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Case Study

ADOLESCENT WITH TYPE 1 DIABETES MELLITUS WITH CAVITATORY PULMONARY TUBERCULOSIS

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ABSTRACTS

Tuberculosis is a major public health problem globally and there is a relative paucity of data on the clinical course of TB in immunosupressed adolescents. We report a case of cavitatory pulmonary tuberculosis in a diabetic adolescent. Although cavitatory lung lesions being not so common in pediatric age group. Co-existense of Diabetes Mellitus and Tuberculosis emphasizes the need for intensive screening for tuberculosis in Type 1 DM children.

KEYWORDS: Adolescent, Cavitatory Tb ,Diabetes Mellitus type 1, Tuberculosis

INTRODUCTION

Diabetes mellitus (DM) is a common, chronic, metabolic syndrome characterized by hyperglycemia as a cardinal biochemical feature. The major forms of diabetes are classified according to those caused by deficiency of insulin secretion due to pancreatic β-cell damage (type 1 DM, or T1DM) and those that are a consequence of insulin resistance occurring at the level of skeletal muscle, liver, and adipose tissue, with various degrees of β-cell impairment (type 2 DM, or T2DM).

T1DM accounts for about 10% of all diabetes, affecting 1.4 million in the United States and about 15 million in the world. It is one of the most common severe chronic childhood diseases; 40% of individuals with type 1 DM are younger than 20 year of age. The incidence of T1DM is highly variable among different ethnic groups. The overall age-adjusted incidence of type 1 DM varies from 0.7/100,000 per year in Karachi (Pakistan) to about 40/100,000 per year in Finland[1].

The link of DM and TB is more prominent in developing countries where TB is endemic and the prevalence of DM is rising.

The first report of the association between DM and TB was documented by Avicenna (980-1027 AD) over one thousand years ago. Since that time, the relationship between diabetes mellitus (DM) and tuberculosis (TB), and the nature of their interaction with regards to comorbidity are largely suggested by numerous epidemiological studies. In the early 20th century, the effect of DM on TB was large concern of investigators, but this was somewhat neglected in the second half of the 20th century with the emergence proper treatment for both diseases[2,3].

The knowledge of the global epidemiology of TB in children is somewhat limited. In 2002, the WHO estimated that 8,800,000 TB cases occurred worldwide, based on data from 209 countries with an estimated mean case rate of 145 per 100,000 population (range, 2–1067 cases)[4].

Incidence rates start to raise in adoloscents and precede a peak in adulthood in developing countries[5].

Although the definite pathophysiological mechanism of the effect of DM as a predisposing risk factor for TB is unknown, some hypotheses are suggested: depressed cellular immunity, dysfunction of alveolar macrophages,low levels of interferon gamma, pulmonary microangiopathy, and micronutrient deficiency[6,7].

Few studies in lower income countries have explored this relationship in light of growing DM prevalence in the developing world.

We hereby report a case of an Adoloscent with Type 1 Diabetes Mellitus with Pulmonary Cavitatory Tuberculosis

CASE REPORT

A 13 year old Indian student with type 1 diabetes mellitus on insulin therapy presented with a three month history of cough, marked weight loss, anorexia and one week history of high grade fever. There was no family history of TB. Physical examination revealed : weight 29kgs , height 146 cm and BMI of 13.6 .She had a Bacillus Calmette –Guerin (BCG) scar. Chest examination revealed reduced air entry with bilateral crepitations and increased vocal resonance in the middle and lower zones of left lung. The tuberculin skin test was positive measuring 14 x 11 mm. The blood count was normal. (wbc count -6300) ESR was 12 mm/hr. blood culture was unremarkable. Her chest radiograph (Fig.1) on presentation showed multiple well defined round opacities and cavitating lesions in the middle zone as well as upper zone of the left lung. Overall, the findings were suspicious for tuberculosis (TB). Given the extensive findings, Computed tomography (CT) of thorax imaging was performed for further evaluation. CT (Fig.2)showed a large area of cavitatory consolidation in left upper lobe, multiple V-Y opacities (s/o endobronchial spread of disease process) in both lungs, predominantly in bilateral upper lobes, superior segment of bilateral lower lobes, right middle lobe and lingula. Multiple enlarged discrete as well as conglomerate, necrotic, non calcified pretracheal, paraortic, prevascular, subcarinal and aortopulmonary lymph nodes. Overall findings were most consistent with active primary TB. Patient`s sputum later confirmed mycobacterium tuberculosis by detection of acid-fast bacilli on ZN stain and culturePatient was isolated and started on standard regime of medications for treatment of tuberculosis including isoniazid, rifampicin, pyrazinamide, and ethambutol. Patient continues to be compliant on medications without complications.

