

ABSTRACT

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LONG-TERM OUTCOMES OF TUBERCULOUS PLEURISY TREATMENT WITH REGARD TO DIAGNOSTIC TECHNIQUE USED FOR PLEURAL EFFUSION SYNDROME DIAGNOSIS

Introduction. Despite the overall positive epidemiological trend, the burden of tuberculosis in Ukraine remains significant. The most common form of extrapulmonary TB is tuberculous pleurisy. The share of the latter in the structure of all tuberculosis forms is within 10–12% or more. The clinical picture of specific pleurisy is diverse, so its diagnosis is often complicated and ultimately leads to various negative consequences. The authors suggested using a diagnostic system based on ultrasound findings to detect pleural effusion syndrome.

Methods. We examined 329 patients with tuberculous pleurisy, who were divided into two groups. There were 142 subjects in the main group and 187 subjects in the comparison group. The radiodiagnostic examination was based on traditional chest radiography. The patients of the main group were examined according to the pleural diseases diagnostic algorithm implemented by the fellows of the department (utility model patent of Ukraine No. 114430).

Results. In the long-term period, residual changes (thickening) in the pleural cavity were found in 6.8% of patients in the main group vs. 19.8% of patients in the comparison group ($p < 0.05$), changes in diaphragmatic skeletopy were observed in 13.5% vs. 25.9%, respectively ($p < 0.05$), and diaphragmatic mobility disorder – in 5.4% vs. 18.5%, respectively ($p < 0.05$). Patients with tuberculous pleurisy who had been examined according to the proposed algorithm developed chronic pleurisy 7.1 times less often (1.4% vs. 9.9%, $p < 0.05$) and pulmonary disease – 2.7 times less often (4.1% vs. 11.1%, respectively, $p > 0.05$).

Conclusion. Taking into account the early detection of pleural effusion and timely verification of the disease, the proposed diagnostic algorithm for pleural diseases allows to reduce the long-term effects on the chest wall, lungs, and pleura.

Keywords: pleural effusion syndrome, pleurisy, tuberculosis, diagnosis, long-term outcomes.

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РЕЗЮМЕ

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Вступ. Попри загальну позитивну епідеміологічну тенденцію, тягар туберкульозу в Україні залишається значним. Найбільш частою формою позалегенових його форм є туберкульозний плеврит. Питома вага останнього у структурі всього туберкульозу знаходиться у межах 10–12 % і більше. Клінічна картина специфічного плевриту різноманітна, тому діагностика його часто ускладнена та призводить, у підсумку, до різних негативних наслідків. Автори запропонували застосовувати для виявлення синдрому плеврального випоту систему діагностики, в основі якої лежить ультразвуко-копія.

Методи. Нами було обстежено 329 хворих із туберкульозом плеври, які були розподілені на дві групи. У основну групу увійшло 142 особи, у групу порівняння – 187. В основі обстеження методом променевої діагностики була традиційна рентгенографія органів грудної порожнини. Хворі основної групи обстежувались згідно з алгоритмом діагностики захворювань плеври, втіленим у життя співробітниками кафедри (патент України на корисну модель № 114430).

Результати. У віддалений період поширеність залишкових змін з боку плевральної порожнини у вигляді нашарувань мали місце у 6,8 % хворих основної групи проти 19,8 % – групи порівняння ($p < 0,05$), порушення скелетотопії діафрагми – у 13,5 % проти 25,9 % хворих відповідно ($p < 0,05$) та її рухливості (5,4 % проти 18,5 % хворих, $p < 0,05$). У хворих на туберкульоз плеври, обстежених відповідно до запропонованого алгоритму, хронічний плеврит розвивається у 7,1 разу менш часто (1,4 % хворих проти 9,9 %, $p < 0,05$), а легеневе захворювання у 2,7 разу (4,1 % та 11,1 % хворих відповідно, $p > 0,05$).

Висновок. Застосування запропонованого алгоритму діагностики захворювань плеври, з урахуванням раннього виявлення плеврального випоту та проведення своєчасної верифікації захворювання, дозволяє зменшити у віддалений період наслідків з боку грудної стінки, легень та плеври.

Ключові слова: синдром плеврального випоту, плеврит, туберкульоз, діагностика, віддалені результати.

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INTRODUCTION/ВСТУП

A serious burden for the healthcare system in the world and particularly in Ukraine is represented by the growing number of socially significant diseases.

