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Case Report

Tuberculous Meningitis in Male Child and Cavitary Pulmonary Tuberculosis in Mother: Concurrent Familial Infective Disease as Evidence of Recent Transmission from Mother to Baby!

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Abstract

Tuberculosis (TB) is one of the leading causes of mortality in children worldwide, but there remain significant challenges in diagnosing and treating TB infection and disease. Tuberculous (TB) meningitis is the commonest infectious disease of the central nervous system in paediatric and geriatric cases. Childhood TB is an indication of failing TB control in the community. It allows disease persistence in the population. Tuberculosis can be prevented in children by diagnosing and treating cases of active TB amongst adults, as paediatric cases always acquire it passively from household contact of adults suffering from TB as disease in adults is multibacillary. Although significant data is available for the prevention of childhood extra-pulmonary and disseminated TB, offering Bacillus Calmette-Guerin (BCG) vaccination, it is still not routinely offered during vaccination. In this case report, a two-year child with a history of failure to thrive and constitutional symptoms diagnosed with disseminated extra-pulmonary TB presenting as TB meningitis with a history of contact with the mother suffering from active sputum positive pulmonary TB receiving anti-TB treatment. Child was evaluated with CT brain plain and contrast and documented meningeal enhancement. Cerebrospinal fluid analysis revealed tuberculous etiology in presence of lymphocytic predominance and raised ADA level in fluid. CSF fluid sent for cartridge based nucleic acid amplification test documented MTB genome with rifampicin sensitivity. We retrospectively analysed mothers' sputum examination and observed higher grades of sputum AFB and her cartridge based nucleic acid amplification test revealed MTB genome with rifampicin sensitivity. Child and mother were treated with standard protocol recommended by NTEP (National Tuberculosis elimination program). In conclusion, we recommend BCG vaccination to all newborns, and tuberculin skin testing and isoniazid prophylaxis to the contact of adults with sputum positive pulmonary TB cases in India to prevent transmission of disease from mother to baby. A high index of suspicion is must while evaluating these cases and all possible measures should be taken to confirm tuberculosis to have successful treatment outcome.

Keywords: Tuberculous meningitis, BCG Vaccination, isoniazid, tuberculin skin test, recent transmission, mother to child.

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INTRODUCTION

Tuberculosis (TB) continues to be a major threat to global health. Cavitation is a dangerous consequence of pulmonary TB associated with poor outcomes, treatment relapse, higher transmission rates, and development of drug resistance. However, in the antibiotic era, cavities are often identified as the extreme outcome of treatment failure and are one of the least-studied aspects of TB [1]. Pulmonary tuberculosis can have diverse presentations ranging from cavitation, consolidation, tumorous lesions, coin lesions, lower lung filed tuberculosis and endobronchial and miliary nodules [2-12]. Similarly, non-tuberculous pathologies can present with abnormalities such as consolidations, nodules, cavitations mimicking tuberculosis [2-14]. Bronchoscopy is a very crucial interventional pulmonology technique in evaluating these cases [2-14]. High risk factors for tuberculosis would be

advanced age, malnutrition, pregnancy, steroids exposure, diabetes mellitus and immunosuppression [9-14]. Tuberculosis in advanced stage may cause cardiac dysfunction and systemic effects which will have poor outcome if timely treatment not received [15-17]. Final outcome in delayed treatment initiation may lead to destroyed lung as post tuberculosis sequel and proportionate number of cases may have lung function abnormalities irrespective of radiological outcome [18-20]. Tuberculosis may be misdiagnosed due to confusing or overlapping clinical and radiological features in high burden setting like India [21-25].

The World Health Organization (WHO) current estimates in 2015 are that one million children currently suffer from TB worldwide (<15 years), and that more than 136,000 die each year [26]. Many people believe that these numbers underestimate the true extent of the problem [27]. About 70 to 80% of children with TB have the disease in their lungs (pulmonary TB). The rest are affected by TB disease in other parts of their body (extra-pulmonary TB). In the high- burden TB setting, it has been reported that 15 to 20% of all TB cases are among children, whereas in the low-burden TB setting, it is estimated that 2 to 7% of all TB cases are among children [27]. Tuberculous meningitis is a common infectious disease of the central nervous system in developing countries. Early diagnosis and treatment with chemotherapy and active management of the complications are of utmost importance to prevent the irreversible neurological sequelae and death. Delay in diagnosis and in the start of effective treatment results in poor prognosis and sequela in up to 25% of cases [28].

