



Case Series

Unmasking childhood tuberculosis – A case series with review of literature

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ABSTRACT

Childhood tuberculosis (TB) remains a major global health issue, particularly in high-burden countries like India, which accounts for 26% of global TB cases. The national TB elimination programme has adopted a focused approach to meet the World Health Organization (WHO's) end TB targets through active case finding and standardised treatment protocols based on updated WHO guidelines. This report presents three paediatric TB cases from a tertiary care hospital, illustrating the diagnostic and therapeutic challenges across varying disease spectrums and age groups. The first case involves a 14-year-old girl with advanced pulmonary TB (PTB), managed successfully with appropriate anti-tubercular treatment (ATT) for non-severe drug-susceptible TB. The second case describes a 5-year-old girl who developed TB during immunosuppressive treatment for nephrotic syndrome. Her condition progressed to severe extra-PTB as grade 3 tubercular meningitis with brainstem tuberculomas, which later got complicated by paradoxical reactions. Management required immunosuppressants, including thalidomide and steroids. Despite intensive care, she remained neurologically impaired and ventilator-dependent, eventually succumbing to ventilator-associated pneumonia. The third case involves another 15-year-old girl, with advanced PTB, diagnosed with isoniazid (INH)-resistant TB through WHO-recommended rapid diagnostic tools (Xpert-*Mycobacterium* TB/rifampicin [RIF] and Line Probe Assay). She was classified as RIF-susceptible, INH-resistant TB and treated appropriately with the WHO drug-resistant TB regimen. All three children underwent contact tracing and received nutritional support, reinforcing the importance of a comprehensive care approach. Two children recovered, whereas the child with TB meningitis succumbed during a prolonged hospital stay. These cases underscore the complexities in managing paediatric TB and the need for adherence to evolving WHO guidelines for effective diagnosis and treatment.

Keywords: Childhood, Paradoxical reaction, Pulmonary tuberculosis, Thalidomide, Tubercular meningitis, World Health Organization

INTRODUCTION

Mycobacterium tuberculosis (MTB) continues to be a significant global health concern, especially in children, accounting for 26% of the global tuberculosis (TB) burden.^[1] Despite advancements in diagnostics, treatments and government efforts, TB remains a major cause of childhood morbidity and mortality.^[2] Children under 14 years constitute 35% of the population in India, but contribute to about 11% of TB cases.^[1] The World Health Organization (WHO) emphasises prevention and treatment as pivotal strategies to meet end TB targets.^[3]

India's National TB Elimination Programme (NTEP)^[2] aligns with WHO recommendations^[1] and focuses on active case finding and treatment retention, especially in high-prevalence areas. Annually, children represent 6–7% of all TB patients treated under NTEP.^[2]

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Pulmonary TB (PTB) is the most frequent form in children, but extra-PTB (EPTB) accounts for a larger proportion of paediatric cases compared to adults.^[1,4] Central nervous system TB (CNS-TB), including tubercular meningitis (TBM), tuberculomas and spinal TB, represents a critical subset, comprising 5–10% of extra-pulmonary cases and 1% of total paediatric TB cases.^[1,5,6]

The introduction of molecular rapid diagnostic tools such as Xpert-MTB/rifampicin (Xpert-MTB/RIF), Xpert Ultra and line probe assays (LPA) improved timely diagnosis, including detection of drug-resistant TB (DR-TB).^[1,7] Stool tests are emerging as a promising alternative with reasonable diagnostic yield in the updated WHO guidelines.^[1] Treatment is weight-based with fixed drug combinations to achieve optimal therapeutic levels and minimise missed doses.^[1,8] New medications for MDR-TB have also improved cure rates.^[1]

Childhood TB is complicated by immunosuppressive conditions such as human immunodeficiency virus (HIV) infection, malnutrition, nephrotic syndrome and diabetes, which increase vulnerability and can be complicated by immune reconstitution inflammatory syndrome (IRIS) or paradoxical reactions (PR).^[5,9-12] PR manifests as worsening TB symptoms or lesion size after initial improvement on therapy.^[5] Tumour necrosis factor- α (TNF- α), interferon- γ and vascular endothelial growth factor may play a key role in the hyperinflammation here, raising the risk of poor outcomes, especially in CNS-TB.^[13-17]

TNF- α inhibitors (thalidomide and infliximab) have shown benefit in addition to steroids in PR in children in different studies over the past decade.^[5,13,18,19] These drugs modify immune responses by suppressing and preventing lymphocyte apoptosis, offering potential benefits when steroids fail or cause adverse effects.^[17]

This case series underscores the complex interplay between MTB infection, paediatric immune status and advanced therapeutic strategies, highlighting the need for tailored management approaches in childhood TB, including drug-resistant forms and PRs as per the updated WHO guidelines.^[1]

CASE SERIES

Details of all three cases are summarised in Tables 1-3.