Among these, tuberculosis (TB) occupies a leading place [1, 2]. In developed countries, the epidemiological situation with tuberculosis is stable and improving. Despite the overall positive

epidemiological trend, the burden of tuberculosis in Ukraine remains significant. In 2018, the prevalence of tuberculosis in the country (new cases and relapses) was 80 per 100,000 population. In Ukraine, the share of pre-extensively drug-resistant TB (pre-XDR-TB) and extensively drug-resistant TB (XDR-TB) cases increased from 47.4 to 51.3% in 2015–2018. Among patients with chemoresistant tuberculosis, multidrug-resistant TB (MDR-TB) with tissue destruction in the lungs predominated over other TB types (57.3%), and only 57.8% were treated effectively [3].

The incidence of TB in the Sumy region in 2004–2019 remained at the same level (46.4 and 47.4 per 100,000 population, respectively). As compared to the Sumy region, there was a decrease in morbidity in Ukraine during these years from 72.0 to 47.6 per 100,000 population. This was not the evidence of positive dynamics, but rather of a negative trend, as it was related to the exclusion of the occupied territories of the Donetsk and Luhansk regions and Crimea from the statistical data. The number of patients with extrapulmonary TB in the Sumy region is 14.6%, and in Ukraine as a whole, it is 10.7%, which is the result of disorganization of medical care provision in general and phthisiatric care in particular, and is an unfavorable indicator of the lack of extrapulmonary TB specialists in Ukraine [4]. The most common form of extrapulmonary TB is tuberculous pleurisy (pleural effusion). The share of the latter in the structure of all tuberculosis forms is within 10–12% or more [5]. In HIV-positive patients, it may reach up to 30–70%, depending on the state of immunity [6]. Considering this, the problem of tuberculous pleurisy diagnosis remains relevant.

Pleural effusion syndrome (PES) is the leading symptom of pleurisy of any origin. Peculiarities of the innervation of the pleural cavity, chest and abdominal walls, peritoneum, lumbar and gluteal areas disguise the first manifestations of the tuberculous process in the pleura which can be mistaken for other pathological processes and conditions. In this regard, the frequency of misdiagnosis amounts to 20–40% [7].

Detection of tuberculous pleurisy includes both clinical and X-ray examination of patients. Along with the latter, another most highly informative, safe, and widely available method is a non-invasive ultrasound examination [8, 9, 10], which is especially useful when the process is localized in limited-access areas of the chest cavity or presents with a small amount of effusion [11, 12].

Objective. To study the long-term outcomes of the treatment with regard to the diagnostic method, which will contribute to the justification of the proposed method for pleural disease verification.

Materials and Methods. We examined 329 patients with tuberculous pleurisy, who were divided into two groups. There were 142 subjects in the main group and 187 subjects in the comparison group. All patients were examined at the Municipal Non-Profit Enterprise of Sumy Regional Council "Regional Clinical Phthisiopulmonology Medical Center". The patients of the comparison group were examined according to the existing standards approved by the orders of the Ministry of Health of Ukraine [13, 14, 15, 16]. The radiodiagnostic examination was based on traditional chest radiography. This group of patients was studied retrospectively. The patients of the main group were examined according to the pleural diseases diagnostic algorithm implemented by the fellows of the department [8, 9, 17]. At the primary level of medical care provision, its components were: a detailed anamnesis with an emphasis on social status, precipitating factors, and comorbidities; physical examination for a possible pleural effusion recognition. In case pleural effusion was suspected, it was necessary to perform an ultrasound examination and traditional chest x-ray examination at the secondary level of medical care provision. After pleural effusion being diagnosed, the patient was immediately referred to a highly specialized institution for verification of the diagnosis. At the tertiary level of medical care provision, a pleural puncture was suggested; if pleural effusion was confirmed and there were no contraindications to thoracoscopy (thrombocytopenia, signs of a recent myocardial infarction, etc.), thoracoscopy with pleural biopsy in 5 areas was performed for cytological, histological, microscopic, bacteriological and gene-molecular research. On the second or third day after elimination of the effusion, plain and lateral chest X-rays were performed to rule out a parenchymal pulmonary process; depending on X-rays and endoscopic examinations results, tomography was considered; if no findings were indicative of tuberculosis, neoplastic process, pleurisy caused by trauma, and cardiac hydrothorax, a blood test was performed using enzyme immunoassay and polymerase chain reaction to check for rare forms of pleural inflammation, and biopsy of relevant body parts was used to rule out systemic diseases.