DISCUSSION

Asia is the epicenter of the growing burden of DM[8] and the largest contribution is from India and China[9].

Notably, pulmonary TB is the ninth most frequent complication of DM[10] and due to a rising prevalence of DM, the relative contribution of DM to the TB epidemic is increasing[8,11].

Tuberculosis (TB) is a major public health problem globally with 8.8 million cases being diagnosed in 2010 of whom 1.1 million died[12]. Incidence rates start to rise in adolescents and precede a peak in adulthood in developing countries[13].

Tuberculosis remains a common worldwide infection causing significant morbidity and mortality, especially in developing nations[14]. Due to effective treatment and public health measures, industrialized countries have an average annual incidence of 23 per 100,000, accounting for only 4% of total notified cases worldwide[14,15].

Pediatric TB, or childhood TB, defined by the World Health Organization (WHO) and Centers for Disease Control and Prevention (CDC) as TB in children less than 15 years of age, presents health care providers with unique challenges[16].

The knowledge of the global epidemiology of TB in children is somewhat limited. Nelson and Wells reviewed recent epidemiologic studies and surveillance data describing trends in the global burden of TB in children. Childhood TB accounted for only 2% to 7% of TB cases in developed countries, compared with 15% to 40% of cases in developing countries[17].

Active disease in younger individuals usually arises among racial and ethnic minorities, or in association with conditions that compromise host immunity (HIV infection, malnutrition, drug and alcohol abuse, co-existent medical conditions, corticosteroid or other immunosuppressive therapy)[18]. As observed in our case child is malnourished and diabetic, hence increasing further chances for co-infection.

There are 5 closely related mycobacteria in the *M. tuberculosis* complex: *M. tuberculosis, M. bovis, M. africanum, M. microti,* and *M. canetti. M. tuberculosis* is the most important cause of tuberculosis disease in humans. The tubercle bacilli are non-spore-forming, nonmotile, pleomorphic, weakly gram-positive curved rods 2–4 μm long[19].

Latent infection: The pathophysiology of tuberculosis is complex. Acquisition of the infection is primarily dependent on exogenous factors; however, reactivation of disease is largely under the influence of immune sufficiency[20].

Transmission: *M. tuberculosis* is person to person, usually by airborne mucus droplet nuclei, particles 1–5 μm in diameter that contain *M. tuberculosis.* Transmission rarely occurs by direct contact with an infected discharge or a contaminated fomite. The chance of transmission increases when the patient has an acid-fast smear of sputum, an extensive upper lobe infiltrate or cavity, copious production of thin sputum, and severe and forceful cough.

Pathogenesis: The primary complex of tuberculosis includes local infection at the portal of entry and the regional lymph nodes that drain the area. The lung is the portal of entry in >98% of cases. The tubercle bacilli multiply initially within alveoli and alveolar ducts. Most of the bacilli are killed, but some survive within nonactivated macrophages, which carry them through lymphatic vessels to the regional lymph nodes. When the primary infection is in the lung, the hilar lymph nodes usually are involved, although an upper lobe focus may drain into paratracheal nodes. The tissue reaction in the lung parenchyma and lymph nodes intensifies over the next 2–12 wk as the organisms grow in number and tissue hypersensitivity develops. The parenchymal portion of the primary complex often heals completely by fibrosis or calcification after undergoing caseous necrosis and encapsulation. Occasionally, this portion continues to enlarge, resulting in focal pneumonitis and pleuritis. If caseation is intense, the

center of the lesion liquefies and empties into the associated bronchus, leaving a residual cavity.

The foci of infection in the regional lymph nodes develop some fibrosis and encapsulation, but healing is usually less complete than in the parenchymal lesion. Viable *M. tuberculosis* can persist for decades within these foci.[19]

It seems that patients with type 1 DM are more susceptible than who have type 2 DM. This higher susceptibility may be related to a longer duration of disease or could be due to the fact that control of hyperglycemia is more difficult among type[21].

Additionally, the risk of TB is higher among patients who are using insulin[22], particularly, those who need higher doses of Insulin[23,24]. Poor glycemic control has been significantly associated with the occurrence of TB[25].