CASE SUMMARY

A 2-year-old male referred to outdoor of pulmonary medicine department from paediatric department with history of fever, and failure to thrive for three months, and mother of child was on anti-TB treatment for three months. Overall physical examination revealed that child was malnourished with scanty hypopigmented hairs over the scalp and most important clinical sign increases the head circumference of the child with open wide anterior fontanel, and multiple enlarged non-tenders, discrete subcentimetric cervical lymph nodes present bilaterally. Neurological examination of the child suggests delayed gross and fine motor signs development with few gross motor signs showing neuroregression. Neck rigidity was positive with Kernig's sign positive. Additionally, plantar reflexes showed extensor response and deep tendon reflexes showed exaggerated response. Respiratory system examination findings are apparently normal. The mother of the child was suffering from sputum positive pulmonary TB and is on supervised chemotherapy as per National guidelines containing four ATT (anti-TB) drugs Isoniazid, Rifampin, pyrazinamide and Ethambutol. She is having respiratory symptoms for four months before initiation of anti-TB treatment, means that baby was exposed to open TB case for four months before start of treatment. She had completed treatment when baby was 24-month-old. Isoniazid prophylaxis to child irrespective of contact with sputum positive pulmonary TB case was not offered, and tuberculin skin test screening was not done. Plain chest X-ray of mother before initiation of anti-TB treatment is at Figure 1.

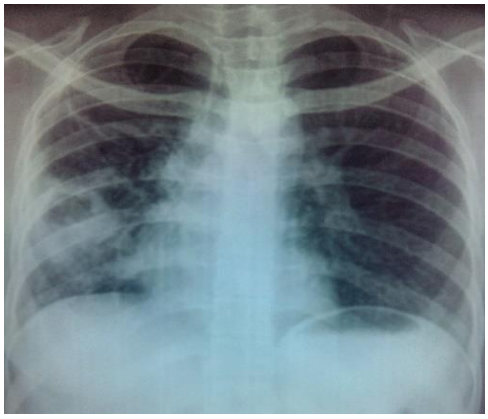

Figure 1: Plain chest X-ray view of mother showing 'thick-walled cavity with pericavitary consolidation with satellite nodules in right middle and lower zone' is an indicator of active pulmonary tuberculosis

A sputum examination acid fast bacillus (AFB) of the mother before initiation of treatment was 3+. After two months of intensive phase of chemotherapy, sputum conversion occurred and sputum for AFB was negative. Sputum conversion remained after completion of ATT for six months as per national guidelines. Chest X-ray was not done after the completion of ATT, as radiological response is not analysed routinely in supervised regimen, only bacteriological response is assessed. Chest X-ray of child is performed in indoor unit is at Figure 2. We performed gastric aspirate for AFB consecutively on five days and collected early morning overnight fasting sample collected with 10 mL of normal saline and assessed after centrifugation of sample. Acid fast bacilli were detected in sample.

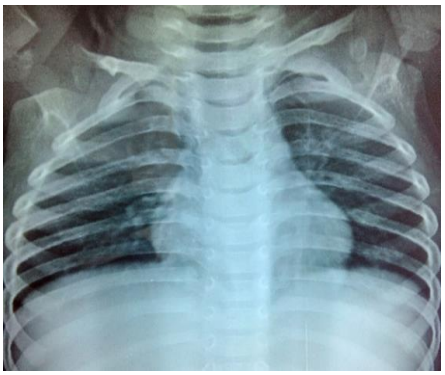

Figure 2: Anterio-posterior chest X-ray view of child showing 'bilateral hilar enlargement with bilateral discrete randomly placed nodular opacities' predominantly in lower fields and paracardiac regions

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Tuberculin skin testing was done with five TU (tuberculin unit) of PPD (purified-protein derivative) given intradermal over volar aspect of left forearm and results were observed after 48 hours after test. Tuberculin test was positive with induration of 14 mm. We performed computed tomography of brain plain and with contrast [figure 3 and figure 4] to look for signs of tuberculous meningitis and its complications. Figures 3 and 4 showing mild dilation of ventricle system seen, i.e., mild hydrocephalous. Also note mild cortico-cerebral atrophy. All these features suggestive of infective etiology and TB needs to be ruled out.

We performed cerebrospinal fluid examination and results were observed as:

- Proteins-110 gm%
- Glucose- 56 mg%
- Total nucleated cells-428/mm^3
- Differential cell count on smear- 90% lymphocytes and 10% neutrophils
- Gram staining and Ziehl-Neelsen staining were inconclusive
- ADA (adenosine deaminase level) in cerebrospinal fluid 24 units/liter
- Cartridge based nucleic acid amplification test showed MTB genome with negative rpo-b mutation which is indicator of rifampicin sensitivity.
- Blood sugar level is 110 mg%.

