

CASE REPORT

The Dreadful Changing Kaleidoscope of Pediatric Disseminated Tuberculosis: A Case Series of TB in Children

S Fouziya Sultana¹, Bela Verma², Amin Kaba³

ABSTRACT

Childhood tuberculosis is a formidable problem in present times. Although the principles of diagnosis and treatment remain the same in children and adults, yet the dissimilarities in the pathology and the host bring up challenges while dealing with pediatric TB. Just as children are not miniature adults, TB in children is also not a miniature version of the adult form. Therefore, it becomes very important to be aware and highly suspicious of infection with tuberculosis especially in endemic countries like India. We present a case series of five cases of different presentations of tuberculosis in childhood. Only one among the five survived the illness and the other four succumbed to the disease. This study highlights the high prevalence and varied clinical spectrum of childhood tuberculosis in Mumbai city.

Keywords: Biopsy, CBNAAT, Pneumonia, Tuberculosis, Tuberculous lymphadenitis.

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INTRODUCTION

World Health Organization (WHO) announced the end TB strategy with the target of reducing tuberculosis deaths by 90 and 95%, and incidence by 80 and 90% by 2030 and 2035, respectively.¹ However, the Government of India has decided to aim for TB elimination from our country by 2025 ahead of the global target.² Childhood tuberculosis is an important area of intervention while drawing the road map to end TB.

Tuberculosis is a common granulomatous disease caused by *Mycobacterium tuberculosis*, which primarily affects the lungs in about 80% of cases.³ Extrapulmonary tuberculosis is defined as tuberculosis of organs other than lungs presenting as disseminated tuberculosis.

Global TB report 2018 reports that in India, an estimated 2.2 lakh children become ill with tuberculosis each year (22% of global TB burden), with a slightly higher burden among males.³ Pulmonary TB is the most common form in children but extrapulmonary TB forms a larger proportion of cases than in adults. It is also known that about 10% of the cases are reported to RNTCP are from children under 14 years of age.³

MATERIALS AND METHODS

On admission, detailed history including TB contact was taken and clinical examination was done. For every patient, in addition to a basic hemogram, a Tuberculin skin test, and chest X-ray were done. Gastric lavage was sent for Gene Xpert, AFB smear, MGIT, and for Gram stain, bacterial and fungal cultures. Further radiological imaging like USG and CT imaging of the thorax and abdomen was done as required. Reports of MGIT were followed up on day 3, 3 weeks, and 6 weeks for further drug sensitivity. Where ever feasible tissue-specific sample was collected and sent for histopathological examination, gene-Xpert, and MGIT. HIV serology was sent for all patients and they were seronegative. Further workup of chronic granulomatous diseases (CGD) was not done as the patients did not have a history of recurrent infections/chronic infections/abscesses or similar family history and the cultures of blood, urine, gastric lavage, FNAC sample of lymph node did not reveal the growth of

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other bacteria or fungi. BAL or biopsy of the lesion was not done owing to their critical hemodynamically unstable condition and unfit for Anesthesia. Two of our patients succumbed to the disease within 48 hours of hospital stay.

CASE DESCRIPTIONS

Case 1

A 5-year-old male child presented with 2 months duration of fever and painful right neck swelling. He had constitutional symptoms such as fever, loss of weight, and loss of appetite. There were no obstructive symptoms of dysphagia, odynophagia, change of voice, or stridor. Furthermore, there was no history of night sweats, chronic cough, and TB contact. On physical examination, there was right neck swelling in the posterior triangle measuring 3 × 3 cm, soft, fluctuant, immobile, non-tender, with head tilt (torticollis) toward the left side and restricted neck mobility. Tuberculin skin test was 3 mm diameter. The chest radiograph was normal. USG neck was suggestive of a well-defined irregular hypoechoic collection in the right upper posterior triangle in the intramuscular plane showing multiple mobile internal echoes with air foci suggestive of a liquefied abscess. CECT neck was suggestive of retro-pharyngeal abscess with extension into the right posterior cervical spine and bony erosion of right occipital condyle, atlas, and mastoid with reactive cervical lymphadenopathy with cold abscess (Figs 1 to 3).

