

A 9 Year Old Female Ethiopian Patient with Stage IV Retroviral Infection and Right Side Hemiparesis

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Abstract

A 9-year-old, 17 kg, female patient was admitted to pediatric ward of a large, teaching referral hospital in Addis Ababa, Ethiopia because of high grade fever (HGF), severe headache & abnormal body movement (ABM) of 1 month duration. The child was taking unspecified Highly Active Antiretroviral Therapy (HAART) regimen from another government hospital ART clinic and unspecified per os (PO) medicines and herbs ordered from private clinics and traditional herbalists, respectively. She was put on Tenofovir/Lamivudine/Efavirenz (TDF/3TC/EFV) fixed dose combination therapy since 8 months back and has been taking phenytoin 50mg PO BID for the last one and half year. The patient has no known drug allergy (NKDA) or allergic diseases. Brain Computed Tomography (CT) scan was done on 27/02/2017 and revealed the presence of Pyogenic Brain Abscess (PBA) with subfalcine Herniation. Abdominal ultrasound was done on 08/03/2017 and showed Hepatomegaly. Head Magnetic Resonant Imaging (MRI) was done on 09/03/2017 and showed Left Frontoparietal Multiloculated Ring Enhancing Lesion with calcification and extensive vasogenic edema & mass effect more likely a Tuberculosis Brain Abscess (TBA). Chest X-ray (CXR) was done on 09/03/2017 with anteroposterior & left lateral position and revealed Left Upper Lobe Opacity more likely Tuberculosis (TB). Patient's hemoglobin (Hgb), mean corpuscular volume (MCV) and mean corpuscular hemoglobin (MCH) all were below normal on two consecutive measurements indicating that patient was suffering from moderate microcytic anemia. The Erythrocyte sedimentation rate (ESR) was also elevated as indication of non specific chronic inflammatory conditions most probably due to TB. Urinalysis was done on date 06/03/2017 and showed slight elevation in Red Blood Cells (RBCs) and White Blood Cells (WBCs) count and serum electrolyte assessment showed potassium was slightly below normal and chloride was increased and serum pH was slightly high causing metabolic alkalosis. Furthermore, alkaline phosphatase (ALP) was slightly elevated indicating involvement of cranial bone and focal hepatic lesions. Based on the clinical, laboratory and imaging evidences, the final working diagnosis was Stage IV RVI on HAART plus Right Sided Hemiparesis Secondary to TBA and PBA plus Focal Seizure. The gradual worsening of ABM of right lower and upper extremities could be due to lack of appropriate titration of the dose of phenytoin. The Initial dose of phenytoin has to be initiated with 5 mg/kg/day orally in 2 or 3 equally divided doses, with subsequent dosage individualized to a maximum of 300 mg PO daily. The maintenance dose should be 4 to 8 mg/kg and for children over 6 years old and adolescents may require the minimum adult dose (300 mg/day). The major drug therapy problems identified in this case was the prescription of rifampin with dexamethasone or prednisolone. Rifampin has been known to decrease the level or effect of dexamethasone-prednisolone by affecting hepatic/intestinal CYP3A4 enzyme metabolism. Hence, avoiding the use or use of alternative drug was recommended. Based on subjective evidences from the patient, now the patient is feeling better. Imaging modalities and laboratory tests are expected to be repeated and further progress report will be reported in future correspondence as short communication or to the editorial note

Keywords: Stage IV RVI; Right side hemiparesis; TB Brain abscess; Pyogenic brain abscess; Focal seizure

Presentation of Case

A 9-year-old female patient was admitted to pediatric ward of a large, central referral hospital in Addis Ababa, Ethiopia-Tikur Anbessa Specialized Hospital (TASH, where clinical pharmacists affiliated with this hospital works) because of HGF, severe headache & ABM of 1 month duration.

The child was a known HIV infected patient for the last 8 years and has been on HAART for the last 7 years. She was referred from Asella Referral Teaching Hospital (ARTH, a referral & teaching hospital 170 km away from Addis Ababa towards South-East Ethiopia) after presented with ABM of right lower extremity (RLE) since one and half year back & ABM of right upper extremity (RUE) since 8 months back for which Phenytoin 50 mg PO twice a day was initiated.

