INTRAPLEURAL APPLICATION OF DIMEXID® WITH ANTIBIOTICS FOR THE TREATMENT OF PLEURAL EMPYEMA/THORACIC EMPYEMA

MIEJSCOWE STOSOWANIE DIMETYLOSULFOTLENKU (DIMEXID®) Z ANTYBIOTYKAMI W LECZENIU ROPNIAKA OPŁUCNEJ

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SUMMARY

Objective: The aim of the study was to analyze the results of conservative treatment for postoperative pleural empyema with the help of dimethylsulphoxide (Dimexid®).

Material and Methods*:* 58 patients with pleural empyema. There were 3 groups: group 1 with complications after heavy lung inflammations (n=17); group 2 with purulent destruction of the lung (n=18); group 3 with postoperative complications after thoracic surgery (n=11), including 7 cases with bronchial fistulas after surgeries for malignant disease; group 4 with purulent destruction of the lung (n=5) that demanded emergency operative intervention; group 5 with posttraumatic empyema (n=7). All the patients received a combination of antibiotics intravenously and, in addition, antibiotics were also administered by infusion into the pleural cavity after dissolution them in Dimexid®. It is a universal solvent and it helps to penetrate inflammatory tissue.

Results: This treatment was well-tolerated, it increased postoperative survival in patients with pleural empyema and it was useful as additional treatment for the management of not only parapneumonic and posttraumatic but also of postoperative empyemas with small bronchial fistulas.

Conclusions: Absence of mortality and a success treatment rate of 95% in our study should be confirmed by a prospective randomised study.

Key words: pleural empyema, bronchial fistula, Dimethylsulfoxide (DMSO).

STRESZCZENIE

Celem badania była ocena skuteczności stosowania do opłucnej wlewów antybiotyków rozpuszczonych w Dimetylosulfotlenku.

Materiał i metody: Leczono 58 chorych z ropniakami opłucnymi spowodowanymi różnymi przyczynami: l grupa (n=17) – powikłania ciężkich zapaleń płuc, 2 grupa (n=18) – ropna zmiana płuc, 3 grupa (n=ll) – powikłania po operacjach torako-chirurgicznych, w tym 7 z przetoką oskrzelową przy chorobach nowotworowych, 4 grupa (n=5) – ropna zmiana płuc, która wymagała doraźnej interwencji chirurgicznej na płucach, 5 grupa (n=7) – ropniak opłucnej z powodu różnych urazów klatki piersiowej.

We wszystkich grupach antybiotyki podawano nie tylko dożylnie ale również do jamy opłucnej po rozpuszczeniu ich w Dimetylosulfotlenku (DMSO), który tkankę w obrębie ogniska czyni przepuszczalną dla antybiotyków.

Wyniki: Opracowana metoda leczenia była dobrze tolerowana przez pacjentów. Pooperacyjne stosowanie miejscowej antybiotykoterapii w skojarzeniu z DMSO zwiększa szansę chorych z ropniakiem opłucnej na przeżycie i prowadzi do trwałego wyleczenia około 95% chorych, nawet z przetoką oskrzelowo-opłucnowej.

Wnioski: Otrzymany przez nas pozytywny rezultat jest podstawą dla prospektywnych badań.

Słowa kluczowe: ropniak opłucnej, Dimetylosulfotlenek (DMSO, Dimexid®).

INTRODUCTION

Dimethyl sulfoxide (DMSO, brand name: DIMEXID) is an amphipathic molecule soluble in both aqueous and organic media. It is one of the most common solvents for the in vivo administration of several water-insoluble substances. DMSO has been frequently used as a solvent in biological studies and as a vehicle for drug therapy [1]. The last is very important as aminoglycosides concentration is not detected in pleural pus after systemic administration because they either do not penetrate the blood-pleural barrier in empyema or are bio-inactivated by the pleural pus.

The aim of the study was to analyze the efficiency of local treatment for pleural empyema with the help of dimethylsulphoxide plus antibiotics.