Case 1

A 15-year-old girl presented with a 3-month history of high-grade intermittent fever, chills, productive cough, decreased appetite and weight loss. There was no history of contact with a known case of TB. She had a *Bacillus Calmette-Guérin* (BCG) scar and showed pallor on examination,

but no lymphadenopathy or organomegaly. Respiratory examination revealed increased vocal fremitus, resonance and crepitations on the left side. Anthropometry showed normal height but low weight and body mass index (BMI). As per the WHO guidelines, the child was fitting into the criteria for active case finding for PTB. Lab tests revealed normocytic anemia, neutrophilic leucocytosis, thrombocytosis, elevated erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) and a positive Mantoux test [Table 2]. Chest X-ray [Figure 1a] showed patchy opacities in the left upper zone, and the sputum acid-fast bacilli (AFB) smear was 3+ positive. Cartridge-based nucleic acid amplification test (CBNAAT) confirmed that MTB was sensitive to isoniazid (INH) and RIF. Other infectious disease workups were negative. High-resolution computed tomography (HRCT) [Figure 1b] showed left upper lobe consolidation with cavitation and tree-in-bud nodules, consistent with PTB. As per the WHO criteria, this child was defined as having extensive (or advanced) PTB disease. She was treated with INH, RIF, pyrazinamide and ethambutol (HRZE) therapy under directly observed treatment short course (DOTS), with nutritional support. Contact tracing was done, and she improved symptomatically, continuing treatment with regular follow-up.

Case 2

A 5-year-old girl undergoing treatment for primary nephrotic syndrome (PNS) developed seizures and altered consciousness during her 5th week of steroid therapy. She had a history of pneumonia resistant to first-line antibiotics, later treated with meropenem and vancomycin. Neuroimaging was done to investigate seizures, which revealed hydrocephalus, raising suspicion for TBM, despite normal cerebrospinal fluid (CSF) findings and negative molecular tests for MTB. She was empirically started on ATT and steroids before being referred to us.

Despite treatment, her neurological status worsened with recurrent seizures and decreased consciousness. When she was received at our hospital, she was awake but unresponsive

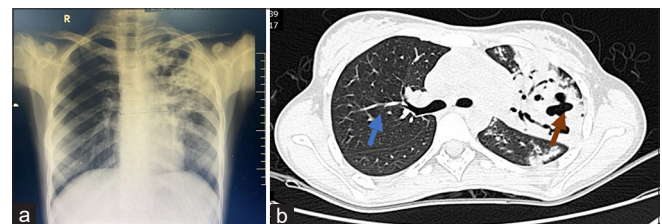


Figure 1: (a) Chest X-ray of case 1 shows ill-defined confluent patchy radio-opacity in the left upper lung zone? infective aetiology, (b) high-resolution computed tomography thorax of case 1 shows 'tree in bud' (arrow on the right side) appearance seen in the right middle lobe and cavities (arrow on the left side) seen in the left middle lobe.

with a Glasgow coma scale of eye opening 4, motor 5 and vocal 2 (E4M5V2), with neurological signs including brisk reflexes, clonus and a positive Babinski sign. An Omayya reservoir for CSF drainage was in place due to raised intracranial pressure (ICP). Magnetic resonance imaging (MRI) revealed a tuberculoma in the parietal cortex, and CSF analysis showed elevated protein and lymphocytosis, but repeated CBNAAT tests were negative [Table 2]. Cultures from blood and CSF grew *Acinetobacter baumannii* sensitive only to polymyxin, which was started alongside ATT and steroids. As per the WHO criteria, this child was categorised as severe EPTB disease, TBM.