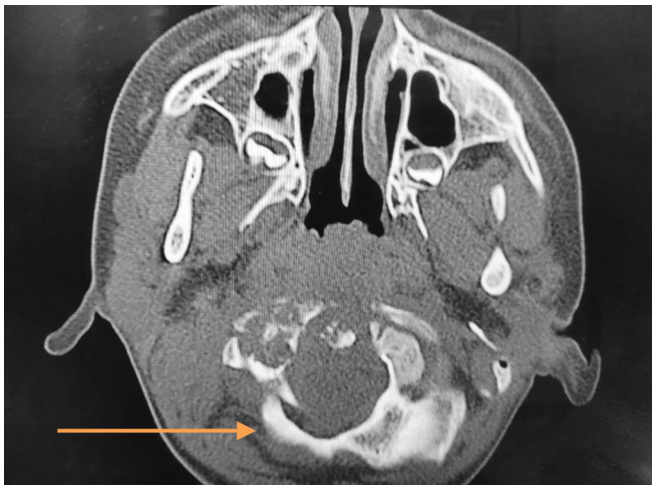


Fig. 1: CT Brain with bone window showing erosion of atlas and occipital condyle

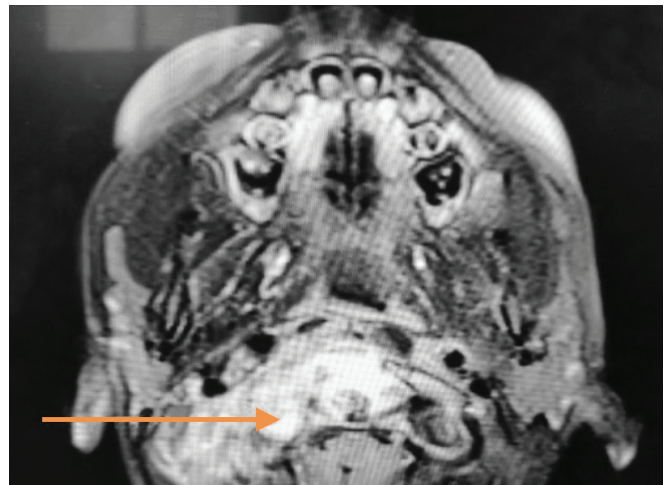


Fig. 2: Post contrast CT enhancement (temporal view) showing retropharyngeal abscess

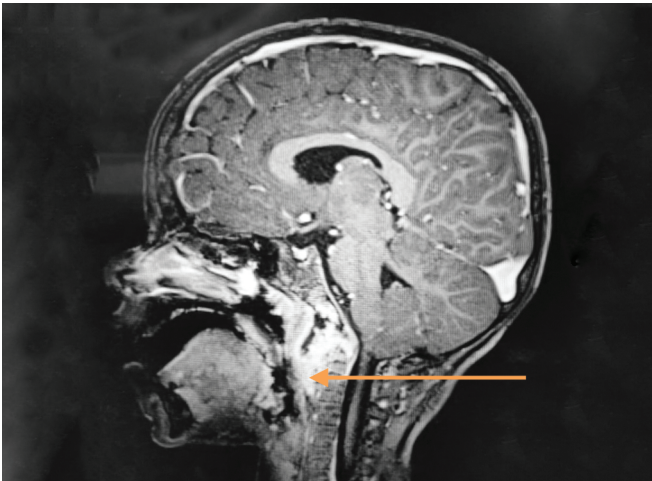


Fig. 3: Post contrast CT enhancement (sagittal view) showing retropharyngeal abscess



Fig. 4: Chest X-ray with bilateral pneumonic consolidation (right side more than left)

He underwent incision and drainage of right neck abscess and pus for gene expert as well as MGIT culture detected *M. tuberculosis* with rifampicin sensitivity. The child was started on treatment with category 1 anti-tuberculosis drugs and a cervical collar was given to wear. Within 2 weeks of starting the intensive phase of the anti-tuberculosis treatment regime, his general condition improved markedly with a reduction in the size of neck swelling and he was discharged on ATT. At present, the child is in the maintenance phase of anti-tuberculosis treatment and doing well.

Diagnosis

Tuberculous right retropharyngeal cold abscess with bony erosion of right occipital condyle, atlas, and mastoid bone.

Case 2

A 3-year-old male child presented with a gradual inability to sit and walk without support for the past 3 months. He also had constitutional symptoms of high fever, cough, loss of weight, and loss of appetite. However, a history of tuberculosis contact was absent. On examination, the child was emaciated with Pectus carinatum, crowding of ribs, an inter-scapular deep swelling,

clubbing, and protruding abdomen. There was tachypnea, tachycardia with subcostal and intercostal retractions. Chest radiograph was suggestive of bilateral pneumonia, right > left (Fig. 4). The child was started on intravenous antibiotics. Gastric lavage smears were negative for acid-fast bacilli, Gene Xpert, and culture revealed no growth of tuberculous bacilli. CECT thorax was suggestive of areas of consolidation with centrilobular opacities giving tree in bud appearance and cavitary lesions in the right upper lobe, right lower lobe, and to some extent in left upper lobe likely to be of tuberculous etiology (Fig. 5). Hence, the child was started on category 1 anti-tuberculosis drugs which included isoniazid, rifampicin, ethambutol, and pyrazinamide along with pyridoxine supplementations. The child showed clinical deterioration even after 1 month of the intensive phase of the anti-tuberculosis regime. Repeat chest roentgenogram was done which showed findings of bilateral pneumonic consolidation with a large bulla in right lower lobe (Fig. 6). Hence, the antibiotics were stepped up and the child was again evaluated for drug-resistant tuberculosis. An intercostal drainage tube was inserted in the right pulmonary cavity. AFB smear, culture, and gene Xpert of pleural fluid sent which did not detect the growth of *M. tuberculosis*. Repeat CECT thorax revealed destruction

