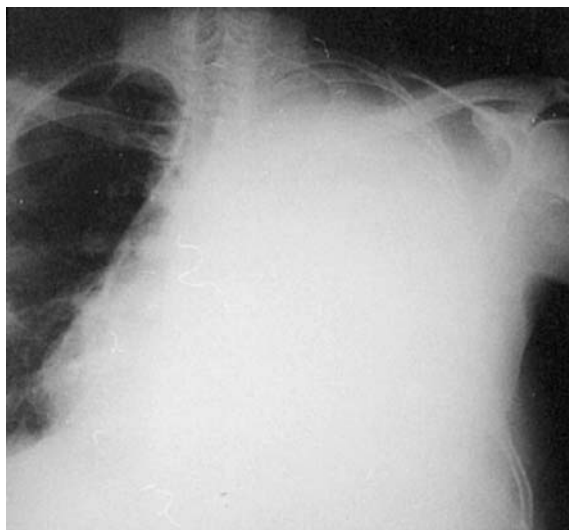


Fig. (4): Massive left sided effusion.



Fig. (5): One month post thoracoscopic talc insufflation.

Table (1): Results of different types of pleurodesis.

Type of pleurodesis	% of success	% of failure
Tetracycline	60	60
Talc slurry	75	75
Talc powdrage	85	85

Table (2): complication rate of different types of pleurodesis.

Type of pleurodesis	Fever and empyema	Chest pain	Total No. of patients	Percentage
Tetracycline	3/20	3/20	6	40
Talc slurry	1/20	2/20	3	15
Talc insufflation	1/20	3/20	4	20

DISCUSSION

According to underlying disease, many patients with malignant pleural effusion may live for months or even years. The quality of life for such patients is therefore of much importance and the aim of treatment should be beside the management of the primary disease, is to relieve symptoms, and to decrease the discomfort of the patient. The necessity for repeated aspirations to relieve dyspnea is both physically and psychologically traumatic to the patient and a burden to the physician [16].

In recent years chemical pleurodesis has become the preferred treatment for symptomatic malignant pleural effusion. Many sclerosing agents have been tried for creating pleural symphysis with variable degrees of success. In this study, sixty patients were available for follow-up, in group I (pleurodesis by tetracycline) 12 patients (60%) showed good response, in group II (pleurodesis by talc slurry) 15 patients (75%) showed good response while in group III (pleurodesis by talc insufflation) 17 patients (85%) showed good response.

The success rate of thoroscopic talc powderage achieved in this study is the same as that obtained by Weissberg 1993 who reported a success rate of 84.5% after performing thoroscopic talc pleurodesis in 169 patients with malignant pleural effusion [9].

Thomas 1993, also reported 90% success rate after performing thoroscopic talc insufflation in 14 patients with malignant pleural effusion [6].

Brungel et al. (2002), achieved success rate of 95.6% following thoroscopic talc pleurodesis, with failure in 2 patients out of 46 [17]. Cardillo et al. (2002) reported success rate of 93% (558 out of 600) after thoroscopic talc pleurodesis [18].

The use of thoracoscopy in talc pleurodesis helps in lysis of adhesions when necessary, insures equal distribution of talc over the pleural surfaces and assesses the effect of positive pressure ventilation on trapped lung to look for it's ability to re-inflate. These advantages contributes to the high success rate of thoroscopic talc powderage if compared with the results obtained after talc slurry.

Webb and associates 1992, achieved 100% success rate after using talc slurry in 28 pateints with malignant pleural effusion. compared with 75% response rate in our study. The procedure was well tolerated without any side effects [15].

The results obtained by Shedbalker et al. (1971), were comparable to the results of this study. They used talc. Slurry in 28 patients with complete success in 20 patients (71.4%), partial success in 2 (7.6%) and rapid fluid re-accumulation in 6 (21%).

These low results were contributed by the authors to be due to clumping of talc over the pleural surfaces [19].

Erickson et al. (2002), showed response rate to tube thoracostomy of 77% compaired to 100% success rate following thoroscopic talc powderage [20].

The major advantage of talc slurry over thoroscopic talc powderage is that in talc slurry, talc is injected into the pleural cavity after making sure that the lung is fully expanded, in contrast to the thoroscopic talc powderage in which talc is insufflated before inflation of the lung takes place, thus the risk of non inflation of the lung as a cause of failure of thoroscopic talc powderage can be abolished if talc slurry is used.