There were 83 (58.5%) city residents and 59 (41.5%) rural residents in the main group vs. 123

(65.8%) and 64 (34.2%) subjects, respectively, in the comparison group. In the main group, there were 41 (28.9%) patients aged 30–39 years and 28 (19.7%) patients aged 40–49 years. In the comparison group, 49 (26.2%) patients were aged 30–39 and 45 (24.1%) patients were aged 40–49. The majority of patients in both groups were males: 115 (81.0%) in the main group vs. 138 (73.8%) in the comparison group. Thus, the groups did not differ significantly ($p > 0.05$) by the place of residence, age, and gender.

Among the patients of the main group, pleural effusion was diagnosed in 134 (94.4%) subjects immediately during the first ultrasound examination. They were immediately referred for a full diagnostic algorithm. In 52 (27.8%) patients of the comparison group, no changes were found in the pleural cavity during the initial X-ray examination. Only 10 (5.3%) patients were diagnosed with pleurisy and were referred for invasive diagnosis at the clinic. 125 (66.9%) patients in the comparison group were diagnosed with pneumonia and underwent treatment at their place of residence in district hospitals. In these patients, pleural effusion was found only during return visits.

In order to study long-term outcomes, we developed the questionnaire "Follow-up of patients who underwent treatment for tuberculous pleurisy". The questions in the questionnaire related to pain character: pain type (dull, aching); the presence of weather-related pain (occurring with changes in barometric pressure, humidity, or other weather phenomena); the presence of exercise-induced pain (occurring or changing with or after physical exertion). Respondents answered "Yes" or "No" to the questions.

Results and discussion. The study of long-term outcomes (2–4 years after the end of the main course of chemotherapy) of the diagnostic and treatment process was carried out by surveying patients of both groups through district tuberculosis offices. Questionnaires were sent to 85 patients from the main group and 93 patients from the comparison group. The questionnaires were sent back by 74 patients from the main group and 81 patients from the comparison group.

The obtained data regarding the subjective sensations of the subjects from the side of the pleural cavity were as follows. 13 (17.6 %) subjects in the main group and 29 (35.8 %) subjects in the comparison group (i.e. twice as much) experienced constant aching pain in the chest on the side of disease location. At the same time, in the main group

pain occurred in the subjects who still had changes in the diaphragm area at the end of the treatment.

6 (8.1%) subjects in the main group indicated that pain used to appear depending on atmospheric phenomena. These patients had been discharged with residual wall changes at the end of the treatment. The same complaints occurred in 17 (21.0%) subjects of the comparison group who had been discharged with similar changes. Therefore, this pain phenomenon was 2.6 times more frequent in the subjects of the comparison group.

The pain appearing during physical exertion and causing a change in the respiratory act (deep breathing, hurried breathing, shortness of breath) was usually observed in patients of both groups with residual changes related to the diaphragm. Among the subjects of the main group, it was indicated by 14 (18.9%) respondents and among the subjects of the comparison group – by 55 (67.9%) respondents ($p < 0.05$). Thus, delayed diagnostics and, accordingly, late treatment were accompanied by greater residual changes at the time of discharge from the hospital and by more pronounced subjective pain in the remote period.

We analyzed the objective data from the medical records of the patients who provided their questionnaires through the district tuberculosis offices (Table 1). The study was conducted based on X-ray morphological changes found in the pleural cavity on the side of the affected hemithorax.

Pleural costal thickening and "blunting" of diaphragmatic sinuses were found in 5 (6.8%) subjects of the main group vs. 16 (19.8%) subjects of the comparison group (2.9 times more). A change in the shape and position of the diaphragm in the convalescents of the main group (defined as "changes in diaphragmatic skeletopy") occurred in 10 (13.5%) subjects vs. 21 (25.9%) subjects of the comparison group which is higher by 1.9 times. Diaphragmatic mobility disorder was observed in 4 (5.4%) subjects in the main group vs. 15 (18.5%) subjects in the comparison group ($p < 0.05$). The difference was 3.4 in favor of the main group subjects, thus, confirming the effectiveness of the proposed algorithm for pleural diseases diagnosis based on ultrasound along with x-ray examination.

There was no recurrence of pleural tuberculosis with effusion among patients in the main group. At the same time, in the comparison group, such a complication occurred in 6 (7.4%) subjects. Due to the fact that the treatment in the main group started 3 to 4 weeks earlier, relapses of the disease were not observed.

