VIA MEDICA

CASE REPORT

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Squamous cell lung cancer in a male with pulmonary tuberculosis

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Abstract

Lung cancer and pulmonary tuberculosis (TB) are highly prevalent and representing major public health issues. They share common risk factors and clinical manifestations. It is also suggested that TB predicts raised lung cancer risk likely related to chronic inflammation in the lungs. However, it does not seem to influence the clinical course of lung cancer provided that it is properly treated. We present a case report of a 57-year old male with concurrent TB and lung cancer. He was diagnosed with positive sputum smear for acid fast bacilli (AFB) and subsequent culture of *Mycobacterium tuberculosis*. Besides, his comorbid conditions were chronic hepatitis C virus (HCV) infection and peripheral artery disease (PAD). Later while on anti-tuberculous treatment (ATT) squamous cell lung cancer (SCC) was confirmed with computed tomography (CT) guided biopsy. Due to poor general condition the patient was not fit for either surgery or radical chemo- and radiotherapy. He was transferred to hospice for palliative therapy. We want to emphasize that both TB and lung cancer should be actively sought for in patients with either disorder. In addition, there is no doubt that these patients with lung cancer and with good response to TB treatment should be promptly considered for appropriate anticancer therapy.

Key words: tuberculosis, lung cancer, clinical course, comorbidity

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Case report

The interaction between lung cancer and tuberculosis (TB) has been long established [1]. There is good evidence that preexisting TB is independently associated with an increased risk of lung cancer [2]. Besides, solid-organ malignancy raises the likelihood of TB reactivation particularly in patients with old healed TB lesions [3].

A 57-year old severe underweight (body-mass-index (BMI) 15 kg/m^2) male was admitted to a respiratory ward with a history of 3-week long anorexia, fatigue, purulent cough and 1-month long fever. His cough started 6 months before. He reported significant weight loss of 15 kilos for 6 months. He had no chest pain and haemoptysis. As an out-patient he received the course of amoxicillin with clavulanic acid with short-lived improvement. Also, the patient complained of intermittent claudication after a short walking distance. He was a resident of the shelter for homeless for a few years. His primary profession was a garage worker whereas his most recent occupation was garbage sorting. There was a history of heavy smoking (30-pack years) and alcohol addiction. He had not been drinking for last 2 years. He had no evident contact with a confirmed TB source. In the distant past he underwent an ear-nose-throat operation for the nose deformity. On examination, he was undernourished, nor-

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motensive (blood pressure — 110/70 mm Hg), non-tachycardic (85/min), slightly tachypneic (16/min) with diminished breath sounds over the left lower lobe. There was moderate pitting oedema of both his legs and worse peripheral circulation in his left foot. His chest X-ray showed irregular consolidation in the upper left lobe and large mass in the lower left lobe (Fig. 1). In the bronchoscopy there were no abnormalities apart from purulent secretions. Computed tomography (CT) of the chest revealed multiple nodules with poorly defined margins in peribronchial distribution in both upper lobes, irregular consolidations and cavities in the upper left lobe. CT showed also a round contrast-enhanced mass in the left lower lobe measuring 92 × 76 mm with a thick-walled cavity with no hilar and mediastinal lymphadenopathy (Fig. 2). Abdominal ultrasound did not show any abnormality. The inflammatory markers were raised (C-reactive protein 100 mg/L, white blood count (WBC 22 G/L). On admission his haemoglobin was low (9.9 g/L) as well as albumin (23 g/L). His sputum smear was positive for acid-fast bacilli (AFB) (++). Anti-hepatitis C virus (HCV) antibodies were detected through ELISA method. He tested negative by ELISA for human immunodeficiency virus (HIV) and hepatitis B surface antigen (HBsAg). Consequently, the patient was transferred to the tuberculosis ward. Anti-tuberculous treatment (ATT) was started with rifampicin (R), isoniazid (H), ethambutol (E) and pyrazinamide (Z). *Mycobacterium tuberculosis* was cultured and identified with MGIT (*Mycobacteria* Growth Indicator Tube). Drug susceptibility testing (DST) proved sensitivity to the all first-line drugs. Later while on ATT persistent severe pain developed in his left lower limb. He was transferred to a vascular surgery ward with the diagnosis of chronic critical leg ischaemia. CT angiography confirmed significantly occluded left popliteal and left iliac internal arteries with the collateral flow. The patient declined any endovascular treatment and was admitted again to the TB ward. Peripheral artery disease (PAD) was managed with aspirin, statin and strict blood pressure control. Whilst continuing ATT the CT guided biopsy of lung mass confirmed squamous cell carcinoma with positive staining for CK-7 and p63 whereas negative for TTF1. Both routine staining and immunohistochemistry were necessary for a precise diagnosis. His clinical staging was T3N0M0. His general condition deteriorated with further weight loss. Eastern Cooperative Oncology Group performance status was 3 which precluded him from any anticancer treatment. Besides he refused any referral to an oncologist. After 2 months well-tolerated ATT was continued only with HR with good radiological response but with an increase of the lung mass (Fig. 3). Sputum samples were positive for AFB after 2 months but converted to negative later after another 1 month. There was persistently elevated WBC (27 g/L, differential: band cells 2%, segmented neutro-