The child's condition deteriorated with persistent seizures suggestive of epilepsia partialis continua, worsening consciousness and feeding difficulties. She required intubation and ventilatory support, with multiple anti-convulsant. Repeat imaging showed worsening hydrocephalus with multiple enlarging tuberculomas in the brainstem [Figure 2a and b]. PR is defined as an immune-mediated worsening despite therapy being suspected. Thalidomide was started as an immunomodulatory treatment alongside continued ATT and steroids. The ventriculoperitoneal shunt (VP shunt) failed and was replaced by external ventricular

drainage (EVD), allowing intraventricular polymyxin administration. Persistent bloodstream infection was noted. The child needed prolonged intensive care, including tracheostomy for long-term ventilation.

Although the fever spikes and seizures subsided, we could not notice any neurological recovery. Unfortunately, she remained ventilator-dependent and expired due to ventilator-associated pneumonia (VAP) [Figure 2c] after 4 months of hospital stay.

Case 3

A 14-year-old girl presented with a 15-day history of low-grade intermittent fever, cough with expectoration, occasional hemoptysis, post-tussive vomiting, decreased appetite and 4 kg weight loss. Her mother had PTB 5 years prior, but the girl did not receive any preventive treatment at that point of time. She had a BCG scar on examination. Further examination showed mild cervical lymphadenopathy, increased respiratory rate, decreased air entry, crepitations and increased vocal fremitus on the right lung. Anthropometry revealed undernutrition (BMI 12.2 kg/m²). Laboratory tests showed anemia, leucocytosis,

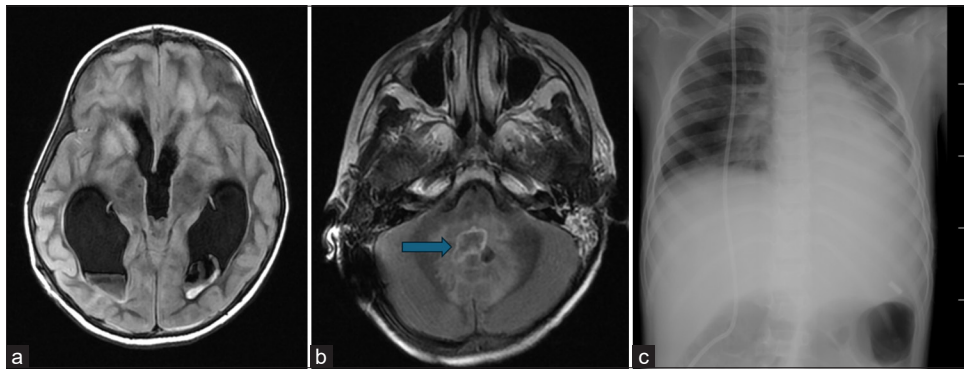


Figure 2: (a) Magnetic resonance imaging (MRI) brain T2 flair axial section of case 2 showing hydrocephalus, exudates in the ventricles. (b) MRI brain T2 flair axial section of case 2 showing multiple tuberculomas in the brainstem (Arrow shows tuberculoma noted in the brainstem in the T2 flair images). (c) Chest X-ray of case 2 showing right mid zone infiltrate on ventilation with tracheostomy tube *in situ* (Ventilator-associated pneumonia). Shadow of ventriculoperitoneal shunt is also noted on the right side.



Figure 3: (a) Chest X-ray of case 3 showing diffuse ill-defined opacities on the right side with cavity lesion beside the hilum on the right side. (b) High-resolution computed tomography (HRCT) images of case 3 showing cavity lesion depicted by arrow over the right lung upper lobe. (c) HRCT images of case 3 showing cavity lesion depicted by arrow over the left lung.

Table 1: Clinical profile of all the three cases.

Parameter	Case 1	Case 2	Case 3
Age/Sex	15-year-old female	5-year-old female	14-year-old female
Presenting symptoms	Fever, cough with expectoration, weight loss	Fever, Seizures, altered sensorium, vomiting	Fever, cough, hemoptysis, weight loss
Duration of symptoms	3 months	5 weeks (during steroid therapy)	15 days
Past/family history	No contact history	Primary nephrotic syndrome; on steroids	Mother treated for TB 5 years back
Nutritional status (BMI)	10 th centile	25 th centile	12.2 kg/m ² (below 3 rd centile)
BCG scar	Present	Present	Present

TB: Tuberculosis, BMI: Body mass index, BCG: Bacillus calmette-guérin

Table 2: Details of the investigations of the three cases.

