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CASE REPORT

CO-INFECTION BY MYCOBACTERIUM TUBERCULOSIS AND KLEBSIELLA PNEUMONIAE IN AN ELDERLY MALE WITH MULTIPLE CO-MORBIDITIES: A RARE ENTITY WITH HIGH MORTALITY

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Abstract:

Klebsiella pneumoniae and Mycobacterium tuberculosis coinfection is one of the most lethal combinations with high mortality specially if there is delay in diagnosis and proper management. Patients with uncontrolled diabetes mellitus are prone to develop this type of serious infection.There is a considerable overlap in the clinical presentation of these critical pulmonary infections hence there is need for a high index of clinical suspicion, appropriate judicious investigations, and promt management to improve survivality. Here, we have presented Mycobacterium tuberculosis and Klebsiella pneumonia co-infection presenting as cough, chest pain, and shortness of breath in an elderly male with multiple co-morbidities, like uncontrolled diabetes mellitus, hypertension, prosthetic aortic valve in situ (for aortic stenosis)& previous history of ishchaemic stroke. This combination is rare and to the best of our knowledge not reported in the literature from Bangladesh.

Key words: *Klebsiella pneumoniae , Mycobacterium tuberculosis* ,Co-infection

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Introduction:

Pneumonia is one of the major causes of morbidity and mortality worldwide, especially in resource-limited settings such as Bangladesh, a lower-middle-income country in Southeast Asia. While the lack of diagnostic microbiology facilities has the limited study of etiologies in Bangladesh, available data suggest that Streptococcus pneumonia, Haemophilus influenzae, Pseudomonas aeruginosa, Klebsiella pneumoniae, Mycoplasma pneumoniae, and Chlamydia pneumoniae are the most common etiologies of community-acquired pneumonia (CAP) in Bangladesh.[1] Mycobacterium tuberculosis infection (TB) is also a major cause of respiratory disease in Bangladesh. The estimated incidence of TB per 100,000 is 221 in Bangladesh, with a mortality rate of 24 per 100,000.[2] On the other hand, coinfection with tuberculosis (TB) and bacteria has not been widely reported. But in populations with a high TB prevalence, co-infection with TB and bacterial pathogens has been encountered.[3]

Klebsiella pneumoniae and Mycobacterium tuberculosis coinfection is one of the most lethal combinations that has not been diagnosed and

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reported properly. Due to the simultaneous occurrence of both infections, diagnosis is delayed, which leads to inadequate treatments and mortality.[4]

Diabetes mellitus is a metabolic disorder with profound negative effects on neutrophil proliferation, maturation, function, and lifespan. So, individuals with diabetes are predisposed to a wide range of opportunistic infections. Again, Diabetes mellitus acts as a predisposing risk factor for PTB and Klebsiella infection. Some hypotheses suggested to explain the phenomenon are of; include depressed cellular immunity, low levels of interferon-gamma, dysfunction of alveolar macrophages, micronutrient deficiency, and pulmonary microangiopathy.[5]

In this case report, we present Mycobacterium tuberculosis and Klebsiella pneumonia co-infection presenting as cough, chest pain, and shortness of breath in an elderly male with uncontrolled diabetes mellitus& hypertension. This combination is rare and to the best of our knowledge not reported in the literature from Bangladesh. If these lethal combinations can be diagnosed early and treatment can be given in a timely manner, then it can save a precious life, as occurred in our case.

