CASE REPORT

Extrapulmonary Tuberculosis, Multidrug-resistant Tuberculosis and Diabetes Mellitus: Two Cases Highlighting the Need for Clinical Screening for Tuberculosis in Patients with Diabetes Mellitus

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ABSTRACT

There is an increased burden of diabetes mellitus (DM) in resource poor setting, coupled with the susceptibility to co-infection with tuberculosis (TB) especially in a high endemic TB area. Programmatic re-engineering of screening for TB amongst patients with DM is needed to ensure a control of an ongoing silent coepidemic of DM and TB. We report two cases highlighting the importance of screening for TB among patients living with DM. Each case had a peculiar characteristic highlighting the role of TB screening and poor outcomes of TB in patients with DM. Case 1 is a 32-year-old nurse with uncontrolled DM, glycated haemoglobin of 16.1% on maximum dose of oral hypoglycaemic agents, who presented with night sweat, fever, weight loss, and left-sided chest pain of 2-week duration. She had a negative sputum GeneXpert for acid fast bacilli (AFB), and a chest radiograph was suggestive of left-sided pleura effusion which responded to TB treatment. Case 2 is a 45-year-old female with uncontrolled DM, who had associated complication of DM. She was diagnosed as pulmonary TB by sputum GeneXpert sensitive to rifampicin; however, by the 5th to 6th month of therapy, she presented with recurrent cough, fever and night sweat. Sputum AFB GeneXpert was positive for AFB but resistant to rifampicin. Undertaking TB screening among patients with DM in clinical practice needs to be intensified in order to improve the outcomes of both TB and control the epidemics.

Keywords: Bidirectional screening, diabetes mellitus, tuberculosis.

INTRODUCTION

Tuberculosis (TB) is a major global health problem with an estimated 8.6 million people developing TB and 1.3 million dying from the disease in 2012 (1). South Africa has the second highest rate of new TB cases in the world and the highest rate of drug-resistant TB (2).

The World Health Assembly endorsed a strategy in May 2014 with the aim to decrease global TB incidence by 90% from 2015 to 2035, which would equate to fewer than 10 cases per 100 000 population in 2035 (1). This was adopted because the initial target set for 2015 for TB eradication is not likely to be achieved because of the changing landscape of TB care and prevention which is caused by global epidemiological and demographic transitions. This has contributed to an increase in the burden of non-communicable diseases and ageing populations, thus changing the importance of different risk factors for TB, and consequently, the profiles of co-morbidities and clinical challenges for people with TB (3, 4).

Despite the role of other risk factors such as human immunodeficiency virus (HIV) infection, malnutrition, silicosis, and overcrowding in exacerbating the spread of TB infection, evidence has shown the importance of non-communicable disease that impairs the host defence system such as diabetes in accelerating TB infection. Currently, an estimated 285 million people live with diabetes mellitus (DM), a number which is expected to grow to at least 439 million by the year 2030 (15).

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 DOI: 10.7727/wimj.2015.212

Diabetes mellitus increases TB infection by threefold principally by impairing the host defences and thereby increasing the risk of progression from TB infection to active disease (5, 6).

A large proportion of people with diabetes and TB are seldom diagnosed, or diagnosed too late. Early detection can help improve the care and control of both conditions. People with diabetes who are diagnosed with TB have a higher risk of death during TB treatment and or TB relapse after treatment as well as poor drug efficacy prone to multidrug-resistant (MDR)-TB. It is recommended by the WHO that all the patients with DM should be screened for TB (1). On average, it is estimated that 30% of the individuals with DM will develop active TB disease over the course of their life time (7).

To achieve the control of TB epidemic, all the patients with known determinants of TB such as diabetes should have an intervention that will identify such patients with TB (8). The benefit of screening for active TB in people with DM is the possibility of earlier case detection, which could lead to earlier therapy and the prevention of its transmission.

The yield (number needed to screen) and cost-effectiveness of different TB tests mainly depend on the TB prevalence in any given setting and the sensitivity and cost of the tests used. The role of clinical symptoms screening is suggested to be a more cost-effective way of preventing TB in patients with DM (9). The role of both clinical symptom screening with chest radiography is operationally feasible in areas of high TB burden, although the role of sputum acid fast bacilli (AFB) GeneXpert/RIF as a screening tool for TB amongst patients with DM is still unclear (9). Despite the cost-effectiveness of clinical symptoms screening, the sensitivity of clinical symptoms screening for TB is higher in a HIV-positive population when compared to a HIV-negative population where the sensitivity appears low (10). However, in the setting of underlying DM, sensitivity can range from 4% to 36% (11) and the relative risk of TB in diabetic patients was 3.11 (95% confidence interval [CI]: 2.27, 4.26) (11).

The effect of DM on the risk of poor TB outcomes has been elucidated. Apart from the risk of increased TB and relapse, the effect of DM on delayed sputum conversion, treatment failure of TB and death was higher in diabetic patients compared to non-diabetic patients. However, the high level of glycated haemoglobin (HBA1C) seems not to have any effect on TB outcomes (11–13).

