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Miliary Tuberculosis with Severe Pneumonia without Abnormal Chest Sounds in a Covid-19 Pandemic

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Abstract

Background: Tuberculosis (TB) is still causing deaths in children in TB endemic countries. Majority (80%) occur in the lungs, with 5% being miliary TB. It is an Interstitial Lung Disease (ILD) with similar clinical, physiological and radiological features to other ILD and affects mainly infants and children with a high mortality rate despite available treatment.

Case Presentation: A three-month old male presented during the COVID-19 pandemic with fever of 2 weeks, cough of one week, fast and difficult breathing of 6 days' duration. He received BCG vaccine 16 days after birth despite being unknowingly exposed to the TB contact from birth. He was acutely ill looking, with severe pneumonia and SPO2 of 76% in room air. Respiratory examination showed broncho vesicular breath sounds with no added sounds. A diagnosis of Severe pneumonia? Pneumocystis Jiroveci Pneumonia (PJP) and R/O COVID-19 was made. Subsequent reviews excluded PJP and COVID-19 and the final diagnosis was Disseminated (Miliary) TB. He was successfully treated with anti-TB medications for 12 months.

Conclusion: Miliary TB presents with common and uncommon manifestations that may be confusing, and so a high index of suspicion with a careful history, focused systemic examination, imaging and bacteriological studies are strongly recommended for its early diagnosis.

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Introduction

Tuberculosis (TB) is an old disease still causing deaths in children in developing countries and TB endemic regions [1-3] and yet childhood TB remains under-diagnosed and under-reported [2]. Majority (80%) of TB in children occur in the lungs, out of which 5% are miliary TB [2]. The term miliary TB was formed in 1700 by John Jacob Manget from the word 'miliarius' which means "related to millet seed" and represents disseminated TB with miliary shadows on CXR [4]. It has been a diagnosis of infants and children since the pre-antibioctic era [5] with a high mortality rate despite available treatment [4]. It is rare in children who have had BCG vaccination as this is known to reduce its incidence [4]. The diagnosis is challenging [4,5,6] because it is an Interstitial Lung Disease (ILD) with similar clinical, physiological and radiological features to other ILD [4]. It can affect any tissues but usually, highly vascularised ones like the lungs, liver, spleen, bone marrow and kidneys are commonly involved [1].

Generally, clinical manifestations range from Adult Respiratory Distress Syndrome (ARDS) to Pyrexia of Unknown Origin (PUO) [6,7] and these include fever (100%), fatigue (91%) and miliary shadows on CXR (88%) [7]. Frequent presentations include fever, loss of appetite, weight loss, crepitations, hepatomegaly, splenomegaly, neurologic manifestations like facial nerve palsy and tuberculous meningitis [2,8,10], but less commonly, chills, night sweats [11], daily morning fevers, haemoptysis, productive cough [4,8], granulomas/tuberculomas, [4,10,12] non-specific [13] and atypical presentations do occur[4]. Hepatosplenomegaly and peripheral lymphadenopathy are more frequent in children than in adults [8] and tuberculous meningitis occurs in 20-40% of cases compared to adults' 15-30% [8] The risk factors for acquiring miliary TB are HIV, childhood infections, malnutrition, chronic kidney disease, organ transplant, immunosuppression [8].

Initially, there's hyperinflation with no classical miliary tubercles in 50% of patients. But generally CXR findings are consistent and identify miliary shadows in 91% of cases of miliary TB [14] with a sensitivity of 59-69% and a specificity of 97-100% [4,5,7,9,11,14,15] Such findings include millet sized tubercles <2mm with 10% having nodules> 3mm which may be asymmetrical, mottled, coalesce or give a snowstorm pattern [4]. Treatment of Miliary TB is with anti-Tb drugs and use of steroids is controversial [4].

Miliary TB therefore presents with a wide variety of common and uncommon manifestations that may confuse even the most experienced Clinician [5], and hence this report aims to add to the available literature of knowledge.

Case presentation

A three-month old male presented in our facility with fever of 2 weeks, cough of one week and fast breathing of 6 days duration.

The fever was initially low grade, intermittent but became high grade and continuous. Cough was insidious in onset, dry, non-paroxysmal but distressing and worsened over time with associated fast and difficult breathing. There's history of contact with a 20 year old aunty who had TB and had been on treatment for 2 months before baby's presentation. Pregnancy was booked at a Primary Health Center (PHC) at 6 months' gestation and mother had regular attendance and was compliant on her routine drugs and vaccinations. Foetal ultrasound scan was normal and HIV screening was negative. The pregnancy was uneventful and carried to term with uneventful delivery and neonatal period. He was exclusively breastfed and immunized for age but noticed to have received BCG 16 days after birth despite being unknowingly exposed to the TB source contact right from birth. The source TB contact was diagnosed and started on Anti-TB treatment one month after his birth. He's the second of two siblings with the senior, a 2 year old female. Mother is 23 year old Secondary School Certificate of Education (SSCE) holder and father is a 31 year old with SSCE. All live in a poorly ventilated 2 room apartment.

