



## THE CURRENT STATE OF DIAGNOSIS, TREATMENT AND PROGNOSIS OF THE COMORBID COURSE OF MALIGNANT TUMORS AND PULMONARY TUBERCULOSIS

(Literature review)

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### ABSTRACT

*One of the urgent problems of modern phthisiology is the combination of tuberculosis with oncological diseases. This is primarily due to the steady increase in the number of patients with malignant neoplasms in recent years against the background of the ongoing tense situation with tuberculosis. In the annual report of the World Health Organization in 2018, tuberculosis was named one of the 10 main causes of death from diseases in the world [6]. Despite the successes in the fight against tuberculosis, the problem of its detection still remains extremely urgent. The combination of tuberculosis with lung cancer changes the clinical picture, making it difficult to carry out differential diagnosis and diagnosis. At the same time, there is a significant increase in morbidity and mortality from cancer [7, 9].*

Tuberculosis "hides" the radiological manifestations of a malignant tumor for a long time, contributing to its progression and the development of high mortality among patients [8].

Despite the long-standing opinion that tuberculosis and lung cancer are antagonists in relation to each other, at the moment it has been reliably established that lung cancer in people with residual tuberculous changes is more common than in people who have not had tuberculosis [9].

In recent years, cases of a combination of cancer of various localizations (RRL) with tuberculosis of the respiratory system have become more common [10]. Thus, in Japan, tuberculosis was recorded in 1.38% of cases in patients with lung cancer [2]. In the USA, tuberculosis is observed in cancer patients 9 times more often than in people without cancer [3]. According to [11], in patients with tuberculosis, RRL is observed in 11.6% of cases. Cases of pulmonary tuberculosis have been described in patients with extrapulmonary cancers: breast, stomach, intestines [12], nasopharynx [7], prostate [1], kidney [9], uterus [5], a case of tuberculosis of the spleen in a patient with skin melanoma [10]. There are few publications on the combination of RRL with tuberculous exudative pleurisy (TEP) [2].



Lung cancer and tuberculosis as a combined pathology in one patient have attracted attention for a long time, back in that distant era when the very concepts of these diseases were in statu nascendi. Thus, G. Bayle (1810) [6] considered "carcinomatous consumption" among 6 different forms of pulmonary consumption. A different point of view was formed by K. Rokitansky and R. Virchow, in whose understanding tuberculosis and cancer are antagonistic and moreover mutually exclusive diseases, since they are based on directly opposite dyscrasias [3].

This view was fully maintained until the middle of the last century, namely, until the seemingly convincing statistics appeared that pulmonary tuberculosis was combined with lung cancer and vice versa was far from an exception [6].

According to I. Roca et al., J. Furin et al. in the absence of adequate algorithms for the elimination of drug-resistant tuberculosis by 2050, mortality from this disease can be compared with mortality from tumor processes [8].

The epidemiological situation for such socially significant diseases as HIV infection, tuberculosis and oncological pathology remains unfavorable. The impact of the prevalence of HIV infection on the manifestations of tuberculosis and oncological diseases requires both special epidemic surveillance and increased clinical alertness [8].

As far as we know, this is the first report on the development of tuberculosis associated with the use of ICI in a large cohort of cancer patients. The incidence rate of TB was 394.4 cases per 100,000 person-years, which is much higher than among the entire population of South Korea in 2018 (51.5 cases per 100,000 person-years) [4], but similar to two previous studies that included cancer patients (361.3 per 100,000 person-years, excluding lung cancer and 307 per 100,000 people per year, including lung cancer) [4].

Lung cancer (RL) is the most common cause of death among all cancers. According to the World Health Organization (WHO) in 2017, more than 1 million new cases of this disease are diagnosed annually in the world. In Russia, RL accounts for 15% of all deaths from cancer - more than 50 thousand patients per year with an average incidence of 60 thousand. Many researchers note that from 60 to 90% of patients with RL are subjected to unjustified treatment at the initial treatment [1].

Tuberculosis (TB) is one of the main infectious causes of morbidity and mortality worldwide [0]. There is currently renewed interest in screening and treatment of latent tuberculosis infection (LTI) as possible means to achieve control over the global tuberculosis epidemic [3]. In most infected people, tuberculosis remains clinically asymptomatic and microbiologically inactive (latent). However, in about 5-10% of latently infected individuals, the infection will cause active tuberculosis at some point in their lives [6]. The risk of TB reactivation is increased in people with immunodeficiency conditions such as HIV infection [7], chronic renal failure [6] or diabetes mellitus [110, p. 000666], as well as in people with immunodeficiency drugs such as tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ) inhibitors [7]. The World Health Organization (WHO) recommends targeted screening of high-risk groups in high-income or upper-middle-income countries with a TB incidence of <100 per 100,000 population per year [6], since preventive TB treatment can significantly reduce the risk of reactivation of tuberculosis [7].