Her ABM was exacerbated in the last one month and her mother took her to different private clinics and traditional healers where many unrecognized orally administered medications were given. The child was diagnosed as 'Stage IV RVI+Right Side Hemiparesis secondary to Pyogenic Brain Abscess+Focal Seizure' at ARTH. Otherwise the patient had no history of cough at night, sweating or contact with active TB patient, no loss of consciousness with or without ABM, no trauma or fall down accident or urinary retention.

The mother claimed that her child has been adhered to the ART medications. The recent (1 month back) CD4 count was 317/mm³ with unknown baseline CD4 count. Her past medical history (PMH) showed no other documented illness except being a known RVI for 8 years and the ABM of one & half year durations. Her social history showed, she was exclusively on breast feeding (EBF) up to one year and was fully vaccinated according to the Ethiopian Expanded Program for Immunization (EPI) schedule. The child is currently a first grade

student. Her family history revealed that she has one older brother (14 year old, also sero +ve) and her both parents were known RVI patients. Her father died before 7 years where as her mother, a business woman and working on a private shop with a monthly salary of one thousand Ethiopian birr (equivalent to ~42 USD), discovered her RVI status after diagnosed as 'a pulmonary TB & herpes zoster patient' before 11 years where her ART initiated immediately the next year. Her mother had no regular antenatal follow-up care (ANC) for any of her pregnancies and all her deliveries were done traditionally at home. Mother was poorly adhered to her ART medication because of loss of hopelessness and financial constraints to nourish her body.

The child was taking unspecified HAART regimen from governmental ART clinic and unspecified per oral (PO) medicines and herbals ordered from private clinics and traditional herbalists respectively. She was the put on TDF/3TC/EFV fixed dose combination (FDC) therapy since 8 months back and has been taking phenytoin 50 mg PO BID since 1 and half year. The patient had NKDA or allergic disease.

The blood group of the patient was O+ and her anthropometric measurements were height of 116 cm; weight 17 kg; mean upper arm circumference 13 cm; weight for age -3SD and height for age, b/n -2 and -3 SD & weight for height was normal (>70%).

Review of Systems

The overall appearance of the patient was chronically sick looking. Her vital signs (V/S) were Blood Pressure (BP), not measured; Pulse Rate (PR), 143/minute; Respiratory Rate (RR), 40/minute; Temperature, 37.9°C & peripheral capillary oxygen saturation (SpO₂), 96% with atmospheric air.

The child had an ABM of RLE & RUE but no signs of rashes or other changes of the integumentary system. The Head, Eyes, Ears, Nose, Throat (HEENT) findings showed no abnormality on physical findings. Her conjunctiva was pale but non icterus. The ears were hearing well and her nose and sinuses were manifesting occasional coldness but without sinus trouble. Patient had no bleeding or redness of the throat, no lumps, goiter, pain or swollen glands on the neck and breasts and no history of cough, wheezing, shortness of breath (SOB) reported; but chest X-ray findings revealed that patient had Left Upper Lobe Opacity that was mimicking Tuberculosis otherwise chest on auscultation was clear & resonant with good air entry.

Cardiovascular assessment revealed that patient had no known heart disease or high blood pressure; dyspnea or orthopnea, chest pain or palpitations. S1 and S2 were well heard with no murmur or no gallop; abdomen was flat and moves with respiration, no signs of fluid collection. Gastrointestinal findings showed that mild appetite score with one episode of vomiting and indigestion with pain symptoms, otherwise no diarrhea or bleeding; no jaundice, gallbladder or liver problems; but detectable hepatomegaly. Liver was 3.5 cm enlarged Below Right Costal Margin (BRCM). Urinary findings showed no Costo-Vertebral Angle Tenderness (CVAT); no frequency, dysuria, hematuria, or recent flank pain.

Musculoskeletal and peripheral vascular examination showed that patient had mild muscular aching pain but no varicose veins. Neurologic findings revealed no fainting but there was repeated seizure episode, and decreased motor activity but sensory was intact. Power was 3/5 on right side and 5/5 on left side (Table 1). The central nervous

system (CNS) assessment showed patient was conscious and alert with Glasgow Coma Score (GCS) =15/15.

Hematologic data revealed no bleeding but there was moderate anemia. On endocrine and psychiatric findings there was no investigated endocrine trouble; no symptoms or history of diabetes; no history of depression or treatment for psychiatric disorders.