Case Report:

A 70-year-old hypertensive, diabetic Bangladeshi gentleman came to tertiary care hospital with the complaints of fever for two weeks with cough, chest pain& breathing difficulties. Fever was low grade, intermittent, not associated with chills and rigor, evening rise of temperature or night sweats. He also complained of productive cough, with whitish, frothy sputum, moderate in amount without any haemoptysis. He also complained of left sided pleuritic chest pain for few days. He suffered progressive breathlessness for last 1 day. Patient is hypertensive for 20 years and has been on antihypertensive drugs since. He is diabetic for 1 year which was incidentally diagnosed and was more or less in control with oral anti diabetic medications. He gave no H/O of any recent travel, exposure to farm animals or birds or prior contact with any tuberculosis patient. Regarding his past history, he was diagnosed with calcified aortic valve with severe aortic stenosis back in 2008 and his aortic valve was replaced with metallic aortic valve in the same year, and he has been on anticoagulantwarfarin since then. He was tested positive for Covid-19 in March of 2021. During his treatment he was withdrawn from Warfarin and suffered Stroke following which he developed left sided hemiparesis. His hemiplegia recovered gradually with several months of physiotherapy and medications.

On general examination , patient was ill looking, dyspnoeic with average built, mildly anaemic, pulse was 90 beats/min, BP was 140/80 mmHg, temperature was 101° F, respiratory rate was 20 breaths/min, Spo2 95% with 3 litres of oxygen. There was no clubbing, cyanosis, and lymphadenopathy. Respiratory system examination revealed left sided moderate pleural effusion as evident by reduced chest movement, reduced vocal fremitus from 4th intercostal space downwards, stony dull percussion note and reduced breath sound over left side of the chest. There was a metallic sound which corresponds with second heart sound. Other systemic examination was unremarkable.

On the basis of above clinical features, our provisional diagnosis was left sided parapneumonic effusion with Ischemic stroke, Diabetes Mellitus, Hypertension, prosthetic aortic valve in situ (for aortic stenosis).

Table I

Laboratory investigations

Name of the test	Finding
Hemoglobin	12.1 g/dl
Total white blood cell count	20.39 K/uL (90%)
Neutrophils	18.35 K/uL (5%)
Lymphocytes	1.02 K/uL (4%)
Monocytes	0.82 K/uL (1%)
Eosinophils	0.20 K/uL
Platelets	315 K/uL
Erythrocyte sedimentation rate (ESR)	104 mm/ Hr
CRP	280 mg/L
SGPT (ALT)	79 U/L
Serum creatinine	1.22 mg/dl
Random glucose	13.5 mmol/ L
Haemoglobin A1c	7.2 %
S. Procalcitonin	1.12 (mg/ml)
Prothrombin time	52 seconds
INR	4.43
D- Dimer	0.8 (ug/mL)
Blood C/S	No growth
Sputum C/S	Organism1. Klebsiela-pneumoniae. Sensitive to Amikacin, Meropenem, Imipenem, Doripenem, Trimethoprim/ Sulfamethoxazole Organism 2 - Candida spp.
Tuberculin test	02 mm
ICT for COVID -19	Negative

Chest xray (Figure- 1) showed left sided pleural effusion and CT chest (Fig 2) showed angular,

loculated pleural effusion with consolidation-collapse in left lung. USG guided pleural fluid aspiration was attempted but only 52 ml reddish color pleural fluid (Fig 3) was aspirated from left pleural space. Complete aspiration was not possible due to septated pleural effusion.