MATERIAL AND METHODS

58 patients with pleural empyema have been divided into five groups (table 1): group 1 with complications after heavy lung inflammations (n=17); group 2 with purulent destruction of the lung (n=18); group 3 with postoperative complications after thoracic operations (n=11), including 7 cases with bronchial fistulas after surgery for malignant disease; group 4 with purulent destruction of the lung (n=5) that demanded emergency operative intervention; group 5 with posttraumatic empyema (n=7).

All of the patients received systemic combination of three antibiotics according to sensitivity of microorganisms. In addition, antibiotics were administered by infusion into the pleural cavity after their dissolution in Dimexid.

The patients in the first group were treated with daily thoracocentesis and saline rinsing (0.9% sodium chloride). The procedure was repeated until the fluid became clear (a total of 200–500 ml of saline), then antibiotics dissolved in DMSO were instilled.

All the patients of the second group were drained on the first day of hospitalization. The irrigation fluids were normal saline containing either the antiseptic Dioxidini 10% or DMSO+antibiotic. After the operation, when negative Gram stain from the pleural fluid was received, the pleural space was filled with Dimexid debridement antibiotic solution (DDAB solution: DMSO, cefotaxime 1000 mg/L, amycacini 500 mg/L, and metronidazole 500 mg/L), and the drainage catheters were removed.

In the third group, malignancy in 7 patients was the indication for pneumonectomy, and chronic pulmonary abscess in 4 patients was the indication for lobectomies. A bronchopleural fistula was present in 7 patients after pneumonectomy. Three patients were treated by chest-tube drainage and pleural cavity lavage via drainage tube. The lavage fluid was normal saline containing either the antiseptic *Dioxidiny10%* or a broad combination spectrum of antibiotics dissolved in 50% DMS. The regimen for treatment of one patient with delayed postpneumonectomy empyema and small bronchial fistula (< 3mm) was parenteral antibiotics and serial thoracocentesis. One case of postpneumonectomy empyema with bronchopleural-cutaneous fistula was treated by systemic antibiotics, daily saline rinse and local instillation of 50% DMSO. In two patients with bronchial fistula, the treatment included parenteral antibiotics, open-window thoracostomy, debridement of the pleural cavity, and open pleural packing with wet dressings of 25% DMSO+antibiotics (150–300 ml). That pleural packing was repeated every second day, until the chest cavity was macroscopically clean, but no more than ten procedures successively.

When the pleural cavity had healthy granulation tissue and no bronchopleural fistula (three- to four-week period), the thoracostomy was closed by obliteration of pleural cavity with DMSO+antibiotic solution.

In the fourth group of patients with community-acquired pneumonia complicated by purulent destruction of a lung, an advanced intoxication and an inefficiency of conservative treatment within 24 hours were indication to pneumonectomy. In the postoperative period, a double lumen tube was used for irrigation with either the antiseptic Dioxidini 10% or a broad spectrum antibiotic combination of usually three antibiotics: β lactam antibiotics (cephalosporins), aminoglycosides (amycacini) and metronidazole initially dissolved in 50% DMSO.

The posttraumatic empyema of the thorax (group 5) was a secondary infection following repetitive drainages of the pneumothorax in two patients and the infection of the retinated haemothorax in three others. Video-assisted thoracoscopy (VATS) was successfully used by us for sterilization, a sufficient lung expansion and, finally, for inserting thoracic drain for lavage of the pleural cavity with DDAB solution.

RESULTS

The average time of hospitalization was 33 days for all the patients with different pleural empyemas.

Table 1. Average time of hospitalization

group	Empyema caused by	Number of patients	Days x±SD
1	Postpneumonia	17	24±4,8
2	Pyogenic lung destruction, delayed operations	18	39±5,6
3	Planned operations (lobectomy, pneumonectomy) for malignant disease and benign lesions.	11 (including 7 patients with bronchopleural fistulas)	45±8,3
4	pulmonary destruction, urgent operations (pneumonectomy)	5	25±4,8
5	posttraumatic	7	27±3,1
total		58	33±10,1

The longest time of hospital stay was observed in the third group. 7 patients in the group had bronchopleural fistulas (p=0.0002, t-test Student). Positive radiological dynamics of treatment of a fistula in patient "A" is presented in figures 1, 2, 3. In this case, the method of systemic antibiotics and DMSO irrigation via chest-tube drainage was applied. A catheter was placed through the fistula, and 10 ml of 50% DMSO with antibiotics were instilled daily into the pleural cavity for 15 days. Treatment was well-tolerated, and the empyema resolved completely with no evidence of recurrence after 7 months of follow-up.