Description	RLE	RUE	LLE	LUE
Power	03-May	04-May	05-May	05-May
Reflex	03-Apr	03-Apr	02-Apr	02-Apr
Tone	NS	NS	NS	NS
Sensory	Intact	Intact	Intact	Intact
NS=normal skin				

Table 1: Motor assessment.

Diagnostic Tools

Imaging modalities

Brain CT scan was done on 27/02/2017 and revealed the presence of Pyogenic Brain Abscess with subfalcine Herniation (Figure 1). Abdominal US was done on 08/03/2017 and showed Hepatomegaly. Head MRI was done on 09/03/2017 and showed Left Frontoparietal Multiloculated Ring Enhancing Lesion with calcification and extensive vasogenic edema & mass effect more likely a Tuberculosis Abscess. CXR was done on 09/03/2017 with AP & left lateral position and revealed Left Upper Lobe Opacity more likely Tuberculosis (Figure 2).

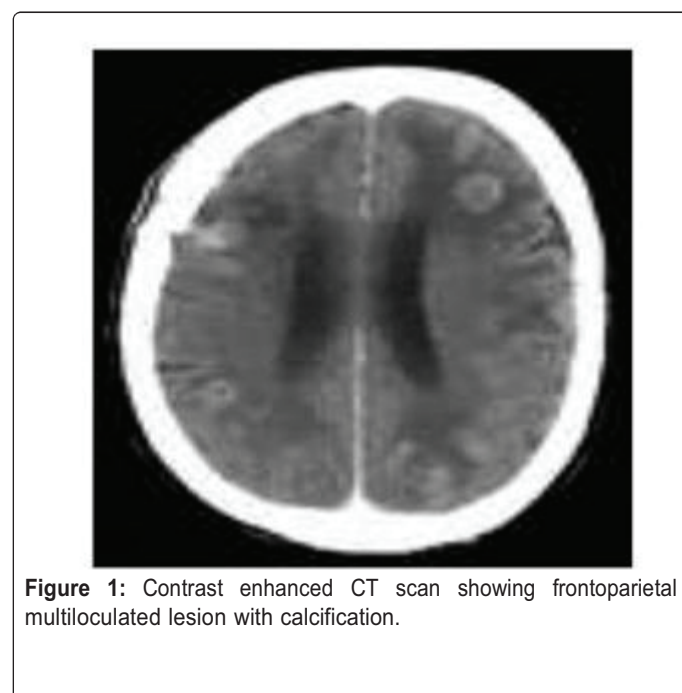


Figure 1: Contrast enhanced CT scan showing frontoparietal multiloculated lesion with calcification.



Figure 2: Frontal CXR: bronchopneumonic opacification and consolidation with cavitations was noted in the left upper lobe. Focal consolidation with cavitations was evident in the right upper zone. Dense nodular opacities were noted in the right lower zone, suggesting calcified granulomas of TB. Aortopulmonary window and right hilar lymphadenopathy was noted, evidence of right lower lobe atelectasis.

Laboratory findings

Data from laboratory investigation (Table 2) revealed that patient's red blood cell count (RBCs) were below normal on date 06/03/2017 but later return to normal on the second investigation done on date 13/03/2017 but patients hemoglobin (hgb), mean corpuscular volume (MCV) and mean corpuscular hemoglobin (MCH) all were below normal on both consecutive date measurement indicating that patient has been suffering moderate microcytic anaemia. The Erythrocyte sedimentation rate (ESR) was also elevated as indication of nonspecific chronic inflammatory conditions most probably due to TB.

Urinalysis was done on date 06/03/2017 and a slight elevation in RBC and WBC count revealed urinary tract infection (UTI) and serum electrolyte assessment showed that potassium was slightly below normal (hypokalemia) and chloride was increased (hyperchloremia). However, serum pH was slightly high causing metabolic alkalosis. Furthermore, alkaline phosphatase (ALP) was slightly elevated indicating involvement of cranial bone and focal hepatic lesions.