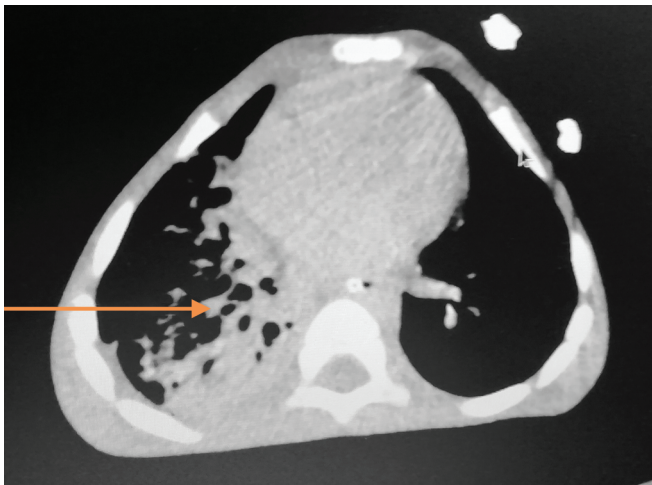


Fig. 5: CT thorax showing right lung centrilobular opacities

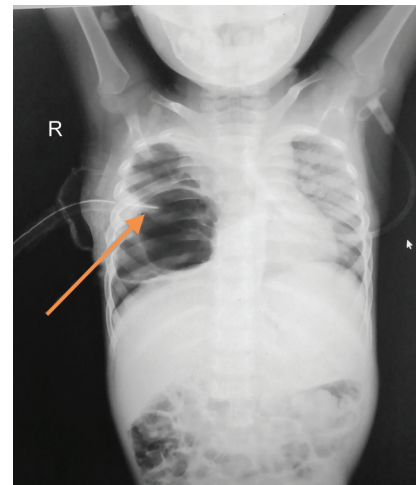


Fig. 6: Chest X-ray showing intercostal drainage tube in the cavity

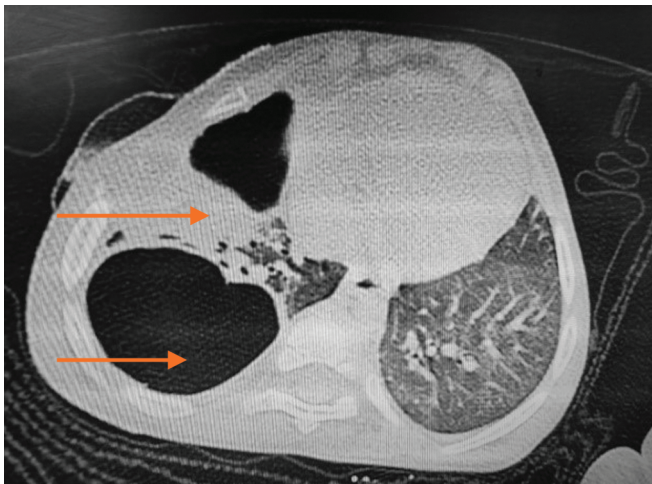


Fig. 7: CT thorax showing lung destruction, extensive fibrosis and cavitary changes

