New onset diabetes in a patient with active tuberculosis

Nowo rozpoznana cukrzyca u chorego na gruźlicę płuc

The authors report no financial disclosure.

Abstract

The present report describes the coincidence of pulmonary tuberculosis (TB) and metabolic disorder such as diabetes. A patient’s bronchoalveolar lavage was found to be positive for acid-fast bacilli (AFB) with following growth of Mycobacterium tuberculosis and complete sensitivity to first line anti-TB drugs. At the same time, the patient presented with typical diabetes manifestation and subsequently required insulin therapy. Combined treatment resulted in significant clinical improvement and gradual resolution of both TB and diabetes symptoms. Therefore, we would like to highlight the value of appropriate medical management of these disorders sharing at least some clinical symptoms and signs such as weight loss and fatigue. Moreover, a growing body of evidence indicates that diabetes may play a role as a risk factor for TB. Consequently, the increasing diabetes prevalence may be a danger to TB control.

Key words: pulmonary tuberculosis, metabolic control, diabetes

Case report

There is firm evidence that diabetes is associated with premature death due to various causes ranging from several cancers and vascular diseases to infections, including pneumonia [1]. Apparently, the incidence of pulmonary tuberculosis is reported to be elevated among diabetic patients [2]. Thus, we would like to report a case of simultaneous development of diabetes and pulmonary tuberculosis.

In June 2010, a 55-year-old, lean (BMI 27) and normotensive man was admitted to the respiratory ward in Wielkopolska Centre of Pulmonology and Thoracic Surgery in Poznań with a month-long history of dry cough, weight loss, fever, with a suspicion of TB or pulmonary abscess. He also reported osmotic symptoms such as excessive thirst and polyuria. His previous medical history was so far unremarkable. His son and mother-in-law had been treated for pulmonary tuberculosis a few years before. As an outpatient he received a course of clarithromycin for supposed community-acquired pneumonia without evident improvement. His chest X-ray showed large heterogeneous infiltration with presumed multiple cavities in the right upper lobe as well as moderate infiltrations in the middle- and lower-zone of the left lung. Subsequently, in order to obtain more precise imaging of the chest and to confirm typical TB abnormalities, computer tomography of the chest was ordered. It showed consolidation, cavities of various sizes in both upper lobes, and multiple small nodules in the right upper lobe — tree-in-bud appearance (Fig. 1, 2). The inflammatory markers were raised (ESR 75 mm/hour, CRP 68 mg/l). Due to non-productive cough no sputum sample was collected. Therefore, the patient underwent a bronchoscopy, and bronchoalveolar lavage (BAL) fluid was obtained. The smear was found to be positive.
was over 20 mmol/l without the presence of ketones in urine. Glycated haemoglobin (HbA1c levels) was consequently 9.1%. In addition, cholesterol levels were elevated as well, e.g. total cholesterol 6.4 mmol/l, HDL 1.5 mmol/l, and LDL 4.1 mmol/l. From the beginning the patient had been treated with an insulin regimen. After two months of extensive antituberculous therapy with four drugs (HRZE) the patient was discharged and treated as an outpatient following the continuation phase for the next four months. Subsequent chest radiography showed moderate improvement. No sputum samples to evaluate the culture conversion with treatment were collected due to the complete resolution of the cough. Bronchoscopy was not carried out either.

**Discussion**

The patient is an example of a common challenge in our clinical practice referring to bizarre constellation of symptoms, which could be attributed at least in some part to either diabetes or tuberculosis. What is more, an acute infection often appears to be a trigger factor for type 2 diabetes. Making a correct diagnosis such as pulmonary tuberculosis in a diabetic patient can be crucial for the appropriate management.

It is acknowledged that diabetes is increasingly common worldwide. However, it has been reported that the incidence of TB has been declining since 2006 [3]. Nonetheless, the prevalence of both conditions varies significantly between ethnic groups. In the UK, the highest number of diabetics was observed among the black and south Asian population [4]. Of interest, the highest estimated number of tuberculosis attributable to diabetes was also found in Asian men and women [5]. In Poland, the incidence of tuberculosis is low (in 2010, 19.7 cases per 100 000 population) and has been gradually decreasing for the last 5 years [6]. With respect to diabetics, the number of diabetic patients is estimated at 2 million, the majority of these being type 2 diabetes.

The intriguing association between diabetes and tuberculosis has been recognized for a long time. In fact, large trials provide clear data that diabetes raises the risk of tuberculosis from moderate to high. According to recent meta-analysis, diabetic patients are 3.1 times (95% CI 2.27–4.26) more likely to develop tuberculosis [7]. As a consequence of this association, there are data to indicate that unsatisfactory diabetic control further elevates that risk. Namely, insulin dependence as a marker for severity of diabetes predicted an increase in that risk [8, 9]. Our patient presented with poor metabolic

(+ + +) for acid-fast bacilli. The patient was treated with the standard regimen consisting of rifampicin (R), isoniazid (H), ethambutol (E), and pyrazinamide (Z). The culture became positive after 8 days and subsequently *Mycobacterium tuberculosis* was identified. Drug susceptibility testing (DST) proved the sensitivity to the first-line drugs. At the same time, the patient was diagnosed with diabetes, fulfilling both the clinical and laboratory criteria (symptoms and random glucose more than 11 mmol/l). The initial blood value of glucose

![](image1.png)

**Figure 1.** Large cavity with air-fluid level with surrounding consolidation in right upper lobe

![](image2.png)

**Figure 2.** Consolidation in right upper lobe with air bronchogram, medium sized cavity in the left upper lobe and multiple nodules
control which required insulin therapy from the onset of the disease (high glycated haemoglobin — HbA1c 9.1%).