CASE REPORTS

A 32-year-old female presented to the outpatient department of the Family Medicine Department with a left-sided pleuritic chest pain of 2-week duration, progressive weight loss, night sweat, and fever. She is a known diabetic patient on maximum dose of dual oral hypoglycaemic agent. She had a positive history of contact with TB; she was a nurse who worked in a TB clinic at a hospital. She was found to have a weight of 60 kg, and body mass index of 30 kg/m^2. She had a stony dull percussion note on the left lower lung zone and an absent air entry on the examination of her chest. Her chest radiograph showed a blunting of the left diaphragmatic angle with an air-fluid level. An assessment of her left-sided pleura effusion was made; effort at diagnostic pleura tap failed to yield a specimen. She was started on oral antibiotics with blood workup done; her HBA1C was 16.1% and sputum AFB GeneXpert was negative. She was reviewed after a week and the symptoms still persisted. Her chest radiograph was repeated and there was no significant change. She was then started on empiric TB treatment based on the clinical findings. Her oral hypoglycaemic agent was changed to insulin therapy (biphasic). She was followed up for 2 weeks and an improvement on her TB treatment was noted; her serial chest radiograph showed left-sided pleura effusion resolved (Figure). In the last visit, HBA1C was 7% and the patient had successfully completed her TB treatment.

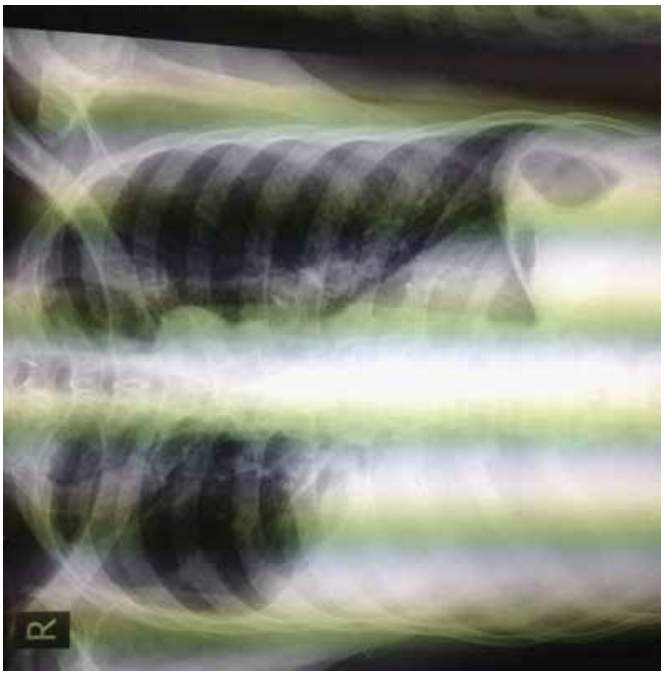

Figure: Chest radiograph showing pleura effusion.

The second case examined was that of a 52-year-old female with uncontrolled type 2 DM who had a diabetic foot in 2013 with subsequent below knee amputation of the right leg. In March 2014, she was diagnosed with pulmonary TB based on her clinical and bacteriological status (mycobacterium TB detected sensitive to rifampicin) and was commenced on TB treatment and then referred back to a local clinic to continue her TB treatment. The sputum check for TB sputum conversion was not done at 7th month. In the 6th month of her TB treatment, she presented with constitutional symptoms of cough, fever and night sweat. Her sputum GeneXpert/RIF was requested and Mycobacterium TB complex was detected, which was resistant to rifampicin. HBA1C at the time of diagnosis of MDR-TB was 12.3%. Her insulin therapy was adjusted, and the patient is currently on MDR-TB treatment awaiting the result of her sputum culture.

DISCUSSION

These two cases reflect the need to incorporate routine clinical screening of TB in patients with DM. Diabetes mellitus increases the general risk of infection, and the precise mechanisms by which DM predisposes patients to TB are still not clear and require further research. Both patients were HIV negative, and unlike the situation with HIV infection, in which cell-mediated immunity is gradually compromised by progressive depletion and dysfunction of CD4 T-lymphocytes, in these two patients with known DM, they might have suffered the impairment of their cell-mediated immunity by DM which impairs the function and activation of the macrophages, monocytes and lymphocytes (6).

These patients were screened for TB as per the National TB guideline using the symptoms screening tool (15). The use of symptoms screening has a reduced sensitivity and specificity in screening for TB cases. However, when patients with positive symptoms, as shown in these cases, are identified, further investigation should be done to diagnose TB. With all our patients, sputum AFB GeneXpert and chest radiology were done. This implies that this approach of using symptoms screening and radiological and sputum AFB GeneXpert is operationally feasible in our setting similar to other reports (9).

To highlight the morbidity pattern associated with TB in people living with DM, the first patient had presented as an atypical TB case, extrapulmonary TB, with an absent AFB in the sputum GeneXpert. Atypical presentation of TB in patients with DM, especially radiological, has been described elsewhere (14). We highlighted an abnormal radiological finding of unilateral pleura effusion as an extrapulmonary manifestation of TB in DM in our case. The poor outcome of TB therapy in our patient with DM was observed in the second case where the patient developed MDR-TB (11, 12), the mechanism of which is not clearly known.

In conclusion, incorporating TB screening among patients living with DM into clinical practice should be intensified in order to improve the outcomes of both conditions and, more importantly, control both epidemics. Our case studies highlight the importance of screening for TB in patients with DM because this will hopefully support the allocation of resources for improved screening in poor resource settings.

ACKNOWLEDGEMENTS

We thank the staff of Department of family medicine, Cecilia Makiwane Hospital (CMH) and National Health Laboratory Service (NHLS), CMH for the quick turnaround time of all the results on the patient.

AUTHORS' NOTE

OOS, OVA and DTG conducted expert analyses of the case and prepared the manuscript. Written informed consent was obtained from the patient for publication of this case report. The authors declare that they have no competing interests.

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