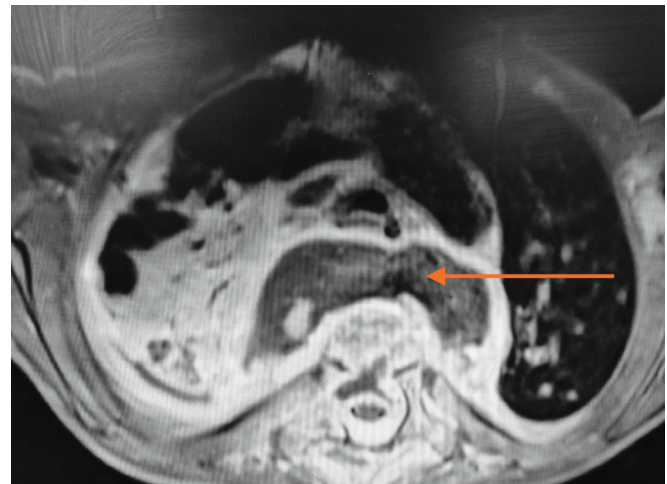


Fig. 8: MRI T1 weighted image (axial view) showing epidural abscess

of anterior and posterior segments of right upper lobe, right middle lobe, and superior segment of the right lower lobe with replacement by large cavitary lesions along with active ongoing infection (Fig. 7). Minimal right pleural effusion with ICD was found. In addition, there were findings of tubercular spondylodiscitis of the D1 to D3 vertebrae. MRI spine revealed D1 to D3 vertebral involvement with erosions, anterior wedging, and near-complete destruction. There was pre- and paravertebral peripherally enhancing collection with local extensions into adjacent scapula and muscles along with an anterior epidural abscess which is seen causing narrowing of the vertebral canal (Figs 8 and 9). The paravertebral abscess was drained and its histopathological examination revealed fibrovascular and fibro-collagenous tissues showing diffuse lymphoplasmacytic infiltrate and occasional scattered epithelioid cells. However, there was no evidence of well-formed granuloma or caseous necrosis and pus for CBNAAT demonstrated growth of *M. tuberculosis* without rifampicin resistance. The child was started on an MDR TB regimen owing to his deteriorating general health condition due to failure of category 1 drugs. The pediatric surgeon and orthopedic surgeon denied surgery for cavitary lung lesion and his Pott's spine with obstructive signs, respectively, as there was a high risk of anesthesia and surgery-related complications including death on the table

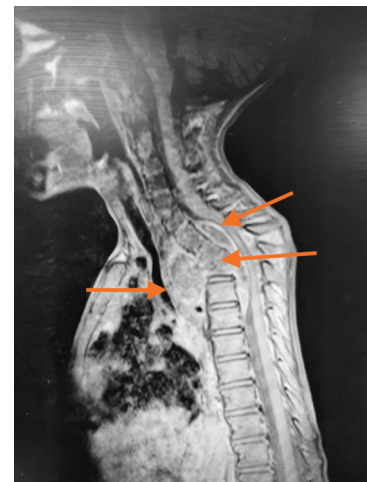


Fig. 9: MRI T2 weighted image (sagittal view) showing spinal cord edema, epidural abscess and collapsed vertebrae

after informed consent signed by the parents. The child did not respond to the management and finally succumbed to the ongoing disease process after a stay of 3 months in the hospital.

Diagnosis

Disseminated tuberculosis with bilateral fibrocavitary pulmonary tuberculosis with Pott's spine involving D1 to D3 vertebra with pre and paravertebral cold abscess with severe acute malnutrition.

Case 3

A 4-year-old female child, unimmunized since birth presented with chief complaints of intermittent fever with loss of appetite and loss of weight for the past 6 months. The child was admitted to a private hospital for 20 days before our hospital visit. The child had developed swelling on both sides of the neck for the past 4 months which increased in size gradually causing difficulty in speaking and swallowing for the past 20 days. Though there was no history of exposure to tuberculosis, the child was under treatment with four drug anti-tuberculous drugs by a private practitioner which was discontinued after 3 months. The child had pancytopenia, elevated ESR and CRP, normal LDH and fibrinogen levels, elevated serum ferritin levels, and a deranged coagulation profile with chest X-ray showing bilateral pneumonia (Fig. 10). Bone marrow biopsy, CD 25, and natural killer cell levels were normal. On presentation to our hospital, the child was in hypotension, bradycardia, SpO₂ 100% on mechanical ventilation, significant bilateral cervical lymphadenopathy presenting as bull neck appearance and

chest had bilateral crepitations and conducted sounds with hepatomegaly and non-palpable spleen. Ultrasonography of the neck revealed multiple enlarged necrotic cervical lymph nodes, most likely to be of tubercular etiology. Gastric lavage did not demonstrate MTB either in AFB staining, culture, or gene Xpert. Category 1 anti-tuberculosis drug regimen with isoniazid, rifampicin, ethambutol, and pyrazinamide along with pyridoxine supplementation was started. Under an anti-tuberculosis regime and wide spectrum antibiotic coverage, the child's general condition partially improved and the child was weaned off from the ventilator support. Meanwhile, the reports of bone marrow biopsy revealed expression of CD56 and natural killer cell activity to be within normal limits. CSF analysis done for seizures demonstrated six total nucleated cells, which were 100% lymphocytic, CEF protein, and sugar values were within normal limits, no growth on its culture, and MTB not detected on gene Xpert. CECT demonstrated consolidation of both the lungs, necrotic abscesses in the neck with necrotic cervical and mediastinal lymphadenopathy, splenic infarcts, granulomas, and microabscesses, and mild hepatomegaly with ascites. The above constellation of findings was suggestive of disseminated infection, most likely to be of tuberculous etiology (Figs 11 to 13). Anti-tuberculosis drugs were continued along with other supportive management. The child developed erosion and