Hematological and biochemistry analysis documented as-

- Haemoglobin 8.6 gm%, total white blood cell counts 6000/mm3, predominant lymphocytes on differential counts, platelets were 4.5 lacs.

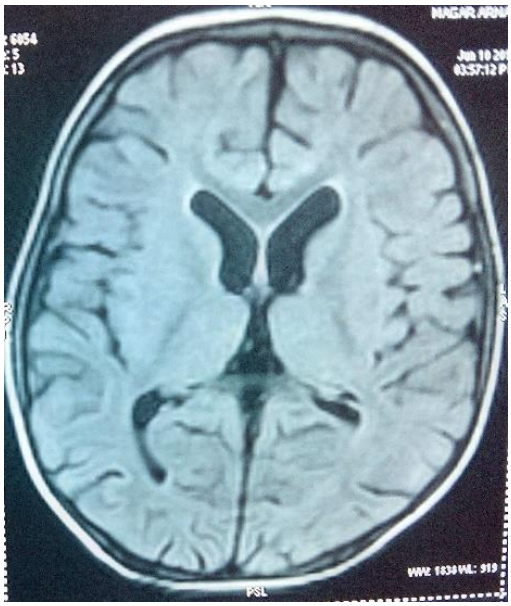

Figure 3: Plain cranial CT (non-contrast) showing dilatation of ventricular system

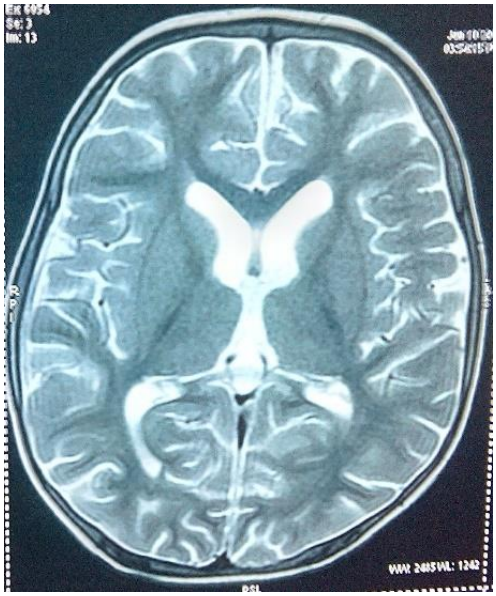

Figure 4: Contrast-enhanced cranial CT showing meningeal enhancement

The child was started on anti-TB treatment consisting of four anti-TB drugs Isoniazid, Rifampicin, pyrazinamide, and streptomycin on the day of admission as per body weight. No cerebral decongestants were required as anterior fontanel was open. In addition to anti-TB drugs, we started dexamethasone and continued it for four weeks in tapering dosages. No seizures or any neurodeficit was observed during hospitalization with complete tolerance and compliance to all three oral anti-TB drugs and one parenteral drug. We discharged child after 20 days of hospitalization with adequate weight gain and advice for compliance and adherence of ATT with high protein diet. We followed child for near complete response to chemotherapy. After four weeks steroids and streptomycin for 90 days discontinued and the rest three oral drugs were continued until six months. After 24 weeks, isoniazid and Rifampin were continued until 12 months of initiation of treatment. Response to ATT is excellent with complete radiological clearance of dilated ventricles on CT brain and no residual neurological deficit clinically.

DISCUSSION

Tuberculous meningitis occurs mainly in developing countries where tuberculosis TB is more common and the wider incidence of the human immunodeficiency virus (HIV) favours the onset of a great number of cases. Children are among the subjects who most frequently suffer from TBM due to their relative inability to contain primary mycobacterium tuberculosis infection in the lung [29]. Tuberculous meningitis is a devastating disease with about 30% mortality in the most severe forms; moreover, 50% of survivors have neurological sequelae, despite apparently adequate administration of antibiotics [30].

Tuberculous meningitis develops in two steps. Mycobacterium tuberculosis bacilli enter the host by droplet inhalation. Localized infection escalates within the lungs with dissemination to the regional lymph nodes. In individuals who develop TB meningitis, bacilli seed to the meninges or brain parenchyma, resulting in the formation of small sub- pial or sub-ependymal foci of metastatic caseous lesions, termed Rich foci. The second step in the development of TBM is an increase in size of a Rich focus, until it ruptures into the subarachnoid space. The location of the expanding tubercle (i.e., Rich focus) determines the type of the central nervous system (CNS) involvement. Tubercles rupturing into the subarachnoid space cause meningitis [31]. Currently, more than two billion people (i.e., one third of the world's population) are infected with TB, of which approximately 10% will develop clinical disease. The incidence of TB is related to the prevalence of TB in the community, and it is still the most common type of chronic CNS infection in developing countries [31].