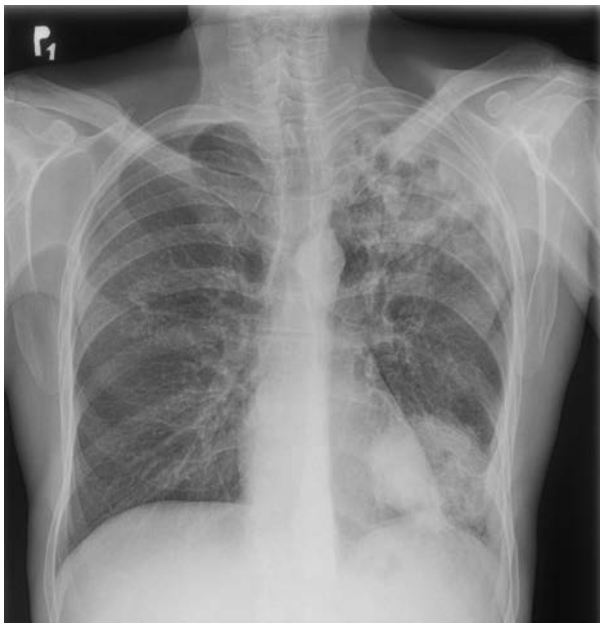

Figure 1. Chest X-ray on admission. Numerous ill-defined consolidations in the upper left lobe. An oval mass measuring 85 mm in the lower left lobe behind the heart

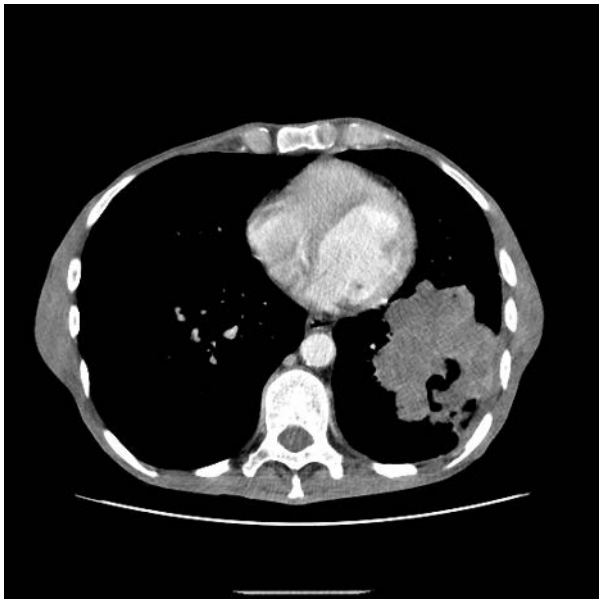

Figure 2. Chest CT. A large oval irregular mass in the lower left lobe with the contrast enhancement