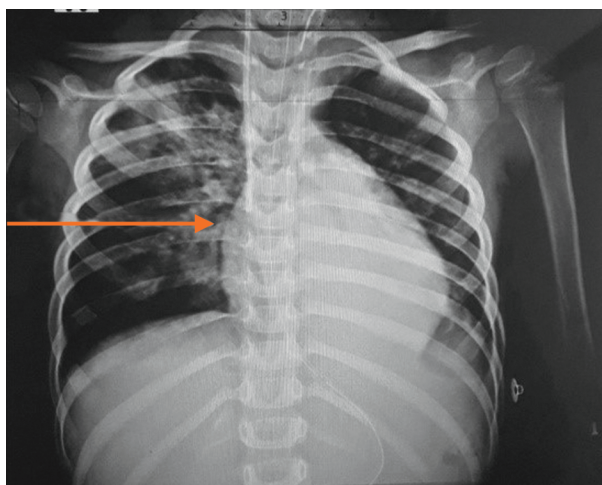


Fig. 10: MRI T2 weighted image (sagittal view) showing spinal cord edema, epidural abscess and collapsed vertebrae

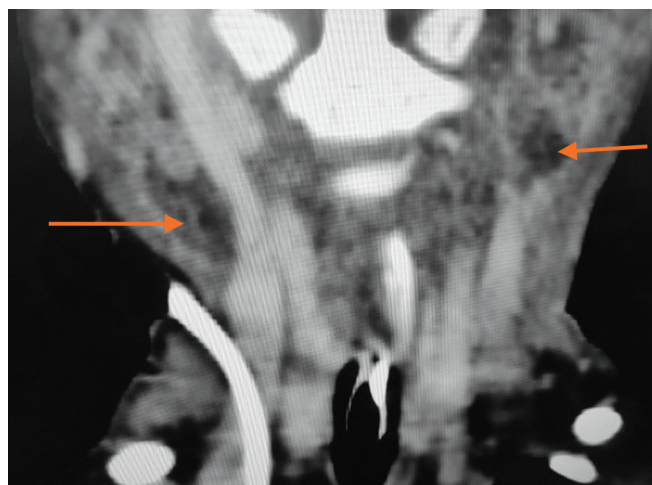


Fig. 11: CT neck (coronal view) showing necrotic collections in neck

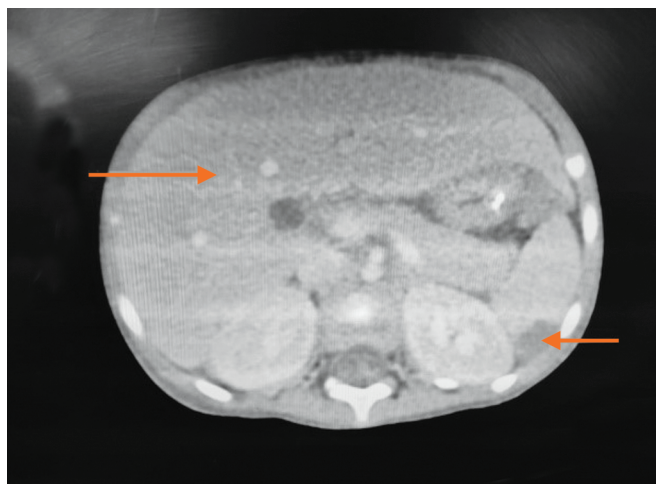


Fig. 12: CT abdomen showing hepatomegaly and splenic abscess

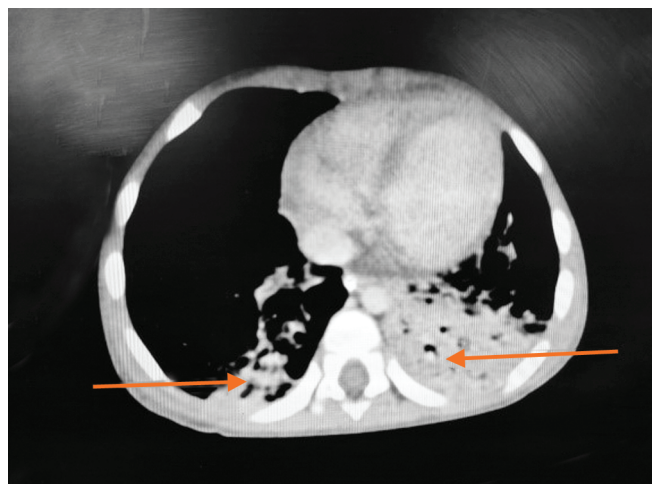


Fig. 13: CT thorax (axial cut section) showing bilateral consolidation

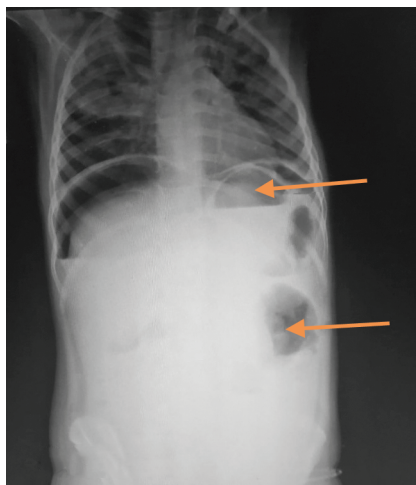


Fig. 14: Chest X-ray showing infiltrates in right para-cardiac region with air fluid level in abdomen



