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TUBERCULOSIS UNMASKED HIDDEN DIABETES MELLITUS TYPE 2 IN A LEAN 48 YEARS MALE

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ABSTRACT
Diabetes Mellitus (DM), a highly prevalent disease, needs rigorous screening to improve patient outcomes. The majority of available screening criteria is validated on Caucasian populations where as the Pakistani population has its unique characteristic e.g. presence of DM at a lower BMI and a high prevalence of vitamin D deficiency (predisposing factor of DM). These factors need to be considered in a suspected case of DM. Late diagnosis of DM may result in complications like infections including active tuberculosis. Infectious processes can unmask DM by decreasing insulin levels and increasing insulin resistance, thereby presenting as one of the first manifestation of diabetes mellitus. The authors report a case of DM2 in a thin, lean patient with tuberculosis complicated by bronchiectasis unmasking DM2.

INTRODUCTION
Diabetes Mellitus (DM) is a world-wide growing health problem with the numbers of patients expected to rise from 336 million in 2011 to 552 million by 2030.[1] Early detection of DM and prediabetes has a great impact on patient outcomes. Asian population has shown a higher prevalence of DM at lower BMI compared to other ethnicities.[2] These factors can result in late detection of DM in such patients which often presents with complications associated with DM2.

Diabetes increases the susceptibility to different kinds of respiratory infections. It is often identified as an independent risk factor for developing lower respiratory tract infections.[3] The relationship between diabetes and pulmonary TB is well known, and the incidence of TB in diabetics is 3 times higher than the non-diabetic population.[4] It is attributed to the malfunction of monocytes in DM which contributes to increased predisposition to TB and ultimately a worse prognosis.[5]

Moreover, DM has been reported as an independent risk factor for TB with a further increased risk of TB with the presence of bronchiectasis in DM.[6] Authors report a case of a thin, lean 48 years old male who presented with tuberculosis complicated by bronchiectasis unmasking DM.

Case presentation: A 48 years old male presented in CMH Hospital out-patient department (OPD) with main complaints of fever, cough, hemoptysis, and right-sided pleuritic chest pain. His symptoms had started one month ago. Fever was low grade, continuous, not associated with any rigors or chills, and night sweats which resolved in 20 days. His cough remained persistent with more bouts in the morning**.** Initially, he had a dry cough. However, on the third day of his illness, his cough became productive with blood-stained sputum and right-sided moderate to severe pleuritic chest pain. The exacerbation of symptoms prompted him to visit CMH.

Along with the above-mentioned symptoms, he also noticed a significant increase in appetite, thirst, urination, and decreased vision since the beginning of his complaints. Despite increased appetite, he had lost about 4kg of weight in one month. On further questioning, he also mentioned the presence of leg cramps for the last 7 months. He had also been a chain smoker with a history of 20 pack-year cigarette smoking which he had quit 10years ago. He had no family history of DM, ischaemic heart disease, asthma, hypertension, or TB. Due to negative DM family history and lean physique, he did not think of screening for DM despite having classic symptoms of polyphagia, polydipsia, and polyuria.

On examination, he was a pale, thin, lean patient with a normal BMI (20kg/m^2), respiratory rate of 17 breaths per min, normal temperature(99F), regular pulse (88 beats/ minute), and, normal blood pressure (120/80mmHg). Oxygen saturation was 90% on room air. Chest expansion was reduced by 2 cm and percussion note was slightly impaired in the anterior axillary line on the right side which suggested underlying consolidation. He had

normal heart sounds and vesicular breathing with no added sounds.

With a provisional diagnosis of pneumonia, high suspicion of pulmonary tuberculosis, and suspected underlying Diabetes Mellitus, he was admitted to the medical ward. He was put on the following treatment while his investigations were being carried out: Humulin(R) (10 units s/c 08 hourly), Injection Rocephin (1 gm I/V twice a day) with tablet levofloxacin 500mg and Injection Tranexamic acid (500mg I/V thrice a day) for hemoptysis.

His Blood Complete Picture showed slightly raised TLC ($10.8*10^9$/L) with a normal DLC. Moreover, his reports also showed low Haemoglobin (9.6 gm/dl), low MCV (60.4 fL), and normal platelet count. Erythrocyte sedimentation rate was 25mm at 1st hour. His liver function tests, renal function tests, and serum ferritin (176 ng/ml) were normal.