Physical examination revealed an acutely ill looking male baby, in respiratory distress with flaring alae nasi, intercostal and subcostal recessions, febrile with temperature 38.5°C, respiratory rate-56/min, pulse rate-154/min, SPO_2-76% in room air, mildly pale, with a weight of 4.4kg, occipitofrontal circumference -38cm, Length-55cm and weight for length 0 to -1. Respiratory examination showed a symmetrical chest, resonant percussion notes, bronchovesicular breath sounds with no added sounds. The central nervous system examination was also normal. The abdomen was full, soft with tender hepatomegaly of 4cm and a splenomegaly of 3cm. The working diagnosis was underweight malnutrition with severe pneumonia? *Pneumocystis Jirovecii* Pneumonia (PJP) and rule out COVID-19. Subsequent reviews excluded PJP and COVID-19 and the final diagnosis was Disseminated (Miliary) TB.

HIV Screening for baby and mother were both negative. SARS COV-2 PCR was negative. CXR had widespread miliary nodules in all the segments and lobes of both lungs with attempts at cavitation in both upper lobes (Figure 1). Full blood count showed a total WBC of $18.3X10^9$/L, PCV-28%, L-36%, N-64% with hypochromasia and microcytosis. Early morning gastric aspiration for Xpert MTB/Rif detected MTB sensitive to Rifampicin.

Patient remained acutely ill, dyspnoeic and tachypnoeic with RR-56/min, having severe pneumonia on intranasal oxygen with SPO_2 ranging from 70-85% in room air and 92-98% on oxygen, yet with bronchovesicular sounds, good air entry bilaterally and no added sounds. Three days into admission and second day after starting anti-TB drugs (Rifampicin, Isoniazid, Pyrazinamide and Ethambutol for 2 months, followed by Rifampicin and Isoniazid for 10 months), he developed generalized tonic clonic seizures with temp 38.3°C aborted with intravenous diazepam. The seizures recurred after 24 hours with 4 episodes in all and a suspicion of tuberculous meningitis was entertained in addition. Phenobarbitone and prednisolone were then commenced after aborting the seizures with diazepam. Lumbar puncture was planned to rule out tuberculous meningitis but he remained very ill.

By the 4th day of anti-TB treatment, the temperature had stabilized for 48hrs, he was tolerating expressed breastmilk and SPO_2 in room air improved to 93-100% and oxygen therapy was subsequently discontinued. He was much improved but still ill-looking, in mild respiratory distress with RR-49/min and the chest examination still remained normal with resonant percussion notes, bronchovesicular and no added sounds. His improvement on anti-TB medications was so sustained that on the 9th day of admission, he was discharged home, to be followed up in the clinic 2 weeks later. He defaulted from the clinic visit for logistic reasons but was however collecting and adhering to anti-Tb drugs as prescribed and presented after 2 months of intensive phase at the age of 5 months. The mother complained of intermittent fever and inability to hold up the neck.

He had attained neck control before the onset of the illness at 3 months of age and was yet to regained it. Weight gain was also slow with only 400g added in 2 months since discharge. Physical examination showed head lag but normal tone, mild pallor, RR-52/min, clear chest with normal cardiovascular system and gastrointestinal tract. Diagnosis remained disseminated TB involving miliary and tuberculous meningitis in an underweight child. Nutritional counselling was reinforced, continuation phase of treatment commenced and steroid therapy with prednisolone which had been interrupted was re-commenced for 4-6 weeks. He has been regular on his Anti-TB medications, seen again three times in the outpatient clinic and had shown sustained improvement. By 9 months of age and 7th month of Anti-TB treatment, he had gained weight up to 6.8kg, regained neck control at 7-8 months and had discontinued prednisolone again after 3weeks. Physical examination was satisfactory with no respiratory distress and a clear chest, diagnosis remained disseminated TB with Miliary TB and probable tuberculous meningitis responding to treatment. A repeat CXR showed interval improvement with hyperinflation, persisting air bronchogram and a residual well circumscribed opacity in the lower lung lobe (Figure 2). His last visit was at 14months of age and 11th month of Anti-TB treatment with sustained and satisfactory improvement. He continues to be followed up in the Childrens' outpatient department, while Anti-TB treatment also continues for a total of 12 months.

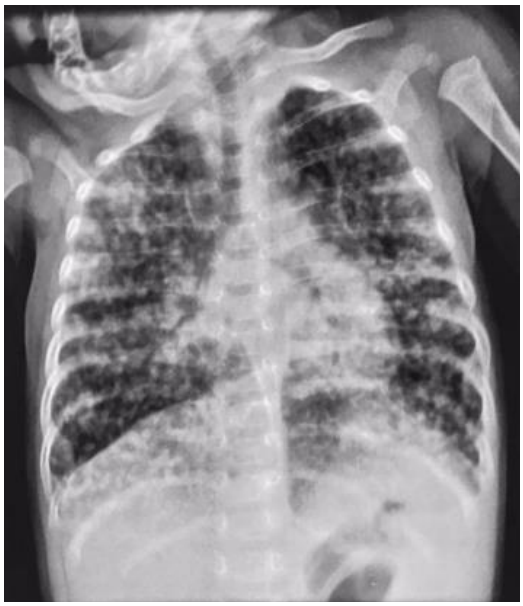

Figure 1: CXR of the 3 month's old male child on admission.
CXR showed widespread miliary nodules in all the segments and lobes of both lungs with attempts at cavitation in both upper lobes.