Fig. 15: X-ray abdomen post surgery with clearance of air fluid level

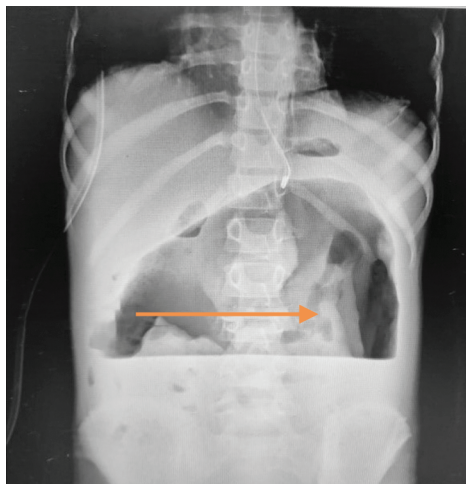


Fig. 16: X-ray abdomen erect view showing air fluid level

hemorrhage of necrotic neck lymph nodes and subsequently developed respiratory failure with disseminated intravascular coagulation and expired due to the severity of the disease process.

Diagnosis

Disseminated tuberculosis with bilateral pneumonia, necrotic eroding abscess of cervical and mediastinal lymph nodes, and abdominal tuberculosis involving liver and spleen.

Case 4

A 9-year-old female child presented with an acute history of high-grade fever, non-bilious-vomiting, and abdominal pain of 3 days. There was a strong history of contact with tuberculosis in two of her older siblings, out of them, one had expired due to the disease, and a cousin who had completed 6-month anti-tuberculosis drug regimen 4 months ago. On physical examination, the child was ill-looking, unstable and in shock with a guarded general condition, tachycardia, tachypnea, hypotension, severe pallor, increased work of breathing, and low urine output. Abdominal examination revealed a rigid board-like abdomen (peritonitis) with diffuse guarding and rigidity and absent bowel sounds. The child was hemodynamically stabilized with fluids, inotropic agents, and blood

transfusion. X-ray of the erect abdomen revealed air under the diaphragm and fluffy shadows in the right lung zone (Fig. 14). The child was taken up for emergency surgery. Exploratory laparotomy revealed perforated ileum and 30 cm ileal resection with ileostomy was performed (Fig. 15). Gastric lavage for gene Xpert detected MTB with rifampicin sensitivity. The child was managed with an anti-tuberculosis regimen with higher intravenous antibiotics and inotropes. The child, however, succumbed due to inotrope refractory septic shock with septicemia secondary to intestinal perforation and disseminated tuberculosis. On autopsy, microscopic examination revealed large areas of caseous necrosis with surrounding epithelioid granulomas, necrotic hilar lymphadenitis suggestive of pulmonary TB. Transmural acute infiltrates of the intestinal wall with necrotic mesenteric and paraaortic lymph nodes demonstrating epithelioid cell granuloma.

Diagnosis

Disseminated tuberculosis-pulmonary and abdominal TB with intestinal perforation and peritonitis.

Case 5

An 11-year-old female child presented with 20 days history of abdominal pain, non-bilious vomiting, and progressively increasing abdominal distension. The past medical and family history was irrelevant except for the death of grandfather due to pulmonary tuberculosis 3 months back. On physical exam, the child looked ill, she was hemodynamically stable, febrile, mild tachypnea, severe wasting with pallor. Abdominal examination revealed distended abdomen with diffuse tenderness and guarding with absent bowel sounds. The child was started on intravenous fluids and intravenous antibiotics. A nasogastric tube with continuous drainage and a Foley catheter was inserted. X-ray of the erect abdomen done at our center revealed a huge air-fluid level (Fig. 16). CT imaging of the abdomen revealed gross echogenic collection in the peritoneal cavity approximately 1 L in volume with mild ascites and conglomerated necrotic lymph nodes along the coeliac and mesenteric axis. The child was immediately taken for emergency surgery. Exploratory laparotomy showed a cocooned collection with approximately 1,500 mL of the fecal collection which was evacuated. Bowel loops adherent with multiple caseating tubercles and multiple perforations of <0.5 cm over 20 cm from