Variable	Dates			Reference range, pediatric
	06/03/2017	13/03/2017	15/03/2017	
White blood cell count (X103/mm ³)	8.64	8.48		5.0–14.5*
Differential count (%)	23.5	27.9		15–61.5*
Lymphocytes (%)	68.1	61.2		40–75
Neutrophils (%)				
Hematocrit (%)	26.1	30.0		35–45*
Red Blood Cell count (per mm ³ X 10 ⁶)	3.53	4.04		4.0–5.2*
Hemoglobin (g/dl)	8.7	10.0		11.5–15.5*
Mean corpuscular volume (fl)	73.9	74.3		76.0–90.0*
Mean corpuscular Hemoglobin (µm ³)	24.6	24.8		26.0–30.0*
Platelet count (per mm ³ X 10 ³)	477	503		150–400
Erythrocyte sedimentation rate (mL/min)		100		<20
Urinalysis (U)	Clear			Clear
Appearance	Yellow			Pale Yellow/colorless
Color	5			4–9
PH	1.025			1.001–1.035
Specific gravity	Neg			Neg

Glucose	Neg			Neg
Ketone	Neg			Neg
Protein	6-7			0-4
RBC (per HPF)	4-6			0-4
WBC (per HPF)				
Anti Hep C Virus Ab	negative			negative
HbsAg-	negative			negative
Serum electrolytes		3.36		3.5-5.5
Potassium (mmol/liter)		141.3		136-145
Sodium (mmol/liter)		114.9		95-105
Chloride (mmol/liter)		7.70		7.34-7.46
PH at 37°C				
Liver Function Tests (U/L) †			35	10-53 ¥
Aspartate aminotransferase			30	10-35 ¥
Alanine aminotransferase			480	175-420 ¥
Alkaline phosphatase				
Renal function Tests †				
Urea nitrogen (mg/dL)			14	5-25 (2-15year)
Serum Creatinine (mg/dL)			0.7	0.12-1.06

* = M/F, 7-12 years; ¥ =M/F 7-9 year; (mm3 =µl); HPF=high power field; U/L=international unit per liter
 To convert the values for urea nitrogen to millimoles per liter, multiply by 0.357. To convert the values for creatinine to micromoles per liter, multiply by 88.4.
 † Reference values are affected by many variables, including the patient population and the laboratory methods used.

Table 2: Laboratory data.

Clinical questions

This 9-year-old female RVI infected patient has been on HAART for the last 8 years. She was presented with gradual worsening of ABM of RLE & RUE. The patient received both conventional and traditional remedies. But, she was not getting well. Hence the clinical questions are: what cause the ABM and what exacerbate it? Did the patient receive appropriate therapy? Was there other related problems managed properly? Was there any drug therapy problem?

Differential diagnosis

Although many correlated differential diagnosis (DDX) were assumed to cause ABM; patient's presentation, laboratory and imaging modalities were important to list only some. These are TBA and PBA.

Brain abscess

Development of a brain abscess (BA) requires inoculation of an organism into the brain parenchyma in an area of devitalized brain tissue or in a region with poor microcirculation, and the lesion evolves from an early cerebritis stage to the stage of organization and capsule formation. Immunosuppression due to disease or therapy is emerging as an important risk factor for development of brain abscess [1]. BA has been identified as one of the most challenging lesions, both for surgeons and internists. However, from the beginning of the CT era,

the diagnosis and treatment of these entities have become easier and less invasive [2].

Hematogenous spread from a remote infectious focus was the most common cause of infection [3]. Fungal infections, *Toxoplasma*, *Staphylococcus*, *Streptococcus*, and *Pseudomonas* spp are identified common etiologic agent in immunocompromised patients with HIV infections, organ transplantation, chemotherapy, or steroid use [4].

A lumbar puncture (LP) is contraindicated in patients with a suspected brain abscess because it can result in transtentorial or transforaminal herniation and subsequent death [1]. Moreover, analysis of cerebrospinal (CSF) fluid does not aid in diagnosis of an unruptured brain abscess. A CT scan of the brain obtained after administration of contrast material shows evidence of a ring- enhancing lesion in a well-defined abscess and features of cerebral edema in the stage of cerebritis [1,5,6].

The modern-day BA therapy generally includes a combined surgical and medical approach. The surgical approaches can be aspiration (free hand, stereotactically or neuroendoscopically guided) or total excision [7]. The outcomes of BA treatment have become better with the improvement of diagnostic techniques, neurosurgery, and broad-spectrum antibiotics [2]. The empiric antibiotics of choice are crystalline penicillin, chloramphenicol, and metronidazole, followed by definitive therapy based on the sensitivity pattern of the causative organisms. There is a recent trend toward the use of third-generation cephalosporins and avoidance of chloramphenicol. If staphylococci are suspected, an antistaphylococcal penicillin should be used, with

vancomycin being the alternative in cases of antibiotic resistance or patient intolerance to penicillin [8].

