



Mini Review

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## Mini Review: Reactivation of Tuberculosis in Patients with Solid Cancer



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### Abstract

The association between active tuberculosis and subsequent cancer development has been investigated for many years. This mini review to estimate the prevalence of latent tuberculosis infection in cancer patient and how chemotherapy can be reactivation of mycobacterium tuberculosis.

### Introduction

Tuberculosis (TB) and malignancy represent global threats calming millions of lives and inflicting formidable suffering worldwide. Tuberculosis (TB) remain the most common infectious disease worldwide and leads to high mortality [1]. Tuberculosis (TB) is an old disease that has affected humans more than 8000years ago [2,3]. The association of TB with carcinoma was initially described 200 years ago by Bayle who considered cavitation cancerous as one of various type of TB [4,5]. For future successful control of TB in the post-2015 era, preventing TB reactivation and transmission in high-risk groups is an important strategy [6]. The WHO suggests the commencement of targeted screening of high-risk groups in high- or upper-middle-income countries with a TB incidence of <100 per 100,000 person-years [7]. cancer has been a well- recognized risk factor for developing active mycobacterium -tuberculosis infection since the 1970s; however, the absolute and relative risk for v different cancer types and the change in risk over time has not been well defined. US and Canadian guideline identify immunosuppression due to human immunodeficiency virus, organ transplant, prolonged therapy with corticosteroids, tumor necrosis factor-alpha inhibitors, hematologic malignancies and head and neck cancer as important risk factors for developing active tuberculosis [8,9].

Patients with solid cancers and hematological malignancies are immunocompromised because of the disease itself, and because of chemotherapy. It is therefore reasonable to assume

that the risk of TB reactivation would be increased in people with cancer and consider LTBI screening and treatment in this group. There is, however, a paucity of information on whether patients with cancer should be screened for LTBI. The British National Institute for Health and Care Excellence (NICE) recommendations state that people who “have a hematological malignancy”, “are having chemotherapy “and” have had a gastrectomy” (for gastric cancer or other reasons) are at increased risk of developing TB, but they do not provide any specific screening and treatment recommendations for these groups [10].

### Discussion

The incidence of tuberculosis in lung cancer patients decreased dramatically over the study period in the United States, with the relative risk decreasing but remaining high after 1980. The increased risk of tuberculosis in those with lung cancer may be due to local immunologic effect of the cancer but also to confounders such as heavy cigarette smoking and alcohol consumption. We do not have an explanation for the dramatic decreased risk of tuberculosis in lung cancer patients over the study period other than lower exposure to active tuberculosis after 1980. Conventional laboratory producers for MTB detection rely upon microscopic examination for presence of acid-fast bacilli (AFB), and culture on solid and /or liquid media. Microscopic examination for AFB is rapid but has a very limited sensitivity.

Although culture is still the gold standard for diagnosis of TB, it may require a turnaround time of 2-8 weeks [11].

Active tuberculosis occurred concurrently or soon after the cancer diagnosis in more than half of the patients with head and neck and lung cancer in 2 large studies included in our meta-analysis [7,12]. The incidence of active tuberculosis in patients with head and neck cancers (HNSCC) decreased by more than 6-fold over the study period in the United States, while the relative risk decreased but remained very high. The increased tuberculosis risk in these patients may be confounded by the association of heavy smoking and drinking as they are independent risk factors for developing active tuberculosis. It is unclear if risk of HNSCC is principally through the direct impairment of antituberculous immunity by cigarette smoking or alcohol consumption or the association of these risk factors with poverty, malnutrition, and low socioeconomic status (SES). The dramatic decrease in incidence of tuberculosis in those with head and neck cancers in the pre- and post-1980 period may be due to decreasing tuberculosis rates, as well as the change in etiology of head and neck cancers associated risk factors and treatment modalities. Non-human papillomavirus (HPV)-associated HNSCC typically occurs in low- to middle-class males who are heavy smokers and drinkers, whereas HPV-associated HNSCC occurs in young nonsmoking males of high SES. Between 1998 and 2004, the incidence of HPV-positive HNSCC in the United States increased by 225%, whereas HPV-negative cancers decreased by 50% [13]. A recently published systematic review and meta-analysis by Cheng et al. [14] on the risk of TB in patients with cancer also had significant methodological limitations. That analysis did not exclude studies that contained information on cumulative incidence of TB only and used annual country-specific TB incidence rates that were unadjusted for potential confounders obtained from WHO for comparison [14].

Comparing the cumulative incidence of TB in patients with cancer (in one included study cumulated over a study period of 25 years [15]). Another systematic review published in 2014 focused on lung cancer only and evaluated the prevalence of TB in those patients [16]. It was not the goal of that review to establish causality (the authors were aware that there is a bidirectional causal link between lung cancer and TB [17]). The primary infection by *M. tuberculosis* is extremely common in areas with high prevalence. It is usually self-limited by the host's immune mechanisms resulting in latent infection and nonspecific or no clinical manifestations. Most cases of active tuberculosis occur due to reactivation of this latent infection in face of impaired immunity. Patients with one episode of tuberculosis are at higher risk of developing recurrent episodes due to reinfection [18]. Lung cancer and tuberculosis are two major public health problems in China. It was demonstrated that there were 28.49 lung cancer-related deaths per 100,000 population in 2014 [19] and 2.6 tuberculosis-related deaths per 100,000 population in 2017 in China [5].

The meta-analysis showed a statistically significantly increased risk of TB in cancer patients, compared to the general

population. Most solid cancers, for which data from three or more studies were available, were associated with an approximately two-fold increase in the risk of developing TB, compared to the general population. This increase was significant for gastric, breast and colon cancer, but not for liver cancer (IRR 2.02; 95% CI 0.83–4.91). Lung cancer was associated with a six-fold increase in TB. The relative risk of TB in gastric cancer (IRR 2.63, 95% CI 1.96–3.52), which is often treated with gastrectomy (associated with malnutrition) [20].

Tuberculosis treatment in cancer patients is still not conclusive, especially for advanced non-small cell lung cancer patients with synchronous anti-tuberculosis and anti-cancer treatments [21]. Hirashima et al demonstrated that in patients with metastatic colorectal cancer, both cancer chemotherapy and tuberculosis treatment could be concurrently administered safely and efficiently [22]. The scholar furtherly demonstrated that anti-cancer and anti-tuberculosis treatments can be safely and effectively administered in patients with different types of malignancies (including lung cancer) and active TB [23,24].

### Conclusion

This review for the clinicians to be aware of the protean manifestation of TB and cancer and maintain a high index of suspicion for simultaneous and/ or misleading presentations, there remains considerable uncertainty about whether patients with cancer should be screened for LTBI, with the intention to offer preventive treatment, if there is evidence of LTBI. The risk of TB in cancer patients remains imprecisely quantified, despite the need for contemporary evidence to inform guidelines and public health policy on LTBI screening and treatment in this setting.

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