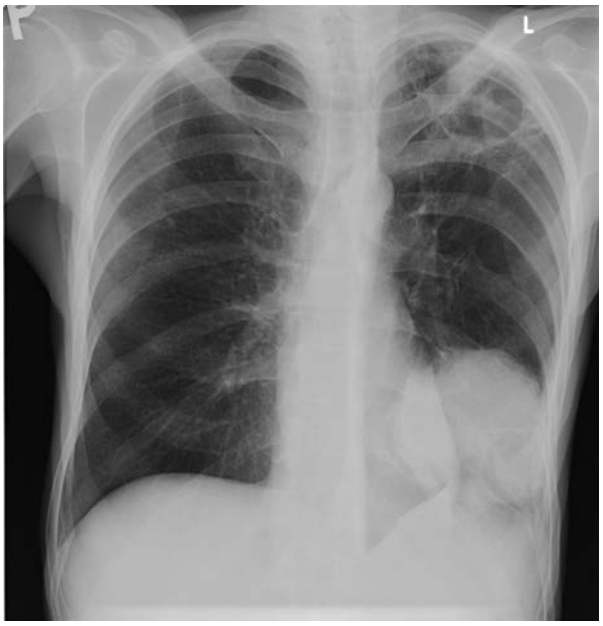

Figure 3. Chest X-ray in the 5th month of ATT. Partial resolution of the consolidations in the left upper lobe. Progression of an oval mass in the left lower lobe

phils 86%, lymphocytes 11% and monocytes 1%). Due to steady decline in haemoglobin altogether 4 units of packed red cells were transfused. Despite lung cancer progression he did not complained of any chest pain, haemoptysis and dyspnoe. When the patient became bedridden he was admitted to a hospice for palliative care. After a few days he died.

Discussion

We present a case of concurrent lung cancer and pulmonary tuberculosis in a heavy-smoking male. Such a cluster in an underweight patient could be a plain coincidence. However, there is robust evidence highlighting the role of chronic inflammation in the pathogenesis of lung cancer. Both these diseases have an enormous public health impact. In 2013 9.0 million people developed TB and 1.5 died form this infection [4]. Whereas in 2012 lung cancer was diagnosed in nearly 1.83 million cases and 1.59 died from it [5]. Globally lung cancer is the largest contributor to new cancer diagnoses and to death from cancer.

In a cohort study adjusted for comorbidities hazard ratio (aHR) for lung cancer in TB patients was 3.32 (95% CI: 2.70–4.09) [2]. The incidence of lung cancer was 11-fold higher than in nontuberculosis subjects. In recent systematic review the independent association between lung cancer and previous TB was confirmed (RR 3.43; 95% CI: 1.93–6.11) [6]. Although the highest risk was during 5 years after TB diagnosis, the overall risk remained still increased 2-fold for 20 years. Consequently, this relationship does not seem to be affected by the early symptoms bias when the first lung cancer symptoms can be wrongly attributed to apparent TB. Zheng et al. found that the odds ratio (OR) for lung cancer associated with former TB was 1.5 (95% CI: 1.2–1.8) [7]. Likewise, it was most elevated after 10 and more years after TB infection (aOR 2.8, 95% CI:1.6–5.0).

TB appears to affect the lung cancer mortality. It remained an independent predictor of lung cancer death (aHR 2.01, 95% CI: 1.4–2.9) [8]. There was no TB association with other malignancies, both related and non-related to smoking. Patients with TB diagnosed before or together with lung cancer had worse prognosis than those with no TB at the diagnosis of lung cancer [9]. In contrast, in one retrospective review TB improved median survival especially in SCC (11.6 vs 8.8 months, $p < 0.01$) [10]. This phenomenon could be explained by the effective T cell immunity nearby tumor. Finally, the only independent prognostic factors for non-localized disease appeared to be its stage and treatment but not any comorbidity such as TB [11].