Tuberculosis brain abscess

Among BA, TBA is a rare manifestation of neurotuberculosis. TBA is characterized by an encapsulated collection of pus, containing collection of pus, containing viable tubercular bacilli without evidence of tubercular granuloma [9,10] and it has been solely a manifestation of dormant tuberculosis (TB) reactivation [11]. Patients may present with features of raised intracranial pressure and focal neurological deficit commensurate with the site of the abscess. A history of pulmonary tuberculosis may be presented [9]. Treatment options include simple puncture, continuous drainage, fractional drainage, repeated aspiration through a burr hole, stereotactic aspiration and total excision of the abscess. Total excision usually becomes necessary in multilocular noncommunicating and thick-walled abscesses. Large brain abscesses are usually surgically treated. Antitubercular therapy is the mainstay of management [9,10].

In one study, thalidomide, a potent inhibitor of tumour necrosis factor alpha (TNF-alpha), was added to the TBA treatment regimen and resulted in marked clinical improvement with resolution of the abscess within 4 months [12]. Another study reported that decreasing the load of tuberculous antigen by draining the abscesses and increasing the pulse exposure of isoniazid resulted in clinical improvement [13].

Pyogenic brain abscess

PBA is a fatal infectious disease characterized by complicated management approaches [14]. Multiple PBA constituted 10-20% of a series of consecutive studies done with brain abscess [3,15].

Atypical bacterial abscesses are more common in patients with HIV infection, and immunosuppression [2]. The clinical presentation of PBA is similar to brain abscesses in general and there is no distinct clinical feature suggestive of PBA over BA [15].

Decompression with stereotactically guided aspiration, antibiotic therapy based on results of pus culture, and repeated aspirations if indicated from results of periodic CT follow-up scans seem to be the most appropriate treatment modality for PBA [2]. Surgical treatment options showed no significant difference with respect to mortality levels, but lower morbidity rates were achieved with stereotactically guided aspiration [2]. Hence, antibiotics alone are insufficient and that surgical evacuation of the abscess is essential. The need for local instillation of antibiotics directly into abscesses is questionable since penetration following systemic administration of antibiotics was adequate when blood levels were high [16].

Final working diagnosis

Based on clinical, laboratory and imaging evidences, the final working diagnosis at TASH was Stage IV RVI on HAART plus Right Side Hemiparesis Secondary to TBA plus Focal Seizure.

Current medications

The patient was started ceftriaxone 750 mg IV BID, metronidazole 176 mg IV TID and vancomycin 255mg IV QID for management of pyogenic brain abscess on 06/03/2017. Dexamethasone 2.6 mg IV QID was started for control of neurologic sequelae and phenytoin 50 mg PO BID was continued for seizure control. TDF/3TC/EFV has been continued while rifampin/isoniazid/pyrazinamide/Ethambutol (RHZE, 150/75/400/100) for treatment of TB abscess (Table 3).

Date Started	Date Stopped
06/03/2017	10/03/2017

Indication	Drug dosage & regimen	Date Started	Date Stopped
Pyogenic brain abscess	Ceftriaxone 750 mg IV BID		
	Metronidazole 176 mg IV TID	06/03/2017	10/03/2017
	Vancomycin 255 mg IV BID	06/03/2017	10/03/2017
Control of neurologic sequelae	Dexamethasone 2.6 mg IV QID	06/03/2017	10/03/2017
Seizure control	Phenytoin 50 mg PO BID	continued	
ART for RVI	TDF/3TC/EFV	continued	
TB abscess	RHZ (150/75/400) 4 tabs PO/d + E 100 mg 3 tabs PO/d	09/03/2017	
Peripheral neuritis due to INH (prophylaxis)	Pyridoxine 25 mg PO/d	09/03/2017	
TB abscess	RHZE (150/75/400/275) 2 tabs PO/d	10/03/2017	
TB prophylaxis	INH 100 mg PO/d 1 tab PO/d	10/03/2017	
Pain management	Morphine 20 mg/ml 1 ml PO PRN	10/03/2017	
Constipation	Bisacodyl 5 mg PO/d	10/03/2017	
Control of neurologic sequelae	Prednisolone 30... 35 mg PO/d	10/03/2017	
Toxoplasmosis and PCP prophylaxis	Cotrimoxazole 480 mg PO/d	10/03/2017	
Symptomatic relief of nausea and vomiting	metochlopramide 5 mg IV PRN	10/03/2017	

Table 3: Current medications.