The method, including systemic antibiotics, daily saline rinse and local instillation of 50% DMSO was used successfully in patient "B" with bronchopleural-cutaneous fistula, and his X-ray changes are presented in figures 4, 5, 6.

Radiological results of treatment of patient "C" with a postpneumonectomy bronchial fistula by means of parenteral antibiotics and serial thoracocentesis are shown in figures 7, 8 and 9.

Patient "D" had an empyema with bronchial fistula on the thirteenth day after pneumonectomy (fig. 10, 11) and the method of the DMSO open-window treatment was successfully applied (fig. 12, 13).

The differences in terms of hospitalization among the patients in the second and fourth groups support the tactic of early radical operation of lung destructive process, however, it is not always possible because of the patients' bad condition and the necessity of preoperative treatment with the application of DMSO and antibiotics.

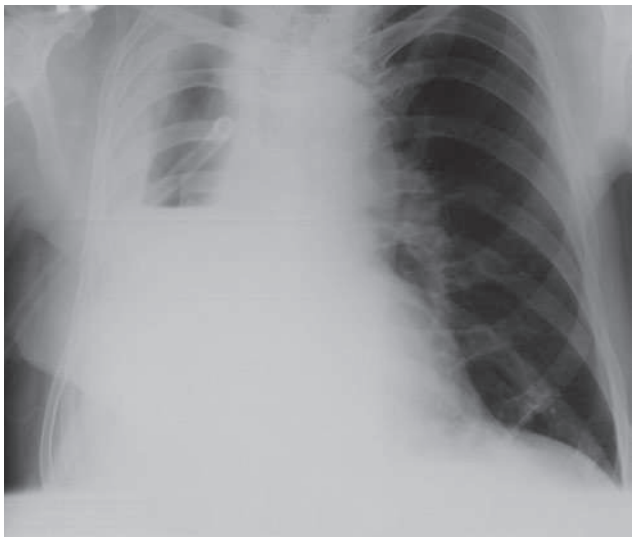

Fig 1. Patient A. 29th day after pneumonectomy (lung cancer). Empyema with bronchial fistula 7mm Ø