On the other hand in populous countries such as India, Peru, and the Russian Federation, with considerable tuberculosis burden a rapid increase in diabetes prevalence has been noticed. [10]. Unfortunately, there are very scarce data on the prevalence of diabetes in other high TB burden countries such as sub-Saharan Africa [11]. However, it was reported that in Tanzania, the prevalence of diabetes among hospitalized TB patients was much higher compared to a control community group (6.5% vs. 0.9%) [12]. Likewise, in another more recent study from Tanzania a higher rate of diabetes was found in culture-confirmed TB compared to a control group (16.7% vs. 9.4%) [13]. Although such findings do not indicate a direct causal relationship, it further strengthens the opinion that in view of the increase in diabetes we may anticipate a rise in TB as well. However, in countries with low TB-prevalence, such as Denmark, the TB risk related to diabetes has been found to be much lower than expected [14]. Moreover, there is no evidence for the association between the glycaemic control and TB in that study.

Although the precise mechanisms increasing the risk of tuberculosis in diabetic patients are not fully clarified, impaired cell-immunity seems to play a pivotal role [15]. Decreased phagocyte and T-cell function as well as vitamin D deficiency are likely contributors. Moreover, diabetic mice were found to have significantly lower production of both interferon-γ (IFN-γ) and interleukin-12 early in the course of M. tuberculosis infection, showing a diminished T helper adaptive immunity. The latter plays a crucial role in controlling tuberculosis infection [16]. Yet immune dysregulation in diabetes does not affect the sensitivity of IFN-γ release assays (IGRAs) in TB patients [17].

According to some studies diabetic patients with tuberculosis may present with atypical radiographic features such as lower-lung and multilobar involvement. In one study these patients had more than twice the chance of having middle- and lower-zone changes compared with non-diabetic controls [18]. Thus, it can be quite challenging not to misdiagnose TB as community-acquired pneumonia. Furthermore, the presence of multiple cavities as well as heterogeneous infiltration were also much more common in diabetic patients [18]. In addition, the duration of therapy was found to be longer as well as a higher rate of drug resistance [18]. However, the cure rates were similar between the groups. Moreover, diabetes was synchronously present in the patients with active TB and diabetes was strongly correlated with TB development. In addition, diabetic patients were significantly older (53 vs. 34 years). Among clinical symptoms, only a cough was found to be more frequent in the diabetic group. Of interest, there were no differences in the frequency of constitutional symptoms such as weight loss and fever between the diabetic and non-diabetic TB groups.

The treatment of tuberculosis in diabetic patients seems to be quite challenging due to a negative effect of poor metabolic control. Consequently, these patients are found to have higher rates of treatment failure and relapse. This may be caused by the altered pharmacokinetics of anti-TB drugs in diabetic patients. In one study, in multivariate analysis, a higher body weight, the presence of diabetes, and higher blood glucose contributed to lower plasma rifampicin concentration [19]. On the other hand, no differences were found in the oral bioavailability and metabolism of anti-TB drugs between diabetic patients and controls despite unsatisfactory glycaemic control (HbA1c 11%) [20]. Therefore, it can be concluded that diabetes itself does not affect the pharmacokinetics of anti-TB medications.

Apparently, diabetic patients seem to have longer conversion times [21]. In addition, initial massive cavitation and positive sputum culture after 2 months of treatment may increase the risk of failure or relapse and justify longer therapy of up to 9 months [22]. Although our patient presented with significant cavitation, his clinical condition soon improved on treatment. Therefore, we decided to adhere to the standard 6-month regimen.

Finally, it may be difficult to classify diabetes in patients with pulmonary TB. Actually, it is usually assessed as type 2, although in the other study the clinical manifestation was closer to type 1 or LADA (late autoimmune diabetes in adults) spectrum of diabetes with normal BMI (20 kg/m²) and a mean age of 47 years [20].

In summary, the number of TB cases has been falling slowly since 2006. Nonetheless, due to the worldwide rise in diabetes we might expect an increase in the numbers of patients with TB and co-existing diabetes. In fact, the rising diabetes prevalence may be a threat to TB control. Thus, it is essential to diagnose both these disorders efficiently, bearing in mind that some of their symptoms are similar. Moreover, according to the guidelines in patients with pre-existing diabetes, screening for tuberculosis is highly recommended [23].
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**Conflict of interest**

The authors declare no conflict of interest.

**References**