Parameter	Case 1	Case 2	Case 3
Haematology	Hb 9.8 g/dl, leukocytosis, thrombocytosis	Hb 8.3g/dl Leukocytosis	Hb 8.5 g/dl, leukocytosis, thrombocytosis
ESR/CRP	ESR 73 mm/hr, CRP 123 mg/L	ESR 80 mm/hr, CRP-33mg/L	ESR 90 mm/hr, CRP 55 mg/L
Mantoux test	Positive	Negative	Positive
Sputum AFB/ CBNAAT	AFB 3+, CBNAAT sensitive to INH and Rifampicin	gastric aspirate -AFB negative, CBNAAT negative	AFB 2+, CBNAAT resistant to INH
Imaging findings (X-ray)	Left upper lobe opacities, cavitation	Right mid-zone infiltrates; VP ^Δ shunt seen	Bilateral patchy opacities: cavities in right mid-zone & left upper zone
HRCT/MRI	Tree-in-bud pattern, cavitation	MRI: hydrocephalus, multiple brainstem tuberculomas	HRCT: cavity in both the lungs (right upper lobe, left middle lobe)
Other relevant tests	HIV, HBsAg, HCV negative	CSF culture: Acinetobacter baumannii	HIV, HBsAg, HCV negative

ESR: Erythrocyte sedimentation rate, CRP: C-reactive protein, AFB: Acid fast bacillus, CBNAAT: Cartridge-based nucleic acid amplification test, INH: Isoniazid, VP: Ventriculoperitoneal shunt; HRCT: High resolution computed tomography; MRI: Magnetic resonance imaging, CSF: Cerebrospinal fluid, HIV: Human immunodeficiency virus, HBsAg: Hepatitis B surface antigen, HCV: Hepatitis C virus

Table 3: Details of the treatment and outcome of the three cases.

Parameter	Case 1	Case 2	Case 3
Anti-TB regimen	2HRZE (sensitive)+2HR	2HRZE+steroids+thalidomide+10HR	MDR regimen (resistant to INH)
Additional interventions	Nutritional support, DOTS	VP ^Δ shunt, EVD*, Mechanical ventilation, Tracheostomy, anticonvulsants	Nutritional support, DOTS
Complications	None reported	Paradoxical reaction, EPC, ventilator-associated pneumonia	None reported
Outcome	Symptomatic improvement, discharged	Prolonged ventilation, Expired (150 days hospital stay)	Started on MDR therapy; follow-up planned
Contact tracing under nikshay	completed	completed	Completed

MDR: Multi-drug resistant, Anti-TB: Anti-Tuberculosis, HRZE: Isoniazid rifampicin pyrazinamide ethambutol, DOTS: Directly observed treatment shortcourse, EPC: Epilepsia partialis continua, EVD: External ventricular drain

thrombocytosis, elevated ESR and CRP and a positive Mantoux test [Table 2]. Chest X-ray [Figure 3a] and HRCT [Figure 3b and c] showed bilateral cavitory lesions. Sputum smear was positive for AFB, and CBNAAT confirmed DR-TB to INH by LPA. HIV and viral serologies were negative,

and the abdominal ultrasound was normal. As per the WHO criteria, she was categorised as RIF-susceptible, INH-resistant advanced PTB disease. She was started on weight-based anti-tubercular therapy under DOTS as per the WHO guideline. Contact tracing was also done in this case.

DISCUSSION

These three cases highlight the spectrum of TB in children from a young age (<5 years) to the adolescent age group, from the immunocompetent to the immunocompromised and from pulmonary to extra-pulmonary manifestations. As per the WHO definitions,^[1] case 1 was categorised as extensive (or advanced) PTB disease, case 2 as severe EPTB and case 3 as a case of RIF-susceptible, INH-resistant TB. We discuss here the challenges of managing these cases as per the updated guidelines published by WHO^[1] in 2024.

Epidemiology and risk factors for TB

According to the WHO Global TB Report 2024,^[1] an estimated 10.8 million people developed TB globally in 2023, with 134 new cases/100,000 population. South-East Asia accounted for the highest burden, contributing 45% of global cases.^[1] In India, a national TB survey across 20 states found a prevalence of 312 cases/100,000 people.^[2,4] Children and adolescents under 15 represent 11% of global TB cases, with 7.5 million newly infected each year.^[1] Around 67 million are estimated to be latently infected, including 2 million with DR-TB and 100,000 with extensively DR-TB (XDR-TB).^[1]

Among children, the pooled prevalence of latent TB infection is defined as an immune response to MTB without active disease, ranges from 33% (5 years) to 40% (6–14 years).^[4] Approximately 5–10% of those with latent infection progress to active TB disease.