Alternatively, it is recognized that cancer patients have higher incidence of tuberculosis. In the retrospective cohort study of cancer patients aHR for TB was 1.67 (95% CI:1.42–1.96) [12]. The highest incidence rate ratio (IRR) of TB was among oesophagus, oral, lung cancers (respectively: 6.4, 3.5 and 2.8) and haematological malignancies (IRR 3.0). In a prospective observation that risk for TB in patients with solid-organ malignancy was over 4.5 times higher compared with non-malignant group [3]. That risk was especially elevated in patients with old healed TB and concurrent chemotherapy.

The explanation of that association is far from clear. Lung cancer may develop autonomously and weaken the local immunity which may result in latent TB reactivation or new exogenous infection. Yet chronic inflammatory response in TB with extensive remodeling of lung tissue may serve as a source of malignancy. That is supported by long-lasting observation of scar cancer. Furthermore, the laterality of TB and lung cancer was considerably correlated [7]. It was also recently shown that chronic TB infection causes cell dysplasia and SCC [13]. *Mycobacterium* infected macrophages play a key role in TB induced carcinogenesis by causing DNA damage. These experimental findings confirm a causal link between TB and malignant transformation.

The clinical course of TB in lung cancer is not very unusual. There is no doubt that respiratory TB if treated appropriately does not affect the clinical course of lung cancer. In a retrospective case-control there was no difference in duration of symptoms between TB group with and without malignancy [14]. There was no difference in CT responses to treatment as well as the morphologic features, either. Hence, the overlapping symptoms, radiological similarities and clinical bias for TB, especially in high-burden TB countries, may result in clinical errors and undue delay in correct diagnosis of lung cancer. Therefore every newly TB diagnosed patient and particularly those with suspected relapse or poor response should be carefully evaluated for coexisting malignancy. On the other hand, during the follow-up new lung lesions especially in a tree-in-bud appearance may be suggestive of active TB [14].

There are conflicting reports on histological subtype of lung cancer associated with TB. In a large retrospective observation SCC was found in over 50% cases of TB and concurrent lung cancer [15]. These patients with old TB lesions and SCC had worse prognosis compared to those without TB lesions [16]. Conversely, Liang et al. found that only adenocarcinoma was significantly associated with TB [6]. Nevertheless, very recent study revealed that the predominant type was still SCC [17]. Though it depends on the regional distribution of lung cancer histology it is rather SCC which is more frequent in TB patients.

While treating those patients the method of choice is the surgery [15]. Patients with more advanced stages of malignancy can be treated with both chemotherapy and ATT [18]. In patients with TB detected during anticancer therapy or shortly after there were no differences in clinical outcomes. All fatal courses were due to progression of the underlying malignancy but not TB itself. However, these patients underwent cyclic chemotherapy with no significant nutritional deficiency and modest immunosuppression. Our patient died due to lung cancer progression while he had a fairly good response to ATT. Therefore chemotherapy is not an obstacle in treating TB [18].

Our patient had comorbidities such as chronic HCV infection and PAD. In Georgia with high TB-burden HCV infection was much more prevalent among TB patients compared with hepatitis B infection or HIV infection (respectively, 21%, 4.3% and 1.8%) [19]. It is also noteworthy that HCV co-infection was not associated with severe drug-induced hepatotoxicity [19]. Indeed, our patient tolerated ATT quite well. PAD in a heavy smoking patient with TB might be a common clinical presentation. Moreover, there has been established genetic link between smoking quantity, nicotine dependence, the risk of PAD and lung cancer [20].

There is little doubt about the association between TB and lung cancer. They share risk factors such as smoking, alcoholism, chronic obstructive pulmonary disease and immunosuppression. TB may raise the lung cancer risk through chronic inflammation both locally and systematically. Also, malignancy may impair infection barriers making patients more susceptible to TB. The latter may serve as a marker of occult lung cancer. Alternatively, TB may mimic other diseases like lung cancer and pulmonary infarction [21]. Then the correct diagnosis in patients with active TB may be challenging. Increased long-term risk of cancer in these patients suggests that it is rather TB which promotes malignancy development. Finally, there is clear evidence that concurrent and treated properly TB does not affect lung cancer course and prognosis.

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Conflict of interest

The authors declare no conflict of interest.

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