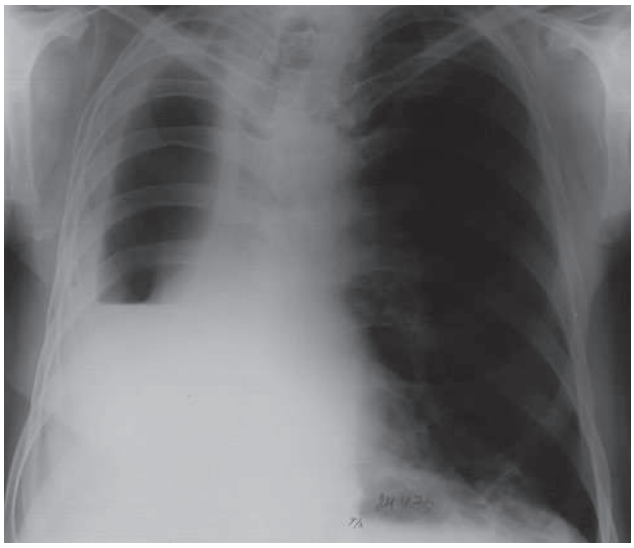

Fig. 2. Patient A. 55th day after pneumonectomy

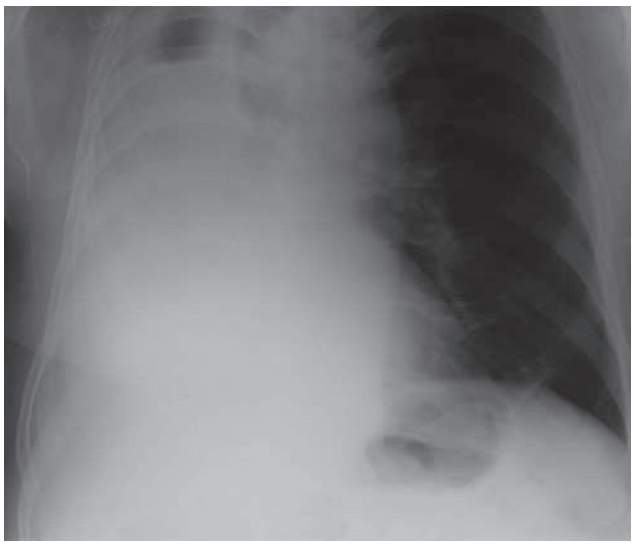

Fig. 3. Patient A. 155th day after pneumonectomy

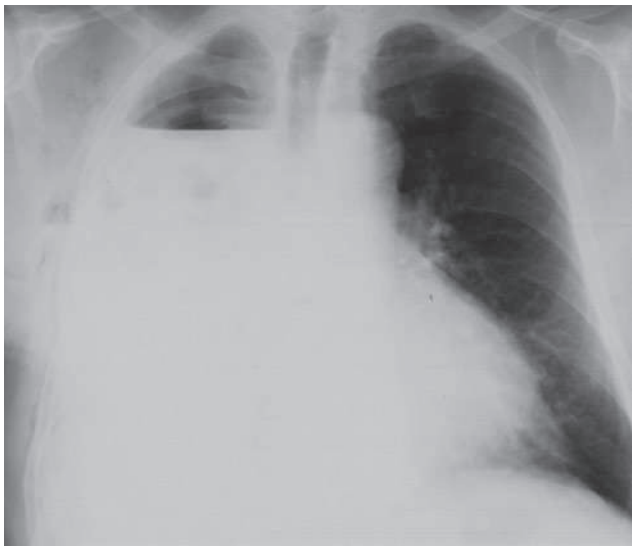

Fig 4. Patient B. 9th day after pneumonectomy (lung cancer). Empyema with bronchopleural-cutaneous fistula

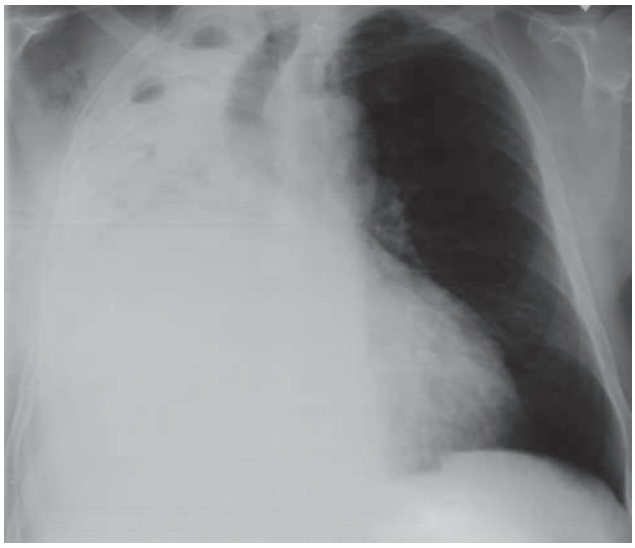

Fig 5. Patient B. 16th day after pneumonectomy (seventh day from the beginning of treatment by local instillation of 50% DMSO)