Under India's NTEP, children make up 6–7% of patients treated annually.^[2] However, a 56% detection gap indicates significant underdiagnosis, particularly of MDR-TB, with only 3% of reported cases in children under 14 years – likely an underestimate.^[1,10,11] Paucibacillary nature of the disease, difficulties in sample collection and underuse of stool X-pert may be possible reasons for this detection gap, which still exists. Among our three cases, only one was DR-TB. Risk factors for childhood TB in India include high population density, poverty, malnutrition, exposure to tobacco and pollutants, immunodeficiency, lack of BCG vaccination and genetic susceptibility.^[2-4,11] We could notice that immunosuppression was the only risk factor in the second case. All the cases had a BCG scar on examination.

The WHO's 2015 End TB strategy^[3] was the first to explicitly include children, leading to improved focus on paediatric TB. India's NTEP uses standardised diagnosis, treatment and prevention protocols, supported by 'Nikshay', a web-based platform to monitor treatment and antibiotic use under the DOTS.^[2]

To reduce child TB mortality, 80% of which occurs in those under five, early diagnosis of infectious adults and timely screening of child contacts is essential.^[8] One study^[11] in eight high-burden countries showed that 12% of household

contacts of MDR-TB cases were diagnosed through contact investigation. Systematic screening, or active case finding, is essential in closing detection gaps, especially in high HIV prevalence settings where HIV testing among TB contacts is also recommended.^[1-3]

Clinical manifestations of TB in children

TB in children can present as PTB or EPTB, with PTB being more common.^[1,20-22] Two of our cases were PTB. However, EPTB, especially TBM, is a significant cause of morbidity and mortality.^[1,16,20,23] Only one child was EPTB, that is, TBM. Across paediatric populations, no major gender differences are observed between PTB and EPTB.^[21,22] We could note that all our cases were girls. Although DR-TB is always an emerging concern,^[11] a high proportion of children with TB suffer from malnutrition in India.^[12]

PTB

Children with PTB typically present with persistent cough, poor weight gain or unexplained weight loss of more than 5% over 3 months.^[1,21,22] This is like our two cases who presented with PTB. In high-risk groups such as infants and HIV-positive children, TB may present atypically, including acute pneumonia or with persistent wheezing.^[1,24] None of our cases were HIV-positive.

The WHO guidelines^[1] recommend classifying such children as presumptive TB and initiating active case-finding using a combination of clinical examination and diagnostic tests. Chest X-ray is usually the first-line investigation in PTB, with a sensitivity of 84% and specificity of 91%. Characteristic findings include miliary shadows, hilar/mediastinal lymphadenopathy and fibro-cavitary lesions in the upper lobes.^[25] However, some radiographic patterns, such as consolidation or bronchopneumonia, are non-specific and require follow-up if symptoms persist despite antibiotics.^[1,25] Two of the three cases (case 1 and case 3) had significant radiological findings on chest X-ray, as depicted in Table 2.

Microbiological testing using molecular WHO-recommended rapid diagnostics (mWRD)^[1,26,27], such as Xpert-MTB/RIF and AFB microscopy, should be done using sputum or gastric aspirates. In both the PTB cases presented here, we could isolate AFB and confirm the diagnosis by Xpert-MTB/RIF. These tests were done simultaneously by sending samples to the regional laboratory for TB in the district. HRCT can be used for complex cases, revealing patterns such as necrotic lymph nodes or 'tree-in-bud' opacities.^[28] This was very classical in our first case, where we could notice a similar HRCT appearance. Drug resistance testing is now universally recommended by WHO upfront using Xpert-MTB/RIF or Ultra, followed by LPAs for further identification of resistance to INH (H), fluoroquinolones

(FQ) and second-line injectables.^[7,29] In the third case, we could confirm the drug resistance by LPA at first contact. This helped us to change the drug regime to a DR-TB regimen.