The presence of classic symptoms of DM prompted for evaluation of diabetic profile which showed raised fasting blood sugar (25.4 mmol/L), random blood glucose (28.2 mmol/L), and high HbA1c (14.6%). His routine urine examination revealed 3 plus sugar with no proteinuria and lipid profile reported high LDL cholesterol (2.82 mmol/L) and low HDL cholesterol (1.1 mmol/L). Thyroid function tests were normal.

X-ray chest showed prominent hilar shadows (fig 1) and CT chest (fig 2,3) showed a patch of consolidation with central air bronchogram in the medial segment of right middle lobe along with mild bronchiectatic changes. Bronchoscopy also displayed bronchiectatic changes in the right middle lobe. However, his sputum and bronchoalveolar secretions culture were negative for any bacteria, TB, or fungi**.**

GENE EXPERT (gold standard investigation for TB) was sent, but his sample collection was insufficient with only the presence of saliva. Consequently, he was asked to provide a second sample, but he could not come due to his occupational commitments. Given the high prevalence of vitamin D deficiency in Pakistan and the presence of leg cramps in the patient, his serum vitamin D levels were also measured which turned out to be low (40 nmol/L). Fundoscopy was normal.

Despite the empiric treatment with antibiotics for 10 days and good sugar control with insulin, he remained sick with persistence of fever and dry cough. Given the high prevalence of TB in Pakistan, chronic nature of his symptoms which failed to respond to initial treatment and strong clinical suspicion of tuberculosis with bronchiectasis in the right middle lobe, he was started on 4 drugs anti-TB treatment on 10th day of his hospitalization. He gradually responded to anti-TB treatment within 10 days with normalization of temperature, lessening of respiratory symptoms, and improvement in general well-being.

As his symptoms showed improvement, he was discharged on the 25th day of his admission on 4 drugs anti-TB regimen along with insulin Humulin 70/30, 20 units s/c in the morning, and 10 units in the evening. He was also prescribed vitamin B6, vitamin D, and iron supplements.

After 1 month, he visited the hospital to collect his medicines and reported no complaints of fever, cough, and pleuritic chest pain. His blood sugar was well controlled with insulin treatment.

On 3 months follow-up, the patient reported decreased polyuria and no hemoptysis in the past 3 months, since his discharge, with good blood sugar control (glycosylated haemoglobin 6.6%). His blood complete picture showed improvement of haemoglobin from 9.6g/dL at the initial presentation to 11.5g/dL. His chest signs of expansion and percussion note were normal. He was advised to continue 2 drug anti TB treatment for another 3 months along with insulin.

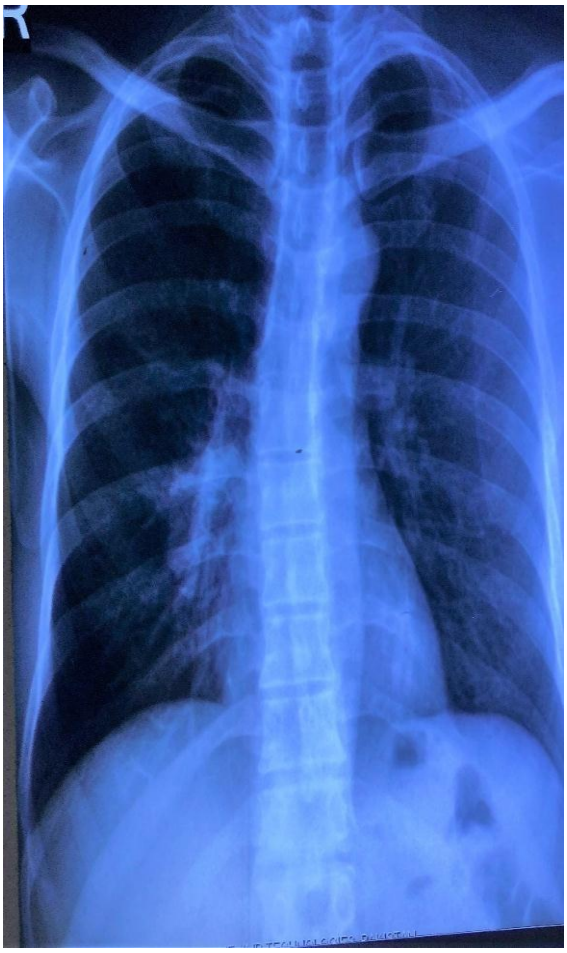

Figure 1: X-ray chest (posteroanterior view) with prominent hilar Shadows.