Although early and rapid identification of TB meningitis is crucial for successful disease management, in most of the cases, diagnosis is significantly delayed. Initial signs and symptoms of disease are non-specific, and the suspicion of TBM usually arises only some days or weeks after the disease's onset and is not different in children who have or have not been vaccinated with BCG. Fever, headache, anorexia, and vomiting characterize the prodromal of the disease in older children, whereas failure to thrive, poor appetite, vomiting, and sleep disturbances are more common in younger ones [32]. Tuberculous meningitis is more easily suspected, when these symptoms are associated with a history of recent contact with a case of documented TB.

Walker *et al.*, [33] reported that BCG vaccination is partially protective against TB meningitis; therefore, a history of BCG vaccination or the presence of a BCG vaccination scar affords some degree of reassurance, when considering a diagnosis of TBM. In patients in whom TBM is suspected clinically, the diagnosis must be rigorously investigated; a history of BCG vaccination does not rule out the diagnosis [33, 34].

In 1948, the British Medical Research Council developed a method for staging the severity of the disease, as follows:

- Stage I describes the early non-specific symptoms and signs including apathy, irritability, headache, malaise, fever, anorexia, nausea, and vomiting without any alteration in the level of consciousness.
- Stage II describes altered consciousness without coma or delirium, but with minor focal neurological signs; symptoms and signs of meningism and meningitis are present, in addition to focal neurological deficits, isolated CNS palsies, and abnormal involuntary movements.
- Stage III describes an advanced state with stupor or coma, dense neurological deficits, seizures, posturing, and/or abnormal movements.

The CSF modifications are common in children with TB meningitis. In these cases, CSF shows a clear appearance, moderate pleocytosis with a predominance of lymphocytes, an increase in protein content and a very low glucose concentration. These findings are different from those usually reported for typical bacterial meningitis in which CSF is opaque, pleocytosis is very high, and neutrophils are predominant. Reduction in glucose content is usually less marked in comparison to purulent bacterial meningitis, where CSF glucose values below 5 mg/dL will often be found. Clear appearance, white blood cell count between 50 and 500 per mL with 50% or more lymphocytes, protein content greater than 1 g/L and glucose content less than 2.2 mmol/L are considered to be indicative of TB meningitis. However, atypical CSF findings have been repeatedly described in children with TB meningitis [34].

The ADA activity test is a rapid test which represents the proliferation and differentiation of lymphocytes as a result of the activation of cell-mediated immunity after TB meningitis. It yields good results in the diagnosis of the pleural, peritoneal and pericardial forms of tuberculosis. When applied to patients with TB meningitis, it was found that ADA activity could not distinguish between TBM and other types of bacterial meningitis; however, it could add useful information to suggest TB meningitis once meningitis due to different pathogens has been ruled out. The ADA values from 1 to 4 U/L (sensitivity >93% and specificity 8 U/L (sensitivity 96%) can improve the diagnosis of TB meningitis ($p < 0.001$). However, values between 4 and 8 U/L are insufficient to confirm or exclude the diagnosis of TB meningitis ($p = 0.07$) [35].

Similarly to clinical and laboratory findings, cerebral imaging can also contribute to diagnosing probable or possible TB meningitis. However, discrimination between TB meningitis and another cerebral disease is frequently very difficult. The most common brain CT or MRI features in children with TBM are hydrocephalus, which can be demonstrated in about 80% of cases, and basal meningeal enhancement, found in 75% of young patients. Infarction, as a result of ongoing vasculitis, particularly of the basal ganglia and of the areas of the medial striates and thalamo-perforating arteries and tuberculoma can be found in a smaller number of TBM paediatric cases. However, a combination of basal meningeal enhancement, infarction and hydrocephalus was found to have a high specificity for the diagnosis of TB meningitis, whereas

basal meningeal enhancement was reported as the most sensitive feature [36].

The evidence of TB infection or disease outside the CNS can significantly increase the probability or possibility that a child with cerebral signs and symptoms can have TB meningitis. However, a great number of patients, particularly when HIV negative, will present with normal chest radiography or negative tuberculin skin testing [37]. Moreover, particularly in high TB prevalence areas, a positive skin test with an unrelated illness has been frequently documented. Taking samples from sites of frequent TB infection such as lymph nodes, lung and gastric fluid can increase the likelihood of a positive culture. Gastric aspiration was positive in 68% of children with TBM [38].