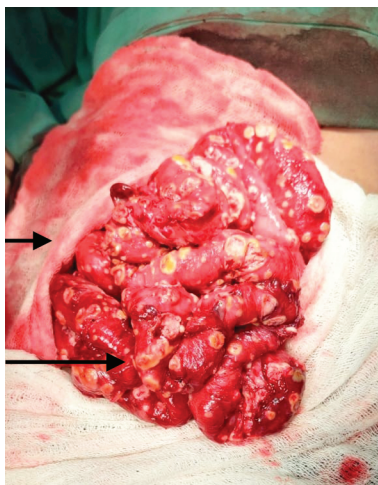


Fig. 17: Intraoperative specimen of cocoon abdomen with its covering and intestine showing caseating necrosis

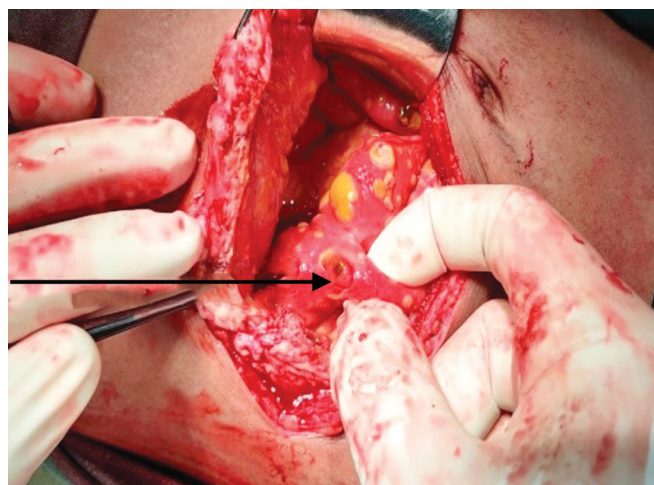


Fig. 18: Intraoperative specimen showing intestinal perforation

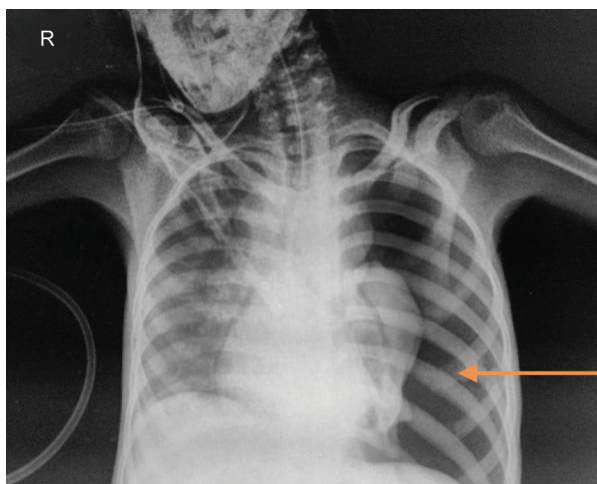


Fig. 19: Chest X-ray showing pneumothorax on left side

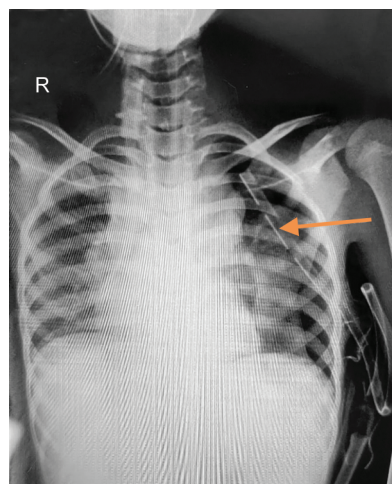


Fig. 20: Chest X-ray with ICT tube *in situ* and resolving pneumothorax

duodenojejunal junction to an ileocecal junction (Figs 17 and 18). Adhesiolysis, with primary closure of perforations and ileostomy with the placement of a pelvic drain, was done. The child was and started on anti-tuberculosis treatment with higher antibiotics. On day 1 post-surgery, the child had developed sudden respiratory distress due to left-sided pneumothorax for which intercostal tube drainage was done (Figs 19 and 20). However, the child developed decompensated, refractory septic shock due to which she collapsed in just 2 days of admission and succumbed to the illness.

Diagnosis

Cocoon abdomen–Intestinal tuberculosis with multiple perforations and adhesions.

DISCUSSION

Table 1 summarizes the clinical profile of the five cases. There were three females and two male patients, aged between 3 years and 11 years. Only one survived, responded well to treatment, and was discharged.

Despite the major advances in understanding tuberculosis, its management, diagnosis of tuberculosis sometimes becomes a dilemma. Hence, the delay in diagnosis, late presentation,

disseminated disease, and complications have led to increased morbidity and mortality. Negative smear for AFB, a lack of granuloma on histopathology, and negative culture do not exclude the diagnosis of tuberculosis. Newer investigations like TBDx system and Capture XT for smear microscopy, Bactec 960 MGIT, BacT/Alert and Micro ESP culture system for culture, IGRA, Gene Xpert, Gene Xpert ultra, Trunat, LAMP (Loop-Mediated Isothermal Amplification Assay) microarray, and gene sequencing methods of nucleic acid amplification tests prove to be useful.