Figure 2: CT chest with a patch of consolidation in the medial segment of right middle lobe

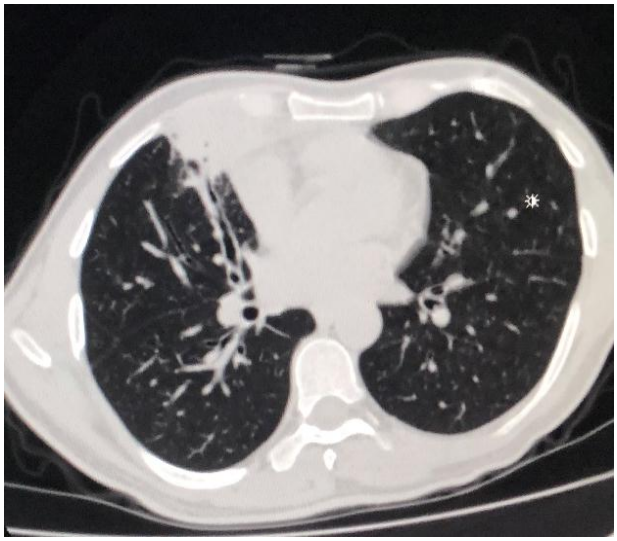

Figure 3: central air bronchogram in the medial segment of right middle lobe along with mild bronchiectatic changes.

DISCUSSION

Diabetes Mellitus (DM) can present in various modes including its classic symptoms (polyphagia, polydipsia, polyuria, and decreased vision), incidentally on routine urine examination, and with its complications.[7] Infection is a stressor that has a role in unmasking DM by promoting insulin resistance via various mechanisms like inhibition of insulin signal transduction by acute phase reactants like IL-6,[8] and decreased insulin concentrations.[9] Moreover, the prevalence of tuberculosis in diabetes has been reported to be high (20%),[10] thus clinicians should have a higher suspicion of DM among tuberculosis patients. High glucose levels at presentation of infection symptoms are also linked with worse outcomes among diabetics hospitalised for lower respiratory tract infections.[11] It highlights the importance of early diagnosis and good control of DM among these patients. Late diagnosis of DM results in poor blood sugar control, which leads to increased risk of complications and poor outcomes of tuberculosis.[12]

A case series described a similar presentation as in the reported patient of TB among diabetics who responded to empirical treatment (anti-TB drugs) without any laboratory confirmation of TB. Twelve percent of the patients in the case series had clinical and radiographic findings suggestive of bronchiectasis, but nearly half of the patients failed to have any bacteriological confirmation.[13] Moreover, uncontrolled diabetes results in more chest cavities and a lack of culture conversion after treatment.[14] Therefore, it is important to manage patients prudently with undiagnosed and poorly controlled DM for suspected TB.

Another under-looked risk factor of DM reported in the patient was Vitamin D deficiency.[15] It needs to be noted that Vitamin D deficiency is highly prevalent among the Pakistani population,[16] however, no study has been conducted to stratify the role of Vitamin D deficiency causing DM in Pakistan. As shown in previous studies, DM has a higher prevalence among the Asian population despite having a lower BMI.[2] Lack of awareness of this peculiar predisposing factor may result in low suspicion of DM among patients. This can result in delayed diagnosis of DM as in the reported patient. A better awareness of distinctive risk factors of DM needs to be addressed among the general population and clinicians.

DM is highly prevalent in Pakistan,[17] despite this the data about DM on the Pakistani population is deficient. Criteria for screening of DM differ among various guidelines, for example, the United States Preventive Services Task Force (USPTF) recommends patients with risk factors like hypertension to undergo screening while the American Diabetes Association recommends broader screening even for individuals without any risk factors above 45 years of age.[18] Screening and early intervention of DM are associated with better patient outcomes but most of the screening guidelines are developed and validated on the Caucasian population. Few studies like RAPID (Risk assessment of Pakistani individuals for diabetes) developed a risk assessment score[19], but a more thorough screening criteria based on the unique characteristics of this population needs to be devised. The role of physicians to improve the quality of life of diabetics is well-known. Better training of physicians in the diagnosis and management of DM is required in Pakistan.[20]

CONCLUSION

Infection has a role in unmasking symptoms of DM by increasing insulin resistance and decreased insulin levels. DM causes decreased immunity which makes lower respiratory tract infections, a mode of presentation of DM. Despite having negative indicators on laboratory evaluation of TB, it is important to have a high clinical suspicion among diabetics with lower respiratory tract symptoms for TB who fail to respond to initial treatment

for bacterial pneumonia in the areas with a high prevalence of TB. Furthermore, the factors like presence of DM at lower BMI and vitamin D deficiency need to be accounted for in assessing the risk of DM in the Pakistani population.

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