Before the emergence of multidrug-resistant M. tuberculosis, three drugs were considered adequate for the first phase. More recently, to address the problem of resistance, four antibiotics for the initial months of treatment are preferred. However, there is no agreement on the duration of each of the two phases and on the total length of therapy. The intensive phase can range from two to six months and total treatment from six months to one year [39]. For several years now, the drugs considered essential by the World Health Organization (WHO) to treat pulmonary TB in children are isoniazid (INH), Rifampicin (RMP), pyrazinamide (PZA), and ethambutol (EMB) [40].

World Health Organization regimen to treat Tuberculosis [40]:

- Isoniazid 10-15 mg/kg/24 h (max 300 mg) orally for 6 months
- Rifampin 10-20 mg/kg/24 h (max 600 mg) orally for 6 months
- Pyrazinamide 15-30 mg/kg/24 h (max 2 g) orally for 2 months
- Ethambutol 15 mg/kg/day orally for 2 months
- Prednisone 2 mg/kg/24 h orally for 4 weeks, followed by a reducing course over 1-2 weeks.

In meningitis, most of the damage derives from the immune response elicited by the presence of bacterial pathogens in the CNS. This leads to a very relevant inflammatory process with significant infiltrative, proliferative and necrotizing vessel pathologies.

The best steroid and the most effective scheme of administration are not known, as no data comparing different regimens are available currently. Moreover, data collected in children are few. According to the suggestions of the American and European Scientific Societies, it can be suggested the use of oral compounds for three or four weeks with subsequent reduction in few days [41, 42].

Issues needs to be considered-

1. BCG Vaccination and role in preventing paediatric disseminated tuberculosis

Following exposure to tubercle bacilli, it takes about 6 to 8 weeks for a primary complex to develop. Six to twelve months after the primary infection, tuberculous meningitis, secondary to hematogenous spread, may occur. The commonest age group for tuberculous meningitis is nine months to three years. BCG vaccination prevents hematogenous dissemination and development of TBM to the extent of 60-80%. Immunity following vaccination takes about eight to ten weeks to develop during which interval exposure to tubercle bacilli can cause disseminated infection. Hence BCG vaccination is must in all the newborns in high TB prevalence setting particularly in India [31].

2. Role of Tuberculin test

The standard tuberculin test recommended for use is the Monteux's test. Commercially available tuberculin's in the country are one, two and five Tuberculin Unit (TU) PPD (RT23 equivalent). It is important to raise a wheal of about 6 mm after the intra-dermal injection and the test is read 48-72 hours after an injection. Ballpoint or palpatory methods are used to read the induration. The width of reaction (induration) in the horizontal plane is noted for interpretation. The Monteux's test or PPD skin test is considered positive, if the duration is 10 mm or more. This cut-off was recommended using a 1 TU PPD RT23. Currently, the laboratories more often use 5 TU PPD (RT23 equivalent), or sometimes even some other higher strengths or types of PPD are used.

The standard cut-off of 10 mm can actually not be justified for any higher strength of PPD used. The reaction evoked is not only dependent on the amount of antigen given, but also does not have a linear relationship with the increasing strengths. Therefore, the current practice may actually lead to an increase in false positive reactions using the 10-mm cut-off with the higher strength of PPD. Efforts should be made to use only 1 TU PPD to decrease the false positives and in no case strength higher than 5 TU should be used. The degree of reaction, including necrosis and ulceration, may not necessarily differentiate infected from diseased [43].

3. INH prophylaxis

TB preventive therapy: The dose of INH for chemoprophylaxis is 10 mg/kg (instead of currently recommended dosage of 5 mg/kg) administered daily for six months. TB preventive therapy should be provided to:

a. All asymptomatic contacts (under six years of age) of a smear positive case, after ruling out active disease and irrespective of their BCG or nutritional status [44].
b. Chemoprophylaxis is also recommended for all HIV infected children who either had a

known exposure to an infectious TB case or are Tuberculin skin test (TST) positive (≥5mm induration), but have no active TB disease [44].

c. All TST positive children who are receiving immunosuppressive therapy (e.g., children with nephrotic syndrome, acute leukaemia, etc.). There is no evidence to support the use of IGRA over TST in young children [44].

d. A child born to mother who was diagnosed to have TB in pregnancy should receive prophylaxis for six months, provided congenital TB has been ruled out. BCG vaccination can be given at birth, even if INH chemoprophylaxis is planned [44].