The general child survival strategies are expected to focus on the diseases with the highest mortality among the under-5 and they include premature birth, perinatal asphyxia, and injuries, pneumonia, and diarrhea. About 10% of these are due to other causes, of which one cause is TB. *Mycobacterium* is perhaps one singular organism contributing to most deaths of under-5 among the world's middle- and lower-income nations, but it does not find a place in the list of causes of death as it is difficult to diagnose and there is a large detection gap. The exact contribution of TB to "Under 5 mortality" is unknown. Many TB-related deaths are possibly reported as pneumonia deaths due to similar respiratory symptoms.

Table 1: Compiled clinical profile of five cases

Serial no.	Age/ gender	Tb contact	Presenting complaints	AFB smear and Gene Xpert	Histopathological exam	MGIT (my- cobacterial growth indi- cator tube)	Treatment given (as per DST, drug sensitivity testing)	Diagnosis	Outcome
1	5 years/ male	No	Painful neck swelling on right	*Pus-MTB detected *Gastric lavage-MTB not detected	*Pus-multiple caseat- ing granulomas with lymphoplasmacytic in- filtration and epithelioid cells	MTB growth +	Category 1 ATT	Right retropharyngeal cold abscess with bony erosion of right occipital condyle, atlas, and mastoid bone	Improved and discharged
2	3 years/ male	No	Gradual inability to sit or walk without support for the past 3 months	*Pleural fluid *Pus from epidural region and *Gastric lavage-MTB not detected	*Pus-fibrovascular and fibro-collagenous tis- sues showing diffuse lymphoplasmacytic infiltrate and occasional scattered epithelioid cells	MTB growth+	Category 4 ATT	Disseminated tuberculosis with bilateral destructing pulmonary tuberculosis with Pott's spine involving D1 to D3 vertebra with pre- and paravertebral cold abscess	Expired
3	4 years/ female	No	Bilateral neck swelling with difficulty in swal- lowing over 6 months	Gastric lavage- MTB not detected	Not done as a child was hemodynamically un- stable and on ventilator support	MTB not grown	Category 4 ATT	Disseminated tuberculosis with bilateral pneumonia, necrotic abscess of cervical and mediastinal lymph nodes, and abdominal tuberculosis involving liver and spleen	Expired
4	9 years/ female	Yes	High-grade fever, vomiting, and pain abdomen	Gastric lavage- MTB detected	Autopsy specimen-ca- seating necrosis in lung and intestines with ne- crotic hilar lymph nodes	MTB growth+	Category 4 ATT	Disseminated tuberculosis pulmonary and abdominal TB with intestinal perforation and peritonitis	Expired
5	11 years/ female	Yes	Vomiting, abdominal pain, and distention	Gastric lavage-MTB not detected Epithelioid granulomas and caseating necrosis	Resected intestinal specimen	MTB growth +	Category 1 ATT	Cocoon abdomen - intestinal tuberculosis with multiple perforations and adhesions	Expired

Since the global strategy has shifted to achieving “zero death by TB”, this obviously could not happen without adding focus to TB in children.¹ National Tuberculosis Elimination Program (NTEP) highlights a stepwise approach to diagnosis and management of tuberculosis so that the diagnosis is not delayed or missed.

CONCLUSION

Despite real progress made by the WHO DOTS strategy in recent years, the global TB epidemic remains an ugly blot on the international public health landscape. TB in children presents particularly difficult challenges, but research priorities and advances in pediatric TB research may also provide wider insights and opportunities for TB control.⁴ High index of suspicion, timely judicious use of invasive diagnostic method and confirmation of the diagnosis, early institution of specific anti-tuberculosis treatment with a low threshold to start the management, and close clinical monitoring for adverse drug reactions are the key to successful management of atypical presentation of tuberculosis. And a new vaccine to prevent tuberculosis should be the ultimate goal. Hence, pediatric tuberculosis should be primarily concerned with the prevention and a child with the tuberculous disease is an opportunity to analyze the failure of the preventive mechanisms.⁵

Index Terms

Tuberculosis, *Mycobacterium tuberculosis*, Pott's spine, cavitation, retropharyngeal abscess, necrotic, lymphadenopathy, exploratory laparotomy, TBDx system, Capture XT, Bactec 960 MGIT, BacT/Alert, Micro ESP culture, IGRA, Gene Xpert, Gene Xpert ultra, Trunat, LAMP, gene sequencing.

ETHICAL CONSIDERATION

Informed consent was taken from the parents of the patients regarding publishing the data.

ACKNOWLEDGMENT

All staff and residents are involved in patient management and treatment.

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