Children may also have concurrent EPTB, and diagnostic material should be collected from these sites when possible.^[27] However, due to the paucibacillary nature of TB in children, treatment should not be delayed for microbiological confirmation, especially in very young or immunocompromised children, who are at greater risk for severe and disseminated forms like TBM.^[8]

EPTB

EPTB involves sites outside the lungs and is seen in various forms, with lymph node TB being the most common, especially in children aged 5–9 years.^[10,12] Cervical lymphadenopathy is frequent, and histopathology or fine-needle aspiration cytology is used for diagnosis.^[1] The tuberculin skin test is often positive but is not diagnostic alone.^[4,6] Although we could get Mantoux positive in the PTB cases, it was negative in the EPTB case, which presented as TBM. Chest X-rays may show associated pulmonary involvement in 5–40% of lymph node TB cases.^[8]

The most severe form of EPTB is TBM, accounting for 5–10% of EPTB cases but carrying a disproportionately high mortality and morbidity,^[14,16,20,25] especially in children under five. This was like our second case who presented with TBM stage 3. TBM progresses through three clinical stages, with prognosis highly dependent on early detection and treatment.^[30] CSF analysis in TBM typically shows lymphocytic pleocytosis, high protein and low glucose.^[31] We could notice similar CSF findings in our second case; the findings were consistent with TBM, although we could not isolate AFB, nor we could get positivity in the molecular tests, as depicted in Table 2. CBNAAT (Xpert MTB/RIF) improves diagnostic accuracy, although the sensitivity is low, whereas X-pert Ultra has better sensitivity on CSF samples.^[1,27,31] Despite this, diagnostic yield remains limited, and lumbar puncture is often delayed due to raised ICP.^[32] Neuroimaging, including contrast-enhanced CT and MRI, is vital.^[33] Common findings include basal meningeal enhancement, hydrocephalus, tuberculomas and infarcts.^[33,34] MRI is more sensitive, particularly for brainstem lesions.^[33] Our second case did show hydrocephalus and basal exudates in the initial CT brain. After 2 months of ATT when the child's condition worsened, we could notice several brainstem tuberculomas in the MRI [Figure 2b] despite the child being on ATT and dexamethasone. Differential diagnoses for TBM include neurocysticercosis, cryptococcal meningitis and CNS malignancies.^[13,34]

CNS-TB manifestations

TBM is the second most common EPTB form after lymphadenitis.^[16,20,30] Historical and modern data highlight

its severity.^[14,15] A study published in the Indian Pediatric Journal in 1966 reported a 51% mortality in children, particularly under 5 years and in the advanced stage of TBM.^[20] TBM still contributes significantly to TB-related deaths (19.3%), with high rates of neurological sequelae (53.9%) among survivors even today.^[16] Intracranial tuberculomas, another form of CNS-TB, presents as intracranial space-occupying lesions and can cause seizures or neurological deficits.^[32-34] This was like our second case. Although rare, it can be seen in about 1% of TB cases.^[16] Risk factors for CNS-TB include young age, malnutrition, immunosuppression and malignancy.^[16,17] We did notice that our second case of TBM was immunosuppressed during steroid therapy for PNS.

TB in the setting of nephrotic syndrome

Children with PNS, especially those treated with high-dose steroids, are at risk of TB.^[9] TB incidence in this group ranges from 1.5% to 10%, mostly occurring after starting immunosuppressive therapy.^[35-37] PTB is the most common form, and frequently relapsing nephrotic syndrome on long-term steroids is particularly vulnerable.^[9,35] This was seen in our second case.

Treatment of TB

Successful TB treatment in children involves more than ATT.^[38] It also includes nutritional support, management of adverse drug reactions, comorbidity care and psychosocial support with decentralised and family-centered care recommended by WHO and integrating TB care with other health services such as maternal and child health.^[1,39] We followed this in the treatment of our patients in our hospital. All these children were attached to 'Ni-kshay' and treated under NTEP.

Standard treatment involves an intensive phase (2 months) and continuation phase (2–4 months).^[1] Children (3 months–16 years) with non-severe drug-susceptible TB may receive a shorter regimen of 2 months of intensive and 2 months of continuation phase (as per SHINE trial results).^[38,40] Adolescents (≥ 12 years and ≥ 40 kg) may be eligible for a 4-month rifapentine-moxifloxacin regimen^[38,40] as per the updated WHO guidelines. As these shorter regimens are still not updated in the NTEP, our first case continued with the standard treatment regime and showed good clinical improvement. Treatment for TBM requires 2 months of intensive therapy (four drugs HRZE) with steroids and 10 months of continuation phase H-Isoniazid, R-Rifampicin (HR).^[1,38] Our second case, although it was on ATT, showed worsening of symptoms after a brief period of improvement.