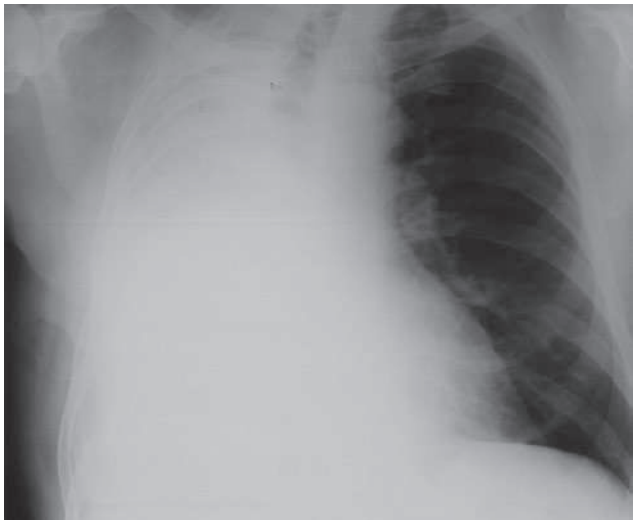

Fig 6. Patient B. 32nd day after pneumonectomy (symptoms of an empyema are absent)

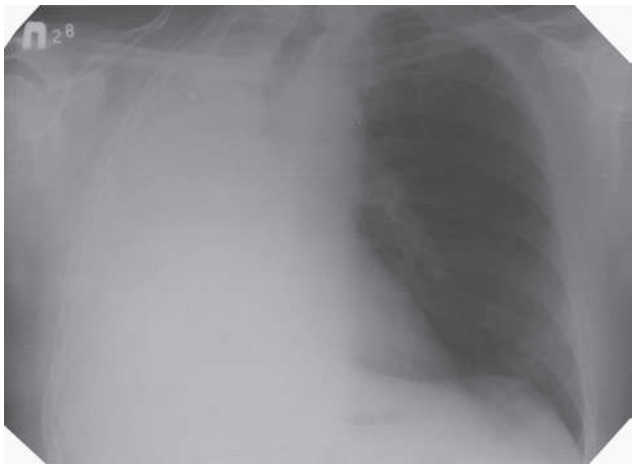

Fig 7. Patient C. 175th day after pneumonectomy (periferal cancer). Empyema with bronchial fistula 1mm Ø after radiotherapy.

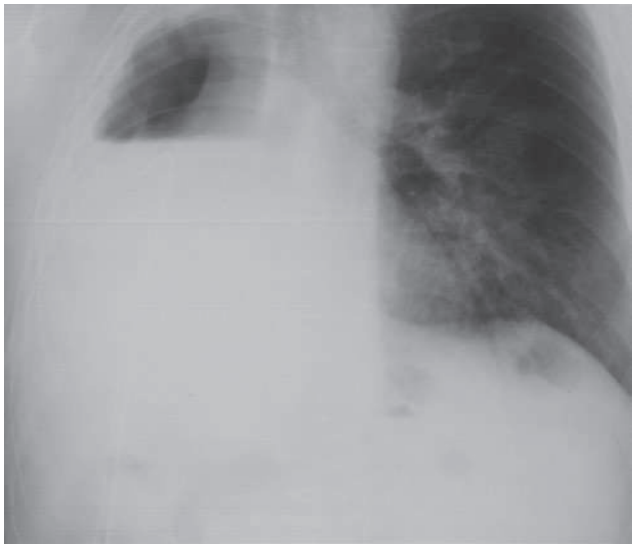

Fig 8. Patient C. 185th day after pneumonectomy. 10th day after serial suction thoracocentesis with saline irrigation and instillation DMSO+antibiotic

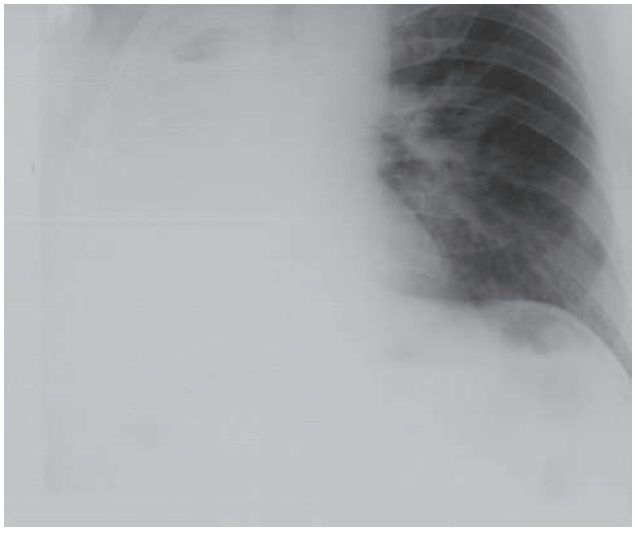

Fig 9. Patient C. 203nd day after pneumonectomy (lung cancer). The patient without clinical and laboratory signs of infection