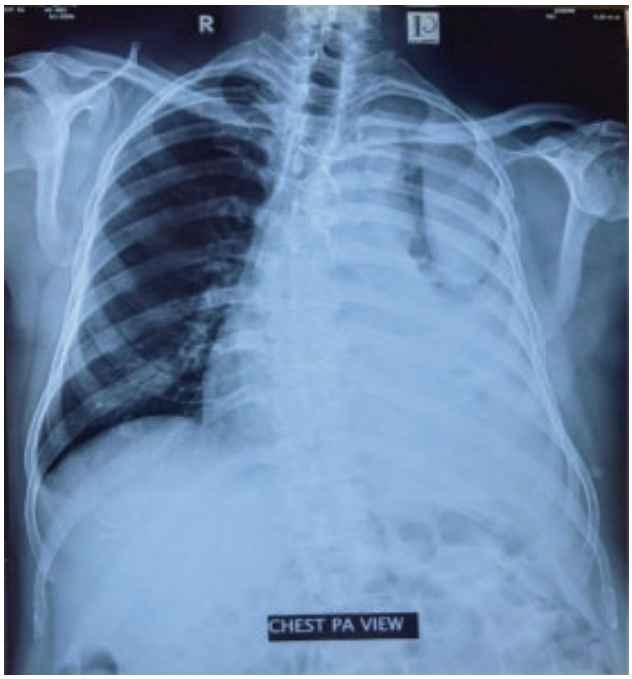

Fig.-1: *Chest Xray (during admission)*

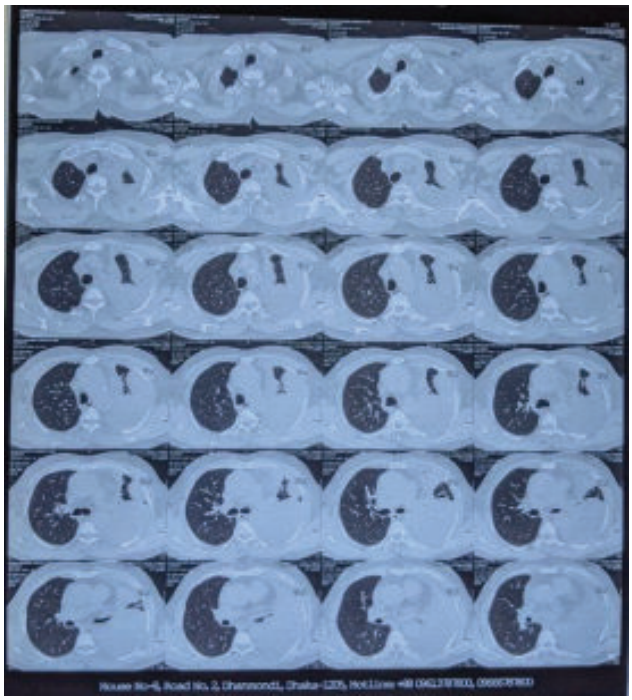

Fig.-2: *CT Chest (during admission)*

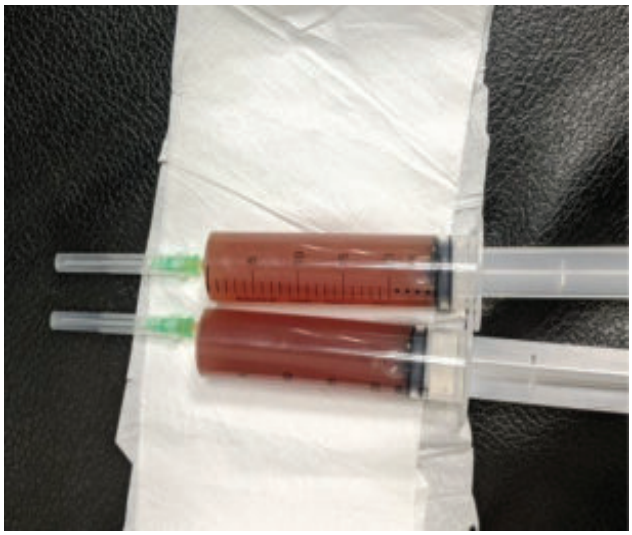

Fig.-3: *Pleural fluid*

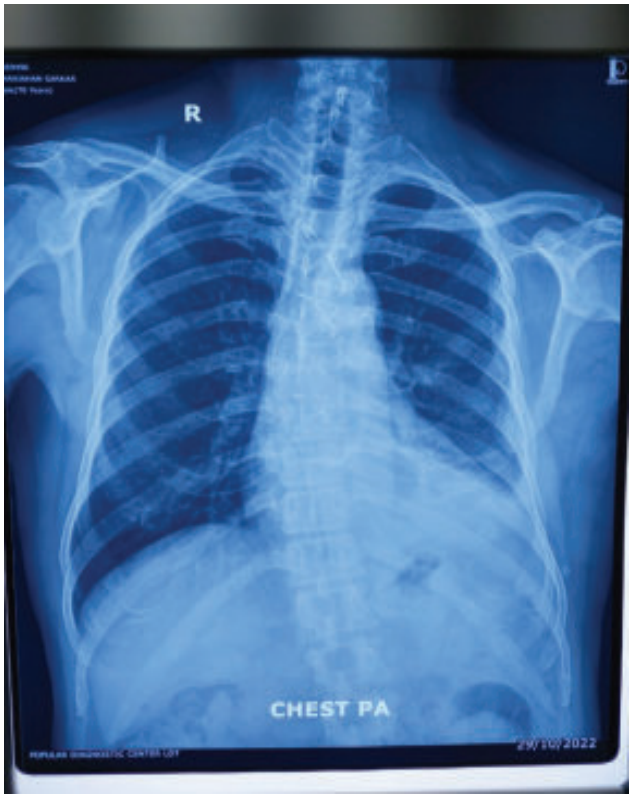

Fig.-4: *Chest xray (during second follow up)*

However, Gene Xpert MTB/RIF assay of the pleural fluid detected Mycobacterium tuberculosis which was not resistant to rifampicin (table 2), although Ziehl-Neelsen staining of the pleural fluid was negative for acid fast bacilli. On the other hand, on sputum culture showed the growth of Klebsiella pneumoniae (table 1).

Table-II

Pleural fluid Analysis

Name of the test	Finding
Physical Examination:	Appearance-Reddish
Cytological test:	Total WBC count: 80000/cumm, Total RBC count: 60000/cumm, Neutrophil: 90% Lymphocytes: 10% Cytopathology for malignant cell: Negative
Biochemical Test:	Glucose: 3.24 mg/dL, Protein: 4.98 g/dL, ADA: 52.26 U/L
Microbiological:	AFB staining: AFB not found Gram staining: Several gram-positive cocci Microbiological (Culture): Culture has yielded no growth of any pathogenic bacteria at 37 degree centigrade
Gene Xpert of Pleural fluid	MTB-Detected, RIF Resistance-Not detected

After proper evaluation and undergoing multiple investigations, we came to conclusion that patient had Parapneumonic Effusion with Klebsiella infection and Tubercular Pleural Effusion. Points in favour for Parapneumonic Effusion with Klebsiella infection were short history of productive cough, neutrophilic leukocytosis in CBC (Table 1) and predominant neutrophil (90%) (Table 2) in pleural fluid. Points in favour for Tubercular Pleural Effusion were low grade fever, detection of MTB in GeneXpert of pleural fluid and increased ADA level in pleural fluid (Table 2).