Corticosteroids reduce mortality and neurological disability in TBM.^[18] In severe cases, surgical interventions such

as a VP shunt and endoscopic third ventriculostomy for hydrocephalus may be needed.^[41] Our second case was started on dexamethasone and was surgically treated for raised Intracranial Tension (ICT) by VP shunt initially and later by an EVD. PRs (worsening of lesions during therapy) are possible, particularly in immunocompromised children during recovery.^[19,24,34,42] Steroids such as prednisolone or dexamethasone are recommended for TBM, TB pericarditis, miliary TB with alveolo-capillary block, TB uveitis and Addison's disease.^[18] They reduce inflammation, prevent complications and are typically used for 2–4 weeks before tapering. Pyridoxine (vitamin B6) is co-administered to prevent neuropathy.^[38] We did notice these PR in our second case, which was treated by thalidomide in addition to steroids.

DR-TB

DR-TB in children resembles drug-sensitive TB in presentation. It should be suspected in children exposed to DR-TB cases, non-responders to standard therapy after 2–3 months, TB relapses.^[29] Types of resistance include INH-monoresistance, MDR-TB (resistant to INH and RIF), pre-XDR-TB (resistant to FQ) and XDR-TB (resistant to FQ + bedaquiline/linezolid).^[1,29] Rapid tests such as GeneXpert and LPAs detect resistance in hours to days.^[27,29,31] The WHO now recommends all-oral regimens using group A drugs such as levofloxacin, bedaquiline, delamanid and linezolid, with over 78% treatment success in paediatric MDR/RR-TB.^[29]

PR^[19] and IRIS^[24] in TB both involve a worsening of TB symptoms during treatment, but they differ in their timing and underlying causes. PR occurs 3–12 weeks after starting treatment and appears as new or enlarging lesions in immunocompromised or immunocompetent children.^[13,16,19] These reactions mimic DR-TB but usually resolve on their own. Proper distinction from DR-TB is essential before labelling a case as PR. TB-IRIS is a worsening inflammatory response seen in HIV-positive children after starting antiretroviral therapy.^[24,42] Similar reactions may occur in children recovering from nephrotic syndrome during tapering of immunosuppression.^[9] These conditions usually improve with steroids but at times in a specific group of children TNF- α inhibitors such as thalidomide or infliximab, which reduce inflammation improve outcomes as shown by several studies.^[13,18,19,43]

Thalidomide, although it was noted to be controversial during its past obstetric use, is currently seen to be effective in treating PR and speeding radiological recovery.^[34] Infliximab, a monoclonal TNF- α inhibitor, is an alternative but has limitations due to cost and poor blood-brain barrier penetration.^[43]

Adverse effects of thalidomide include rash, neuropathy and elevated liver enzymes. It is noted that these adverse effects are often dose-dependent and seen commonly with high-

dose thalidomide.^[19] A meta-analysis showed 91% clinical and 90% radiological improvement with thalidomide.^[19] Although thalidomide is not mentioned in any guidelines, strong randomised controlled trial evidence in children is still lacking. Other common drugs like aspirin have also shown benefits in PR due to their anti-thrombotic and anti-inflammatory properties.^[44] TB care is incomplete without emphasis on preventive therapy^[45] and management of malnutrition with proper nutritional and psychosocial support^[39] to the affected family as per the Nikshay Poshan Yojana of the NTEP.^[2]

CONCLUSION

In India, despite efforts under the NTEP, significant delay or underdiagnosis still exists. Non-specific symptoms, paucibacillary nature of the disease, and high incidence of EPTB make diagnosis more challenging. The need for molecular tests and imaging cannot be overemphasised and should be prioritised in CNS-TB and drug resistance. Emergence of stool X-pert as a non-invasive tool for diagnosis in young children needs to be recognised. Nutrition and psychosocial support should always be a part of the treatment of paediatric TB in addition to strengthening contact screening, preventive therapy and access to mWRDs as envisioned under NTEP and WHO end TB targets. Corticosteroids and immunomodulators like thalidomide for PRs in selected cases may be considered if supported by well-designed clinical trials in children, as illustrated through our case series.

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