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COEXISTING PULMONARY TUBERCULOSIS AND INTERSTITIAL LUNG DISEASE: A TALE OF TWO DISEASES

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ABSTRACT

Background
Tuberculosis (TB) remains a common lethal infectious disease globally. On occasion, it occurs alongside interstitial lung disease (ILD), or following treatment of ILD.

Report
We report a case of a 21-year old male with a history of chronic cough, weight loss, bilateral leg swelling, hypoxaemic on room air and on supplemental oxygen with central cyanosis whose chest radiograph and high resolution computed tomography chest scan showed features of both tuberculosis and non-specific interstitial pneumonia. He was treated with a course of prednisolone and azathioprine and anti-TB medicines leading to significant improvement of his symptoms.

Conclusion
Tuberculosis, a common treatable infectious disease, may coexist with ILD. Treatment of TB contributes to the overall prognosis of ILD.
Key words: Pulmonary tuberculosis, interstitial lung disease, hypoxaemia, anti-TB

INTRODUCTION

Worldwide, tuberculosis (TB) remains an important, deadly disease[1]. A third of the world's population harbour a latent infection of tuberculosis and factors responsible for shifts in the immunity of this at-risk population may result in a surge in the incidence of the disease.[1,2] These factors include immune compromise from infections (HIV), non-communicable diseases (diabetes mellitus), use of immune-modulating drugs and underlying diseases such as bronchogenic cancer or interstitial lung disease (ILD).[2,3] An estimated one-third of persons with HIV suffer from tuberculosis and it is the leading infectious cause of death in this group of persons.[1,4] Nigeria ranked 6th amongst the list of 30 countries with the highest TB burden, according to the WHO global TB control report of 2018.[1] Tuberculosis mimics the clinical and radiological features of many of the interstitial lung diseases, leading to a spate of misdiagnosis, treatment delays and deprivations.[5,6] The incidence of culture positive Mycobacterium tuberculosis in interstitial lung diseases has been shown to be up to 5 times higher than in the general population.[6]

Interstitial lung diseases (ILD), a term used for a heterogenous group of more than 200 conditions that share similar signs, symptoms, anatomic and pathophysiologic mechanisms, remain largely undiagnosed, especially in this part of the world.[7] Few reports have been made about ILD in Nigeria and as such the true prevalence cannot be estimated.[8-10] In many instances, due to their diagnostic challenge, they are misdiagnosed and managed as TB before the error is spotted.[6]

We present herein a unique case of coexisting active TB and ILD in a 21- year old male which posed diagnostic and clinical challenges.

CASE PRESENTATION

We present a 21-year old male Nigerian of Igbo origin, a secondary school leaver, who presented with an 18-month history of insidious onset, progressive breathlessness, and weight loss and a 3-month history of cough and fever. He had worked as an assistant to a mason and painter in the 6-months preceding the onset of his symptoms shortly after leaving secondary school and while awaiting admission into the university. The dyspnoea progressed to occur at rest leading to temporary discontinuation from the job. He subsequently developed cough, fever, drenching sweat and weight loss with worsening breathlessness 3 months prior to presentation. There was no haemoptysis or contact with persons with chronic cough nor had he been previously exposed to anti-TB medicines.

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There was orthopnoea and leg swelling but no paroxysmal nocturnal dyspnoea. He had no history of tobacco or illicit drug use. He had no significant medical or surgical history prior to this presentation. He presented with a chest x-ray done at a private hospital which was interpreted as pulmonary tuberculosis.

His physical examination findings were those of a chronically ill looking young male, with central cyanosis, bilateral pitting leg oedema up to the knees; significant respiratory distress with a respiratory rate of 50 cycles per minute, SpO_2 of 45% (room air) and 73% (on intranasal O_2 at 8L/min),widespread coarse crackles in the mid and basal lung zones especially; pulse rate of 134b/min, blood pressure of 140/80mmHg with a loud pulmonic component of the second heart sound. The rest of the physical examination was unremarkable.

He was admitted as a case of acute on chronic respiratory failure secondary to probable interstitial lung disease with possible Koch's disease and initially commenced on stat IV hydrocortisone then tabs prednisolone 40mg daily and omeprazole 20mg daily, IV frusemide, and oral spironolactone. Anti-TB medicines (CAT-1), viz HRZE, were commenced along with intermittent intranasal O_2 to achieve saturations of >90%. Intensive care unit admission, though desirable, was not pursued because of the potentially infectious nature of the condition.

Chest X-ray on presentation showed an in homogenous opacity in both hemithoraces with background cystic streaky and nodular lesions obscuring in the right and left cardiac borders, but with a preserved lung volumes (figure 1).A high resolution computed tomography (HRCT) scan of the chest was requested and showed extensive areas of consolidation in both lungs with the air-bronchogram sign in both lung bases with areas of reticulation, nodularity, and cystic bronchiectasis in both upper lobes. An impression of interstitial lung disease (non-specific interstitial pneumonia) coexistent with pulmonary tuberculosis was made (figure 2).