CONCLUSION

In the present case report, we have reported a 2-year male child presented with constitutional symptoms, failure to thrive and neurodevelopmental issues and history of mother on ATT with active pulmonary cavitary lung disease in mother. Microbiological workup of mother showed drug sensitive tuberculosis and CSF analysis of baby documented MTB genome with sensitive disease. Child is treated with ATT as per NTEP guidelines and showed excellent response.

Learning points:

1. Tuberculosis in a child represents recent and ongoing transmission of TB bacteria. Young children particularly below six years of age are most likely to become exposed and infected with TB by close contacts, such as family members. Active screening of all family members is must if child is having tuberculosis to rule out chances of transmission form parents to child and is considered as evidence of recent transmission form parent to child.
2. Extra-pulmonary tuberculosis (EPTB) is fairly more common in paediatric cases with CNS involvement a predominant site. Possibility of tuberculosis should be kept as differential in cases with failure to thrive and malnutrition with or without family history of tuberculosis.
3. The BCG vaccination is must to all newborns in India, as it will prevent childhood TB and its complications. Although BCG has shown variable efficacy in preventing childhood tuberculosis, it has shown major role in prevention of disseminated tuberculosis and CNS tb in childhood.
4. Tuberculin skin test has valuable role in childhood TB as it is one of the indicators of active disease, irrespective of BCG vaccination in paediatric cases below six years in high TB burden country such as India.
5. The INH prophylaxis has best possible measure in close contacts of known sputum positive case, and to be considered routinely to all paediatric cases after ruling out active TB. This prophylaxis has major role in preventing progression of disease and preventing chances of dissemination.
6. Response to ATT is excellent in paediatrics with improvement in clinical and radiological and neurological parameters. Compliance is adequate and is not a issue of great concern due to adequate counselling of care takers and importance of ATT in curing disease with significant mortality and morbidity.
7. Side effects are relatively less common and ATT is very well tolerated in paediatric cases. Rational for same is not known. May be this is related to adequate care, diet and supportive care children receive during entire course of ATT from parents of care takers which will prevent ATT related adverse events.
8. TB remains a major threat to child health worldwide and considered as health issue of global concern due to rising trends of drug resistant tuberculosis. Again, primary drug resistant tuberculosis is not very common in paediatric cases and similarly, as in our case, majority of cases by a large occurs as parent to child transmission during household contacts.
9. Duration of treatment and treatment outcome is similar to adults as per NTEP guidelines. We recommend extended regimens for EPTB, i.e., up to 12 months in TB meningitis cases observe complete clinical and radiological improvement and prevent relapse with short regimes.
10. A high index of suspicion is must while evaluating paediatric cases with constitutional symptoms and all possible measures should be taken to confirm tuberculosis as underlying cause to have successful treatment outcome.
11. Counselling and awareness of importance of infections control policies to prevent household transmission, importance of INH prophylaxis, trainings of family members for prevention of transmission of TB to child by utmost precautions during routine livings in house is must to prevent this deadly disease in children.

Conflicts of Interest: Nil
Research Funding: Nil

REFERENCES

1. Urbanowski, M. E., Ordonez, A. A., Ruiz-Bedoya, C. A., Jain, S. K., & Bishai, W. R. (2020). Cavitary tuberculosis: the gateway of disease transmission. *Lancet Infect Dis.*, *20*(6), e117-e128.
2. Shital, P., & Halkanche, G. (2014). "Cavitary Lung Disease: Not Always due to Tuberculosis! Primary Lung Cancer with Smear Positive Pulmonary Tuberculosis- A Case Report." *American Journal of Medical Case Reports*, *2*(8), 164-166.