Abdulmoez et.al concluded among the children with diabetes (110), 4 (3.8%) were found to have positive tuberculosis results by tuberculin skin test, whereas 2 (1.8%) were found to have positive tuberculosis results by Ziehl Neelsen staining on sputum[26], in our case both were positive.

Radiologic diagnosis of TB allows for early intervention in infected patients, as acid-fast bacilli are found in the sputum of only a limited number of patients (20-55%) with active pulmonary TB[27].

Primary TB progresses to active disease within one year of infection in approximately 5% of individuals.

However, findings classically associated with postprimary TB include an affinity for the upper lobes, cavitation, and absence of LAD[28]. Multiple cavities are common, and are imposed upon an area of consolidation. Endobronchial spread is the most common means of spread in postprimary TB, and results in tree-in-bud opacities on CT which is seen in our case and both cavitation and the tree-in-bud sign are signs of an active disease process[27].

Even though cavitary tuberculosis is rare among children, on an average 6 cases were seen every year. In children, cavitary lesions may arise by one of the following mechanisms: (a) acute cavitation from extension of a recent primary focus and evacuation of the contents, *(b)* evacuation of the caseous material from a slowly growing round focus, *(c)* rapid lung destruction following bronchial spread and *(d)* exogenous reinfection following hematogenous spread. Cavitation arising out of exo-Ogenous reinfection and progression of the primary lesion are more common in populations with increased prevalence of tuberculosis, like in India[28,29].

The importance of cavity formation in tuberculosis lies in the communication it provides for the organisms with the outside environment. It results in a continuous supply of well oxygenated air to the interior of the cavity that stimulates rapid extracellular bacterial multiplication and provides a means for spread of disease both to other part of the lung and to other individuals[30].

Intensive screening for tuberculosis in Type 1 DM children, higher incidence in type 1 due to more difficulty in controlling of hyperglycemia.

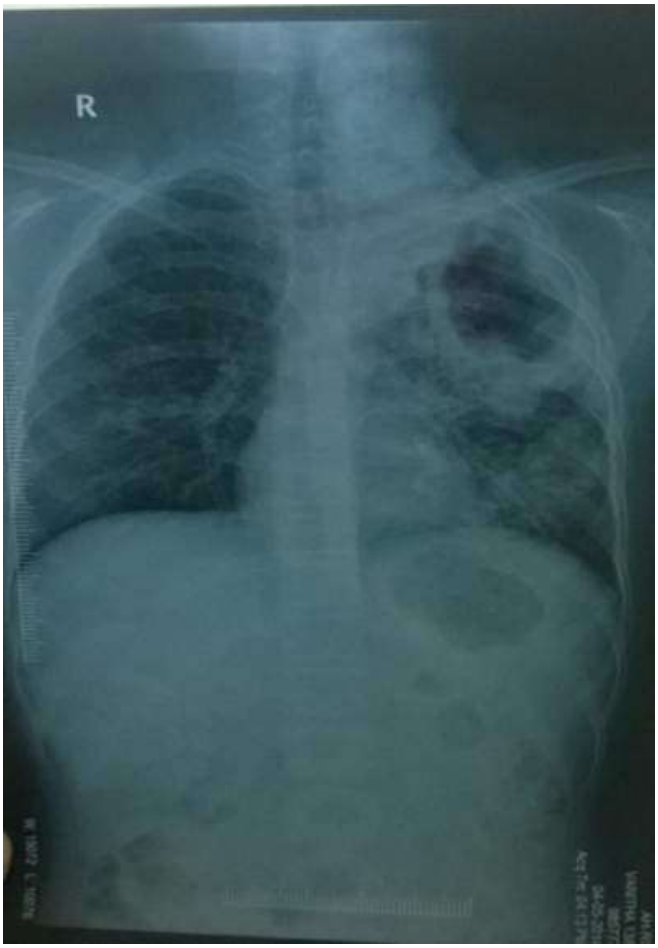

Figure 1:*13 year old female with primary active tuberculosis. Posteroanterior chest radiograph: multiple well defined round opacities and cavitating lesions in the middle zone as well as upper zone of the left lung.*

CONCLUSION

Figure 2:*13 year old female with primary active tuberculosis.Chest CT shows large area of cavitatory consolidation in left upper lobe, multiple V-Y opacities (s/o endobronchial spread of disease process) in both lungs, predominantly in bilateral upper lobes, superior segment of bilateral lower lobes, right middle lobe and lingula.*

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