He was started treatment with combination Antibiotics for the Klebsillea pneumonia infection according to his sputum culture sensitivity report along with the proper management of his other co-morbidities. We had consulted with the Thoracic surgeon for the management of encysted multiloculated effusion and he advised VATS (Video Assisted Thoracoscopic surgery) decortication. But, due to presence to multiple co-morbidities, patient did not give consent for the VATS intervention.

After full course of two weeks combination antibiotic treatment for Klebsillea pneumonia, patient came for first follow up. Full blood count showed total WBC count reduced to 13.28 K/uL with 82% Neutrophil count, but ESR was remain high, 104mm/Hr. After the first follow up, Anti-TB medication had started according to national guideline category of 'new case' for 6months along with the steroid for two months.

Then, his cough, shortness of breath gradually subsided. The fever abated and he was able to perform all activities of daily living with an overall improvement in glycemic control. He came for second follow up after 18days ongoing treatment of Tuberculosis. On the second follow up, Chest xray (Fig4) showed much improvement with regards to the effusion. Pleural effusion is reduced to the lower zone only of the left lung and ESR reduced to 31mm/hr(which was previously 104 mm/hour).

Patient is now continuing his Anti-TB treatment and is currently in his 2nd month of treatment along with the management of other co-morbidities.His overall well being improved along with all biochemical & radiological parameters.