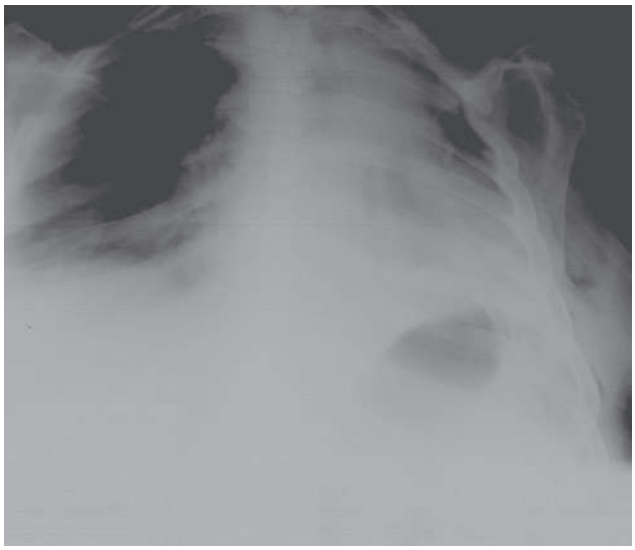

Fig.10. Patient D. 5th day after pneumonectomy (lung cancer)

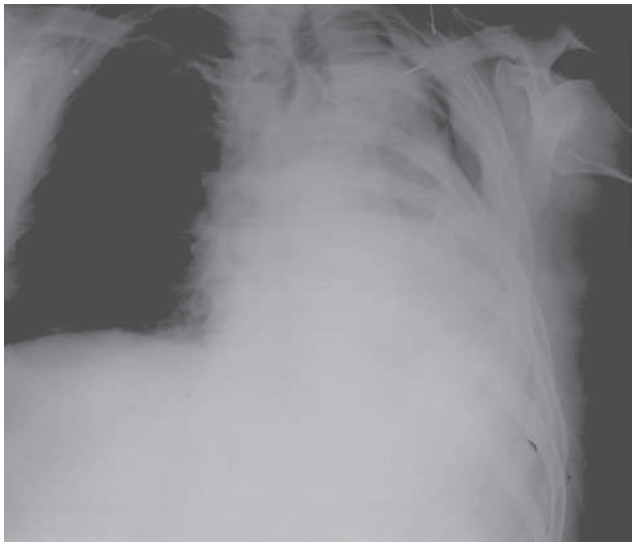

Fig 11. Patient D. 13th day after pneumonectomy (lung cancer). Empyema with bronchial fistula

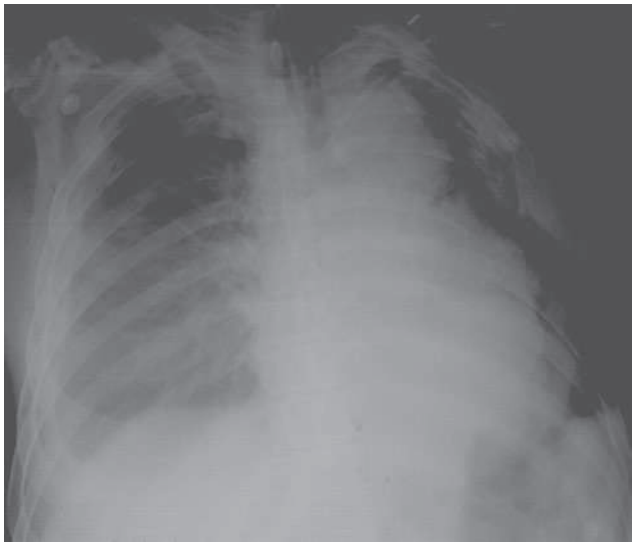

Fig. 12. Patient D. 18th day after pneumonectom (lung cancer). Empyema with bronchial fistula. Open-window thoracostomy