According to M.V. Shelyakhovsky, at the first treatment of patients with RL, in 29% of cases, the diagnosis of "pulmonary tuberculosis" is established, the role of which in the global structure of morbidity and mortality is also significant. Tuberculosis is still a common cause of morbidity and mortality worldwide. One of the key epidemiological determinants of tuberculosis is migration, the causes of which are diverse and include economic, socio-political and climatic factors [1].

Comparing, the combined incidence of tuberculosis in cancer patients (in one included study, the study period was 25 years [5]) with an annual incidence of TB in the general population would have led to an overestimation of the risk of tuberculosis in cancer patients. Similarly, using the general population as a comparison group, without any correction for potential distorting factors, especially age, led to an overestimation of the risk of tuberculosis in cancer patients. The conclusion of the authors of the study is that people living in the United States with hematological cancer, head and neck cancer, lung cancer, the benefits of targeted screening and treatment of LTBI, therefore, should be questioned. Another systematic review published in 2014 focused only on lung cancer and assessed the prevalence of TB in these patients [7].

Despite the fact that there is a certain amount of information in the literature about the combination of lung cancer and tB, there is no clarity in the causal relationship between these diseases [2], nevertheless, according to a number of authors, tB prepares a bed for the development of cancer. According to the materials of I.V. Lesunova (2011), this is due to changes in the morphology of the bronchopulmonary system in TB, primarily squamous cell metaplasia of the cylindrical epithelium of the bronchi [7]. According to other authors, lung cancer develops more often in patients with active forms of tB, which are characterized by a chronic course with pronounced fibrous changes in the bronchi and lungs [8]. A number of authors suggest that tB patients should be considered as a group at increased risk of developing tumors [4]. According to the literature, lung cancer in patients with lung TB is 4.5–7 times more common than in the rest of the population [9].

According to a report by the World Health Organization (WHO), in 2018, about 10 million people fell ill with tuberculosis in the world, of which 57% were men, 32% were women, and 11% were children under the age of 15. The number of deaths from this terrible disease among HIV-negative patients amounted to 1.2 million people, among HIV-positive — 251 thousand people. More than 80% of all cases of tuberculosis occur in 30 countries from the WHO list with a high tuberculosis burden, among them India, China, Indonesia, and the Philippines occupy leading positions (WHO, 2019). The countries of America and Europe account for only 3-6% of cases of tuberculosis from the total number of cases in the world (WHO, 2018). Drug-resistant tuberculosis remains a serious problem of domestic and foreign healthcare. According to WHO (2019), in 2018, resistance to rifampicin (a first-line drug) was detected in half a million people, who were diagnosed with multidrug-resistant tuberculosis (MDR-tuberculosis) in 78% of cases. Half of all cases of drug resistance are M. tuberculosis to rifampicin and MDR-tuberculosis is registered in three countries — India (27%), China (14%) and Russia (9%) [3].

The combination of lung cancer and tuberculosis is more common in men in old age and senility. Cancer occurs in the lung on the side of the tuberculous lesion with active tuberculosis in 75.0%, with inactive tuberculosis — in 83.3% of cases. Microbiological and morphological



research methods are the most effective for verifying the diagnosis of a combination of tuberculosis and lung cancer [9].

Currently, the most radical point of view has spread, according to which tuberculosis and lung cancer are not only combined with each other, but also pathogenetically related [2]. In fact, there is evidence that the incidence of lung cancer in tuberculosis patients is 0.4—8.2%, which is 4.5—7 times higher than in the general population [8]. Thus, N. Dacosta and S. Krinare [9] showed that in India, various forms of active and inactive tuberculosis were present in 30% of patients with bronchogenic tumors, while in the general population the combination of tuberculosis and lung cancer did not exceed 7%. Similar statistics are provided for Japan [9]. According to the latest data from A. Tamura [5], active pulmonary tuberculosis occurs in 2-5% of patients with lung cancer, and lung cancer occurs in 1-2% of patients with active pulmonary tuberculosis. Some "special" forms of lung cancer, such as "cancer in the rumen" in non-smoking women, are directly associated with previously suffered pulmonary tuberculosis [4].

It was found that the relative risk of developing lung cancer in tuberculosis is 11.14 times within 1-5 years [9].

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