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3. Shital, P., Anil, J., Sanjay, M., & Mukund, P. (2014). Tuberculosis with Diabetes Mellitus: Clinical-Radiological Overlap and Delayed Sputum Conversion Needs Cautious Evaluation-Prospective Cohort Study in Tertiary Care Hospital, India. *J Pulm Respir Med*, *4*, 175.
4. Patil, S., & Laxman, K. (2014). "'Tennis Racket cavity' on Chest Radiograph: Strong Predictor of Active Pulmonary Tuberculosis! – A Case Report." *American Journal of Medical Case Reports*, *2*(9), 167-169.
5. Shital, P., Choudhary, C. R., Kasture, L., & Rujuta, A. (2015). Endobronchial Tuberculosis Presenting as a Post-obstructive Pneumonia, Para-hilar Mass Lesion in Chest Radiograph and 'Tumorous' Endobronchial Lesion during Bronchoscopy: A Case Report. *American Journal of Infectious Diseases*, *3*(5), 147-151.
6. Patil, S., Dahiphale, J., Raka, V., Narkar, S., Choudhari, S., & Gondhali, G. (2023). „Coin Lesion" in Chest Radiograph Presenting as Round Pneumonia with Eccentric Cavitation in HRCT Thorax: Tuberculosis or Malignancy-A Real Puzzle. *South Asian Res J Med Sci*, *5*(2), 33-40.
7. Patil, S., Dahiphale, J., Raka, V., Narkar, S., Choudhari, S., & Gondhali, G. (2023). „Stepladder Lung Cavities" with „Starry Sky Pattern" in HRCT Thorax with Constitutional Symptoms: A Strong Predictor of Active Pulmonary Tuberculosis. *SAR J Med*, *4*(2), 32-42.
8. Patil, S., Narwade, S., & Mirza, M. (2017). Bronchial wash Gene Xpert MTB/RIF in lower lung field tuberculosis: Sensitive, superior, and rapid in comparison with conventional diagnostic techniques. *Journal of Translational Internal Medicine*, *5*(3), 174-181.
9. Patil, S., & Gondhali, G. (2018). Short course of high dose steroids used for non-pulmonary indication like anaphylaxis caused flare up of tuberculosis & presenting as acute pulmonary tuberculosis with pleural effusion: a case report. *European Journal of General Medicine*, *15*(1), 37-42.
10. Patil, S., & Mirza, M. (2018). Tuberculous Lymphadenitis of Hilar Lymph Nodes as a Cause of Right Middle Lobe Syndrome: A Case Report. *Respiratory Case Reports*, *7*(2), 90-96.
11. Patil, S., & Patil, R. (2018). Fleeting pulmonary infiltrates in allergic bronchopulmonary aspergillosis Misdiagnosed as tuberculosis. *Int. J. Mycobacteriol*, *7*, 186-190.
12. Patil, S., & Jadhav, A. (2019). Short course of high-dose steroids for anaphylaxis caused flare up of tuberculosis: a case report. *Journal of Translational Internal Medicine*, *7*(1), 39-42.
13. Patil, S., & Gondhali, G. (2021). Pulmonary Melioidosis Masquerading as Tuberculosis: A Case Report. *Electron J Gen Med*, *18*(5), em310.
14. Patil, S., & Gondhali, G. (2021). COVID-19 pneumonia with pulmonary tuberculosis: double trouble. *The International Journal of Mycobacteriology*, *10*(2), 206-209.
15. Shital, P., & Mirza, M. (2018). Laryngeal & Lower lung field tuberculosis in pregnancy: A case report. *Electronic Journal of General Medicine*, *15*(2), em06.
16. Patil, S. V., Toshniwal, S., & Acharya, A. (2023). GondhaliG. Cardiac dysfunction in active pulmonary tuberculosis: Mysterious facts of TB's pandora. *Electron J Gen Med.*, *20*(2), em452.
17. Patil, S., Gondhali, G., & Bhadake, M. (2022). Disproportionate tachycardia and tachypnea in pulmonary tuberculosis: A marker of concurrent cardiac dysfunction. *Journal of Association of Pulmonologist of Tamil Nadu*, *5*(3), 124-9.
18. Patil, S. V., Narwade, G., & Gondhali, G. (2020). Cardiac Dysfunction in Active Pulmonary Tuberculosis: Double Trouble!!. *European Respiratory Journal*, *56*, 1604.
19. Patil, S., Patil, R., & Gondhali, G. (2020). Cardiac Dysfunction in Active Pulmonary Tuberculosis: Underestimated, Missed Routinely and Have Impact on Clinical Outcome! Prospective Study of 600 Cases in Tertiary Care Setting in India. *Am J Respir Crit Care Med*, *201*, A5435.
20. Patil, S., Narkar, S., Raka, V., Dahiphale, J., Choudhari, S., & Gondhali, G. (2023). Destroyed lung'as Post Tuberculosis Sequel: A Preventable Stigma of 'disease of concern'of Millennium. *Saudi J Med*, *8*(3), 112-119.
21. Patil, S., Patil, R., & Jadhav, A. (2018). Pulmonary functions' assessment in post-tuberculosis cases by spirometry: Obstructive pattern is predominant and needs cautious evaluation in all treated cases irrespective of symptoms. *The International Journal of Mycobacteriology*, *7*(2), 128-133.
22. Patil, S. V., Toshniwal, S., & Gondhali, G. (2023). Cavitating lung disease is not always due to tuberculosis! Wegener's granulomatosis with mycetoma with deep vein thrombosis lower limb: Case report with review of literature. *Electron J Gen Med.*, *20*(1), em425.
23. Patil, S., & Gondhali, G. (2022). Bronchus sign on HRCT thorax: presenting sign of Wegener granulomatosis with lung involvement—misdiagnosed as TB in presence of acino-nodular pattern on imaging. *The Journal of Association of Chest Physicians*, *10*(2), 105-11.
24. Patil, S., & Patil, D. (2022). Wegener's granulomatosis mimicking like pulmonary tuberculosis and presenting as cavitating lung disease with mycetoma: A case report with review of literature. *Med Sci Res*, *13*, 103-9.
25. Patil, S., Gondhali, G., & Patil, D. (2022). Chronic febrile respiratory illness with acino-nodular consolidations as presenting feature of granulomatosis with polyangiitis: A case report with review of literature. *Journal of Association of Pulmonologist of Tamil Nadu*, *5*(3), 116-20.