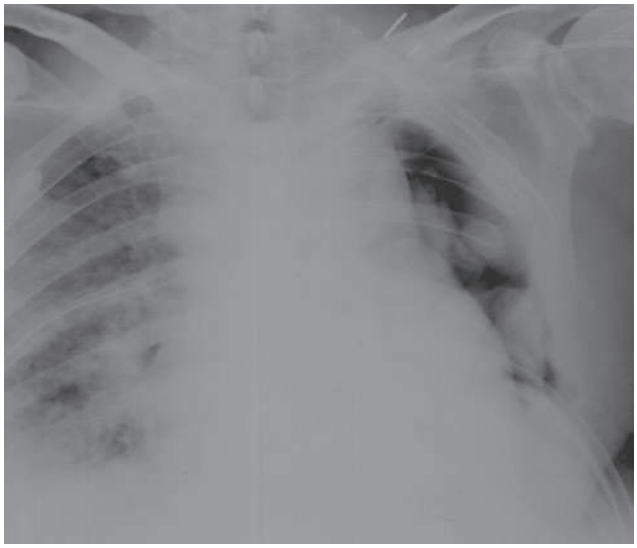

Fig.13. Patient D. 30th day after pneumonectomy. 12th day after thoracostomy and threatment with open pleural packing with DMSO

DISCUSSION

Treatment of pleural empyema depends on the etiology and the staging of the disease that is, the duration of the infection before the diagnosis, the appearance and location of the pleural fluid in the pleural space, and the results of microbiological investigations. The published reports contain data on these aspects of empyema.

The principle of treatment with local instillation of antibiotics into the pleural space is supported by experimental [2] and clinical studies [3].

Systemic administration of antibiotics achieves adequate drug concentrations in normal, uninfected pleural fluid but fails to do this in the case of empyema [4], which may explain the advantage of the local instillation of antibiotics, fibrinolytic agents (streptokinase, urokinase or recombinant deoxyribonuclease) [5] and antiseptics [6].

Teixeria L.R. et al. have shown, using rabbit model of empyema, that the degree to which the different antibiotics penetrated into the infected pleural space was highly variable. Penicillin penetrated most easily, followed by metronidazole, ceftriaxone, clindamycin, vancomycin, and gentamicin [7].

Various antiseptics solutions can be used for pleural space irrigation/sterilization for example saline-iodine [8], gentian violet [9], dioxidini et cetera.

The choice of the DMSO is also caused because of its anti-inflammatory [10] and antiseptic properties [11].

In a clinical study, patients treated by cyclical irrigation of the pleural space with antibiotics had

a shorter hospital stay and duration of wound drainage than those who underwent decortication or thoracoplasty [12]. Pleural space irrigation followed by obliteration of the pleural space with an debridement antibiotic solution required one surgical procedure and resulted in significantly shorter hospitalization and decreased morbidity in patients with early postpneumonectomy empyema [13].

In conclusion, treatment with systemic antibiotics, repeated thoracocentesis, saline rinsing, and local instillation of antibiotics dissolved in DMSO seems to be appropriate for many patients with empyema of different etiologies. Moreover, a minimally invasive approach might achieve satisfactory results in selected patients with a postpneumonectomy empyema even when there is minor bronchopleural fistula presenting [14].

CONCLUSIONS

Our result confirms researches of other authors as far as efficiency of application of DMSO for treatment of a surgical infection [15].

Intrapleural application of solutions DMSO with antibiotics improves the efficiency of treatment of advanced pleural empyema and can be useful as additional treatment for the management of not only parapneumonic and posttraumatic but also postoperative empyemas with small bronchial fistulas.

Absence of mortality and a success treatment rate of 95% in our study should be confirmed by a prospective, randomised study.

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