Discussion:

Bangladesh has one of the highest incidence of TB cases in the world with high TB and MDR-TB burden [6]. Though, coinfection with tuberculosis (TB) and bacteria has not been widely reported but superadded bacterial infection can occur in TB patients and the simultaneous occurrence of both infections leads to delayed diagnosis and inadequate treatment.

The coexistent infections of Klebsiella and Mycobacteria have been diagnosed but not frequently reported.[7] A study conducted in Japan in 2016, reported 128 cases of TB with coexistence of infectious agents. Amongst which the second highest coinfection was with K. pneumoniae that exhibited significant mortality rate than the others.[8] Coexisting Klebsiella and Mycobacteria infections have been reported in India and worldwide as well.[3,5,9,10]

Diabetes mellitus is a global health problem and over 80% of affected people living in low-middle income countries (LMICs) where tuberculosis is widespread.[11] On the other hand, Tuberculosis (TB) and diabetes mellitus (DM) have synergetic relationship. It has been seen, diabetic patients are 2–3 times at higher risk of getting active TB disease. Recent studies from Bangladesh have reported an increasing frequency of diabetes among persons with tuberculosis. Prevalence of TB among patients with DM attending diabetic care centres in Bangladesh was 3.4%.[12]

Klebsiella pneumoniae is an encapsulated gram-negative bacterium found in the environment and a member of the human intestine flora. It has been associated with pneumonia in patient with diabetes mellitus and in alchoholics. Diabetes mellitus is a major growing risk factor for pulmonary infections with Mycobacterium tuberculosis[13] and Klebsiella pneumoniae[14] both of which our patient had.

In general, patients with TB and DM are not treated differently than patients with only TB. Patients must be treated according to standard category.Rifampicin, isoniazid, ethambutol, and pyrazinamide remain the first- line drugs for the treatment of susceptible Mycobacterium tuberculosis strains. Almost all the anti-TB drugs are safe in diabetic patients with TB without other comorbidity. Before starting anti-TB therapy, baseline renal, and liver function should be assessed. Careful and frequent monitoring is required as there is increased chance of hepatotoxicity, and our patient was already on Warfarin therapy for which PT was prolonged for therapeutic purpose and also initially liver enzymes were higher. But eventually, liver enzyme went down and Anti-TB drug didn't cause deterioration of liver function test of our patient.

Given the low occurrence of *K. pneumoniae* in the community, the treatment of pneumonia should follow standard guidelines for antibiotic therapy. Once infection with *K. pneumoniae* is either suspected or confirmed, antibiotic treatment should be tailored to local antibiotic sensitivities. Current regimens for community-acquired *K. pneumoniae* pneumonia include a 14-day treatment with either a third or fourth-generation cephalosporin as monotherapy or a respiratory quinolone as monotherapy or either of the previous regimes in conjunction with an aminoglycoside. If the patient is penicillin-allergic, then a course of aztreonam or a respiratory quinolone should be undertaken. For nosocomial infections, a carbapenem can be used as monotherapy until sensitivities are reported.[15]

In our patient, initially we treated the Klebsiella infection with full course of 2weeks treatment of antibiotic. After that, we had started the anti-TB medications according to the guideline for the treatment of Tuberculous pleural effusion. Patient is responding well so far as had evidenced by clinical well-being and improvement of the effusion.

Conclusion:

TB and Klebsiella pneumoniae lung infection can coexist in patients with diabetes mellitus. There is a considerable overlap in the clinical presentation of these serious pulmonary infections hence the need for a high index of suspicion, appropriate investigation, and treatment in relevant situations. And if the patient can be diagnosed early and managed judiciously, then we will be able to combat the mortality associated with these lethal combination of Klebsiella and Mycobacteria, as occurred in our patient.

Conflict of Interest:

The author stated that there is no conflict of interest in this study

Funding:

No specific funding was received for this study**.**

Ethical consideration:

The study was conducted after approval from the ethical review committee. The confidentiality and anonymity of the study participants were maintained

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