26. Global Tuberculosis Report", WHO, Geneva, 2015 www.who.int/tb/publications/global report/en/.
27. "Childhood Tuberculosis Roadmap", 11th November 2012 www.stoptb.org.
28. Garcia-Monco, J. C. (1999). Central nervous system tuberculosis. *Neurologic Clinics*, *17*, 737-60.
29. Lewinsohn, D. A., Gennaro, M. L., Scholvinck, L., & Lewinsohn, D. M. (2004). Tuberculosis immunology in children: diagnostic and therapeutic challenges and opportunities [Childhood TB]. *The International Journal of Tuberculosis and Lung Disease*, *8*(5), 658-674.
30. Farinha, N. J., Razali, K. A., Holzel, H., Morgan, G., & Novelli, V. M. (2000). Tuberculosis of the central nervous system in children: a 20-year survey. *Journal of infection*, *41*(1), 61-68.
31. Udani, P. M. (1985). Management of tuberculous meningitis. *The Indian Journal of Pediatrics*, *52*, 171-174.
32. Khemiri, M., Bagais, A., Becher, S. B., Bousnina, S., Bayoudh, F., Mehrezi, A., ... & Barsaoui, S. (2012). Tuberculous Meningitis in Bacille Calmette-Guerin–Vaccinated Children: Clinical Spectrum and Outcome. *Journal of child neurology*, *27*(6), 741-746.
33. Walker, V., Selby, G., & Wacogne, I. (2006). Does neonatal BCG vaccination protect against tuberculous meningitis?. *Archives of disease in childhood*, *91*(9), 789-791.
34. Starke, J. R. (1999). Tuberculosis of the central nervous system in children. *Semin Pediatr Neurol*, *6*, 318-31.
35. Tuon, F. F., Higashino, H. R., Lopes, M. I. B. F., Litvoc, M. N., Atomiya, A. N., Antonangelo, L., & Leite, O. M. (2010). Adenosine deaminase and tuberculous meningitis—a systematic review with meta-analysis. *Scandinavian journal of infectious diseases*, *42*(3), 198-207.
36. Theron, S., Andronikou, S., Grobbelaar, M., Steyn, F., Mapukata, A., & du Plessis, J. (2006). Localized basal meningeal enhancement in tuberculous meningitis. *Pediatric Radiology*, *36*, 1182-1185.
37. Akhila, K., Mahadevan, S., & Adhisivam, B. (2007). Qualitative evaluation of tuberculin test responses in childhood tuberculosis. *The Indian Journal of Pediatrics*, *74*, 641-644.
38. Doerr, C. A., Starke, J. R., & Ong, L. T. (1995). Clinical and public health aspects of tuberculous meningitis in children. *The Journal of pediatrics*, *127*(1), 27-33.
39. Donald, P. R. (2010). The chemotherapy of tuberculous meningitis in children and adults. *Tuberculosis (Edinb)*, *90*, 375-92.
40. Treatment of tuberculosis: guidelines – 4th ed. World Health Organization 2010.
41. Centers for Disease Control. (2003). Treatment of tuberculosis. *MMWR Recomm Rep*, *52*, 1-77.
42. Thwaites, G., Fisher, M., Hemingway, C., Scott, G., Solomon, T., & Innes, J. (2009). British Infection Society guidelines for the diagnosis and treatment of tuberculosis of the central nervous system in adults and children. *Journal of infection*, *59*(3), 167-187.
43. Chadha, V. K. (2001). Tuberculin test. *Indian J Pediatr*, *68*, 53-8.
44. IAP Working Group. (2010). Consensus statement of IAP Working Group: status report on diagnosis of childhood tuberculosis. *Indian Pediatr*, *41*, 146-55.