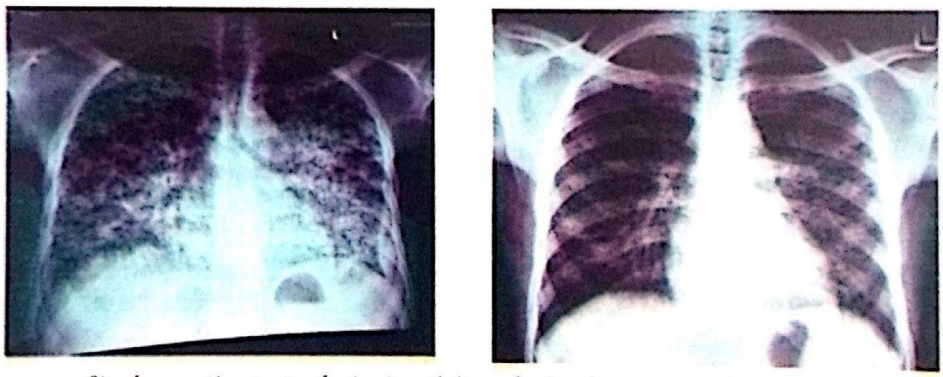

Fig.1 (a)Chest x-ray of index patient at admission (a) and after intensive phase of anti-TB (b)

His sputum XpertMTB-Rif result was negative for TB. His other laboratory results are shown in table 1.

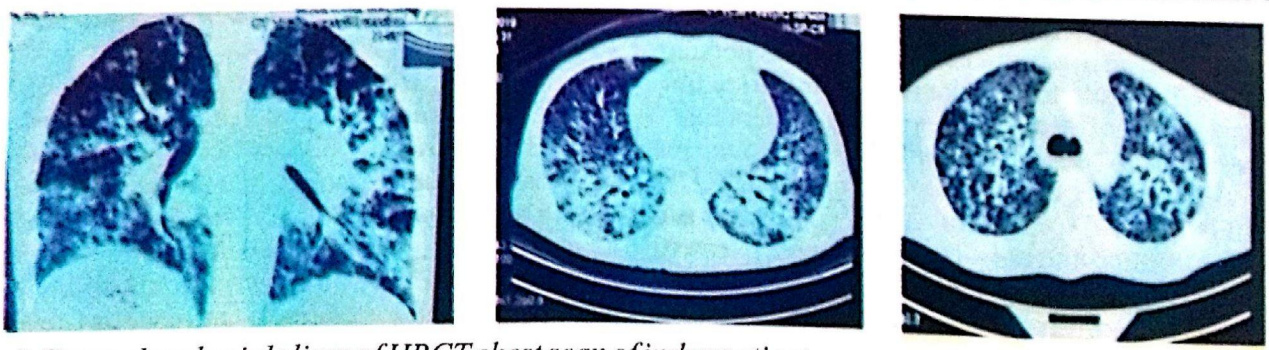

Fig.2 Coronal and axial slices of HRCT chest scan of index patient

He made significant clinical progress and was discharged to the outpatient department after 16 days on inpatient anti TB and immunosuppressants. Oxygen Saturation SpO_2 on room air on discharge was 98%. He has been gradually weaned off Prednisolone and placed on Azathioprine during his follow up. Presently, he has completed the intensive phase of anti-TB medicines and is on the continuation phase of the treatment. His latest CXR at the end of the intensive phase of treatment demonstrates remarkable improvement in the radiographic features compared to the pre-treatment image(figure 1b). He continues his treatment and follow up as at the time of writing.

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TABLE 1 Investigation results of index patient

Hb (g/L)	111	(120 – 180)
WBC (x 10^9/L)	18.4	(3– 10.8)
Diff (%)	Neutrophils – 66	(40 – 75)
	Lymphocytes – 33	(20 – 45)
	Eosinophils – 1	(1 – 5)
Platelets (x10^9/L)	159	(100 – 400)
ESR (mm/1st hour)	72	(0 – 7)
ALT (IU/L)	11	(3 – 12)
AST (IU/L)	24	(3 – 12)
ALP (IU/L)	102	(9 – 35)
Total Bilirubin (mg/dL)	1.5	(<1)
Conjugated bilirubin (mg/dL)	0.8	(0.4)
Na+ (mmol/L)	137	(135 – 150)
K+(mmol/L)	3.3	(3.5 – 5.0)
Cl- (mmol/L)	96	(96 – 108)
Urea (mmol/L)	7.38	(2.5 – 6)
Creatinine (i mol/L)	44.2	(44.2 – 132.6)
Fasting blood glucose (mmol/L)	4.2	(3.33 – 6.67)
Urinalysis	Proteinuria +	
Sputum M/C/S	Moderate growth of Streptococcus spp after 48 hours incubation sensitive to Augmentin (3+), Ceftriaxone (3+) and Cefuroxime (3+)	
Sputum GeneXpertMTB/Rif	No MTB detected	

DISCUSSION

We have highlighted the case of a 21-year old male with active TB infection complicating a background interstitial lung disease with the attendant challenges in correctly diagnosing and treating both conditions.