The results obtained after the use of sclerosants other than talc are generally lower. Bayly et al. (1978), reported a success rate of tetracy-

cline pleurodesis of 67% in 12 patients with malignant pleural effusion [21], which is comparable to our results. Tag El Dien et al. (1985), reported a success rate of 60% after tetracycline pleurodesis in 12 patients with malignant pleural effusion [14].

The advantages of tetracycline over talc powder as a pleural sclerosant is its easy use and a fewer side effects other than fever and pain.

Different doses of talc have been recommended by many authors, Hartman et al. (1993), reported that the intrapleural administration of 3-6gms of aerosolized talc controlled the pleural effusion in 95% of patients in their series. comparable results have also been obtained after performing talc slurry [22]. Webb and associates (1992), reported 100% success rate of talc slurry, after using 5gms of talc and 3gms of thymol iodine in 50ml saline solution [15].

Many complication have been noticed after the use of talc as a pleural sclerosant. The degree of pain associated with talc has been variously reported from non existing to severe. Walke-Renard and colleagues (1994), reported a pleuritic chest pain after thoracoscopic talc insufflation in 9 out of 131 patients (7%) with malignant pleural effusion that responded to mild analgesics [23]. In our study although all patients complained of mild pain related to thoracoscopic procedure and intercostal tube drainage that responded to simple analgesics, only five patients (12.5%) experienced severe chest pain which necessitates the use of strong analgesics. Fever following talc pleurodesis is common. Aelony and co workers (1991), noted temperature elevation varying from low to high grade in 21 out of 39 patients (54%) [24] which is comparable to 63% percent incidence noted in the study of Lisa and colleagues [11]. They stated that temperature elevation was not a predictor of other complications such as respiratory failure or empyema. The incidence of fever after the use of talc pleurodesis is 5%, which is much lower than that described in above mentioned studies.

Todd and colleagues (1980) reported an incidence of empyema of 3% after performing thoracoscopic talc powderage in 163 patients with malignant pleural effusion [25]. Two patients (5%) developed empyema in our study.

Cardillo et al. (2002), reported this complication in 3.1% of patients following thoracoscopic talc powderage [18].

Asbestos-free talc powder is not widely available in Egypt, we have not used talc as a sclerosant except in patients with malignant pleural effusion, as the life expectancy of such patients is much less than the latent period needed for the development of asbestos-related neoplasia. There has been some concern about the use of talc pleurodesis in patients with benign disease, as respiratory functions may be impaired.

Lang and associates (1988), observed only mild restrictive impairment 22-35 years after talc pleurodesis for spontaneous pneumothorax, total lung capacity averaged 89% of the predicted value [26]. This complication needs long follow-up period and was not studied in this series

In Conclusion:

Talc powder is the most effective pleural sclerosant. It has the best results among all chemical agents used. The administration of talc during thoracoscopy (powderage), is better than talc slurry. Thoracoscopy provides better visualization of the pleural cavity, thus ensuring equal distribution of talc, allows biopsy taking if needed, cutting of adhesions if present and coagulation of any bleeding vessel. The least side effects were reported with thoracoscopic talc powderage. Talc dusting during thoracotomy, although has a better results, carries the risk of major operation and so, has no advantage over the thoracoscopic talc powderage. Before performing thoracoscopic talc powderage the ability of the lung to reexpand should first be detected by noting relief of dyspnea and a radiological evidence of re-inflation after a simple thoracocentesis has been carried out. Also, a C.T. of the chest to exclude pleural thickening and fiber-optic bronchoscopy to exclude endobronchial lesion that will prevent lung aeration are very important for proper selection of cases. The procedure under local anesthesia is much easier, well tolerated by the patient and has fewer side effects.

Any patient with malignant pleural effusion, can get benefit of this procedure provided that the effusion is drained completely and the lung is fully expanded after evacuation of the effusion.

The difference in success and complication rates of different types of pleural sclerosants did not reach a statistical significant value, however, there is a trend to use talc powder for plerodesis in malignant pleural effusion preferably by thoroscopic talc powderage due to its higher success rate.

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