Table 1 – Long-term results of diagnosis and treatment of tuberculous pleurisy in the main group and the comparison group

Group of patients	Changes in pleural cavity						Recurrent pleural disease		Pulmonary disease		Chronic pleurisy	
	Pleural thickening, "blunting" of diaphragmatic sinuses		Changes in diaphragmatic skeletopy		Diaphragmatic mobility disorder							
	abs.	%	abs.	%	abs.	%	abs.	%	abs.	%	abs.	%
Main group n = 74	5	6.8	10	13.5	4	5.4	-	-	3	4.1	1	1.4
Comparison group, n = 81	16	19.8*	21	25.9*	15	18.5*	6	7.4	9	11.1	8	9.9*

Note: * – a statistically significant difference between the values of the main group and the comparison group ($p < 0.05$)

Pulmonary tuberculosis developed in 3 (4.1%) subjects of the main group and in 9 (11.1%) subjects of the comparison group ($p < 0.05$), which was 2.7 times more than in the main group. Among patients with complicated pleurisy, pulmonary tuberculosis became multiresistant in 2 (2.7%) patients of the main group and 7 (8.6%) patients of the comparison group ($p < 0.05$).

The reason for the development of the pulmonary process obviously lies in the etiopathogenesis of tuberculous pleurisy, which is one of the disseminated forms of tuberculosis. Still, the main factors that contributed to the spread of the process from the pleural cavity to the lungs were treatment non-compliance and antisocial behavior which is known to put such people at risk for tuberculosis development in general and pulmonary tuberculosis, in particular.

Despite it, the difference in the frequency of pulmonary tuberculosis between the main group and the comparison group (2.7 times) eloquently confirmed that the timely therapy of pleural tuberculosis (which started 3 to 4 weeks earlier in the main group) was an essential condition for preventing the process spread to the lung parenchyma and presented a strong justification for the advantages of the proposed algorithm for diagnosing pleural diseases.

CONCLUSIONS/ВИСНОВКИ

Taking into account the early detection of pleural effusion and timely verification of the disease, the proposed diagnostic algorithm for pleural diseases allows to reduce the long-term effects, such as residual changes (thickening) in the

Chronic pleurisy was reported in 1 (1.4%) subject of the main group and 8 (9.9%) subjects of the comparison group.

In addition, we studied the influence of past tuberculous pleurisy on the respiratory function. Type I respiratory insufficiency was detected in 16 (21.6%) subjects of the main group vs. 40 (49.4%) subjects of the comparison group, which was 2.3 times more often. Type II respiratory insufficiency occurred in 3 (4.1%) subjects of the main group vs. 8 (9.9%) subjects of the comparison group, which was 2.4 times more often. Thus, respiratory insufficiency (both type I and type II) developed in 59.3% of subjects of the comparison group and 25.7% of subjects of the main group. The 2.3-fold difference between the studied groups confirmed the advantages of the proposed algorithm for pleural effusion syndrome diagnosis, which is identical to a pleural disease, since all pathologic processes of the pleural cavity are accompanied by pleural effusion syndrome.

Of the extrapulmonary forms of tuberculosis, tuberculous spondylitis developed during the remote period in one (1.4%) subject from the main group and in 3 (3.7%) patients of the comparison group ($p > 0.05$); however, this difference was not statistically significant.

pleural cavity (6.8% of patients in the main group vs. 19.8% of patients in the comparison group, $p < 0.05$), changes in diaphragmatic skeletopy (13.5% vs. 25.9%, respectively, $p < 0.05$), and diaphragmatic mobility disorder (5.4% vs. 18.5%, respectively, $p < 0.05$), and to prevent recurrence of

pleural disease. Patients with tuberculous pleurisy who had been examined according to the proposed algorithm developed chronic pleurisy 7.1 times less

often (1.4% vs. 9.9%, $p < 0.05$) and pulmonary disease – 2.7 times less often (4.1% vs. 11.1%, respectively, $p > 0.05$).

CONFLICT OF INTEREST/КОНФЛІКТ ІНТЕРЕСІВ

The authors declare no conflict of interest.

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None.

AUTHOR CONTRIBUTIONS/ВКЛАД АВТОРІВ

All authors substantively contributed to the drafting of the initial and revised versions of this paper. They take full responsibility for the integrity of all aspects of the work.

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