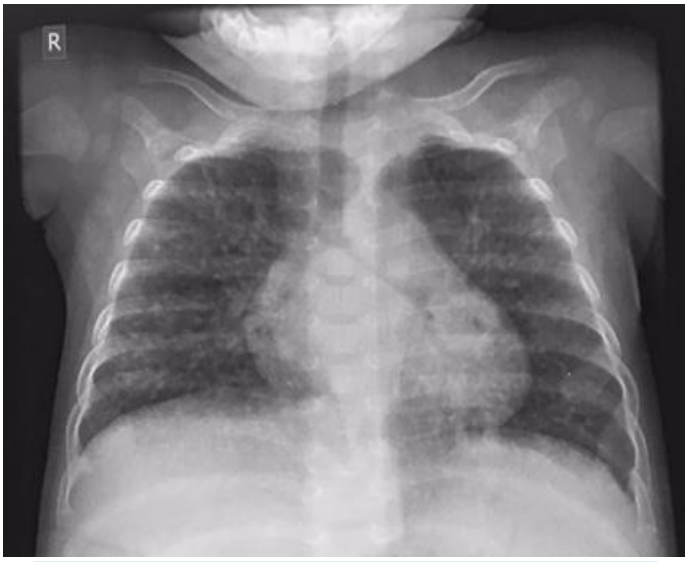

Figure 2: Repeat CXR of same patient 7th month on Anti-TB treatment.
A repeat CXR showed interval improvement with hyperinflation, persisting air bronchogram and a residual well circumscribed opacity in the lower lung lobes.

Discussion

Our case presented with fever, cough, difficult and fast breathing with clinical features of severe hypoxia recording very low oxygen saturation in room air. This severe pneumonia with desaturation in the present pandemic was so confusing that our closest differentials were COVID-19, as reported by studies [16,17] followed by PJP. Both were excluded by their negative test results and outcome.

He was acutely ill looking, in respiratory distress, febrile, mildly pale, with a clinically clear chest. Even though studies have shown the non-specific symptomatology and presentation of miliary TB [4,6,14], none have reported persistently clear chest despite such severe pneumonia associated with desaturation as found in our patient.

RDS as found in our patient is a known complication of miliary TB and has been closely associated with tuberculous meningitis [2,18]. Again, known risk factors for developing military TB are young age, lack of BCG, malnutrition and contact with Tb case [18], all of which were found in our patient. He did not receive BCG until 16 days after birth which exposed him to the TB bacilli before the BCG vaccine. Miliary TB is rare in children who have had BCG vaccination as this is known to reduce its incidence [4,8].

A tender hepatosplenomegaly as found in our case was a common finding reported in several studies [1,2,9].

Again, being a male child is supported by studies showing that males are more frequently affected by miliary TB in studied childhood and adult series [4].

Our patient developed episodes of convulsions. Studies have reported seizures in military Tb either due to associated hypoxia or complicated by tuberculous meningitis [18].

The uniqueness of the case is the persistently clear chest findings with the total absence of added sounds in spite of the severe illness and hypoxia. Other studies have documented crepitations, among other findings [9,19].

CXR findings had widespread miliary nodules as seen in several studies [7,14,19]. The presence of residual opacities in the repeat CXR done at 7 months of treatment buttresses arguments to support extension of anti-TB treatment beyond 6 months for miliary TB which is what is currently being practiced in Nigeria [20-22].

The diagnosis of miliary Tb could be very challenging in resource poor settings, but as much as its possible every effort should be made to support CXR and bacteriological investigations in these areas for early diagnosis and prompt treatment [5,19].

Conclusion

Miliary TB presents with a wide range of common and uncommon manifestations that may confuse even the most experienced Clinician, and so a high index of suspicion with a careful history, focused systematic physical examination, imaging and bacteriological studies are strongly recommended for its early diagnosis. Prompt treatment with standard Anti-TB drugs is life-saving.

Ethical statement

The study was conducted according to the principles of the World Medical Association Declaration of Helsinki and written informed consent was obtained from the parent for publication of this case report.

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Authors' contribution

AUE-Conceptualization, collection of data, Resources, Writing–Original Draft Preparation, and Supervision, GEB-Resources, collection of data, Writing–Review & Editing, UAU-Investigation, Resources, Writing–Review & Editing, EUA-Resources, collection of data, Writing–Review & Editing, KAC-Resources, collection of data, Writing–Review & Editing, BEE-Investigation, Resources, Writing–Review & Editing. All authors agreed to the final version of submitted manuscript.

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