Idiopathic pulmonary fibrosis (IPF) is the most common chronic ILD of unknown aetiology and occurs more commonly in the 5^{th} – 6^{th} decades.[7] While enormous effort has been made to control and eradicate tuberculosis, it has remained a prevalent health challenge in the 21^{st} century.[1] The incidence of tuberculosis amongst patients with ILD appears to exceed that of the general population. Shachor*et al* retrospectively studied 162 cases of chronic ILD and found the incidence of MTB infection amongst their cohort to be 4.5 times that of the general population.[6] Park *et al* also reported an increased incidence of both pulmonary TB and non-tuberculous mycobacterial (NTM) infection amongst 795 patients with IPF.[11] Part of the increased incidence of tuberculosis in this population is due to the use of immunosuppressant medications such as prednisolone, azathioprine, tumour necrotic factor (TNF)-alpha inhibitors and Pirfenidone, to mention but a few.

Several reports have demonstrated the tendency to manage eventual idiopathic pulmonary fibrosis as smear negative TB in the past, usually unsuccessfully.[2,3,6,12] Akhter *et al* reported that 28 (38.35%) of 73 patients eventually managed at a ILD clinic in Pakistan were initially diagnosed and erroneously managed for TB before the correct diagnosis was made.[12] Only 2 (2.74%) of the patients in their series were found to have smear-positive TB on a background of silicosis.[12] The age of our index patient, lack of smoking and features of predominantly basal, subpleural involvement on imaging make it very unlikely that the specific type of ILD he had was IPF.

The exposure of our index patient to cement dusts and possible chemical solvents in paint in the months prior to the earlier manifestation of predominant breathlessness and weight loss argue strongly for a possible interstitial process. Workers in industries such as mining, tunnel construction, glass production, sandblasting, ceramic production and cement and concrete manufacturing are at risk of exposure to silica dust.

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The association of occupational exposure to silica and pulmonary tuberculosis has been established incontrovertibly, with the odds of tuberculosis being 2.8 – 39 times more in those with silica exposure than in otherwise healthy individuals.[12–15]

Interstitial lung disease coexisting with TB poses a diagnostic challenge, not least due to its infrequency of occurrence. Overlap exists in the symptoms of both conditions and no clear guidelines exist to distinguish both at presentation.[2,12] Due to the high prevalence of TB in our clime, it is understandable that part of the work up for patients presenting with chronic cough, weight loss and other constitutional symptoms and radiographic shadowing invariably includes TB. Neglect of any underlying ILD process however, leads to a poorer outcome such as that reported by Wong et al.[2] This is especially so amongst primary care providers and non-specialist health care providers where there is a lack of awareness of the possibility for such concomitant existence.[12]The sputum GeneXpertMTB-Rif assay result of our patient was negative and contributed to the diagnostic dilemma. It is known that the sensitivity of this investigative modality approaches 98 – 100% in smear and culture positive samples but falls significantly to about 74 – 77% in smear negative but culture positive TB.[16]Our patient made a remarkable recovery following prompt institution of immunosuppressant therapy and anti-TB medication.

Recognition of the possibility of both conditions due to his significant oxygen desaturation on room air, central cyanosis, and bilateral pitting leg oedema, as well as the presence of cough, fever, weight loss and drenching sweat informed the choice of initial therapy and led to the resolution of his oxygen dependence within 48 hours of the commencement of immunosuppressant therapy.The response of the non-fibrotic ILDs to immunosuppressive therapy is known to be much better than those of the fibrotic forms, reflecting the generally better prognosis of the former.[10,12,17] Therapy with this class of drugs is also known to lead to reactivation of tuberculosis and accounts for a significant proportion of TB in the context of ILD.[2,10,11] Our index patient had no history of exposure to immunosuppressants prior to his presentation but may have had a possible impairment of macrophage clearance function following his exposure to silica-containing cement dust. The age at presentation and presence of typical features of Tuberculosis might be considered serendipitous as it ensured that TB was considered in the differential diagnosis with institution of appropriate anti-TB medicines early enough as to preclude death.[2] A high index of clinical suspicion alongside a pragmatic approach should influence diagnostic thinking in presentations of either condition, especially in the presence of atypical features.

CONCLUSION

This article highlights the unusual presentation and successful management of TB with ILD in a young male adult. TB can coexist with ILD, either de novo or as a result of therapy of the latter and should be considered in every such presentation of ILD due to its inherently treatable nature.

DISCLOSURES

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Conflict of interest: Nil

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