Pharmaceutical care plan (SOAP approach)

The goal of pharmaceutical care (PC) plan is to control the clinical signs and symptoms; prevent further complications; manage and stabilize patient; restore normal activities; prevent long-term complications; modify lifestyle/risk factors and monitor patient improvement. Several studies of children with HIV type 1 infection have demonstrated sustained increases in CD4+ cell count, even when virological failure has occurred after receipt of highly active antiretroviral therapy (HAART). Hence, long-term HAART allowed for restoration of CD4+ cell counts and control of viral loads in HIV-1-infected children. Initiating HAART after severe immunosuppression could have an impact on restoration of the CD4+ cell count [17]. For example, in our case there were no repeated measures of CD4+ cell counts and viral load results that could help us to tell patient improvement. Growth failure has been a common feature of children with HIV-1 infection [18] even though in our case the patient maintains normal weight and height.

First-line ART in children should consist of two nucleoside reverse transcriptase inhibitors (NRTIs) plus a non-nucleoside reverse-transcriptase inhibitor (NNRTI). TDF+3TC (or FTC)+EFV as a fixed-dose combination is recommended as the preferred option to initiate ART (strong recommendation, moderate-quality evidence) [19]. In resource-limited setting, the combination of tenofovir, lamivudine plus efavirenz is the most affordable first line once-daily regimen. Tenofovir disoproxil fumarate (TDF) is approved for children but concerns remain about long-term renal and bone toxicity [20]. The use of efavirenz is not registered for children less than 3 years of age [21]. CYP2B6-G516T polymorphisms significantly affect the clearance and bioavailability of EFV in children. Changes in hepatic enzyme activity by age may need to be considered when evaluating the impact of genetic variants on antiretroviral pharmacokinetics in children [22]. Continuous monitoring of clinical, virologic and immunological parameters to assess treatment failure is mandatory in this patient. Because treatment failure is likely, unless a high level of adherence is achieved. Nonadherence to therapy has been the major impediment to successful treatment of children infected with HIV-1 [23].

TB treatment in children must be individualized and based on susceptibility studies [24]. When TB is diagnosed in patients already receiving ART, TB treatment should be started immediately. There are two issues to consider in such cases: whether ART needs to be modified because of drug–drug interactions or to reduce the potential for overlapping toxicities, and whether the presentation of active TB in a patient on ART constitutes ART failure that requires a change in the ART regimen.

Prophylaxis with isoniazid has an early survival benefit and reduces incidence of tuberculosis in children with HIV. Prophylaxis may offer an effective public health intervention to reduce mortality in such children in settings with a high prevalence of tuberculosis. Extrapulmonary tuberculosis should be managed according to the principles and with the drug regimens outlined for pulmonary tuberculosis, except for children who have miliary tuberculosis, bone/joint tuberculosis, or tuberculosis meningitis who should receive a minimum of 12 months of therapy [24,25].

During TB treatment, isoniazid causes the greatest early reduction in organisms and is considered to be one of the two most important TB drugs, along with rifampin [26]. However, its prophylaxis use has to be stopped to decrease the incidence of liver toxicities due to overlap of medications and increased dose of INH.

Hemiplegia is a physical impairment that can occur in childhood following head trauma, cerebral vascular accident or transient ischemic attack (stroke), brain tumor, or congenital or perinatal injury [27]. Forced use, or constraint-induced, movement therapy has shown some efficacy in the rehabilitation of adults with chronic hemiparesis as a result of stroke (Table 4). Some studies have tried their effect in children and forced use therapy can be an effective rehabilitation technique in children with chronic hemiparesis (Table 5) [28,29].

Phenytoin initial dose 5 mg/kg/dose in 2-3 divided doses; maintenance dose is 4-8 mg/kg and for children 6 years and above may require taking the minimum adult dose of 300 mg/day.

Sr.#	Problems	Subjective data	Objective data	Assessment	Plan*
1	Retroviral infection	HGF, Pain,	CD4 count	Stage IV RVI	Plan1
2	Tuberculosis	NK	Chest X-ray (CXR)	Pulmonary TB	Plan2
3	Hemiparesis	Weakness of Right upper & lower limb, difficulty of urination	Poor motor reflexes	Right side hemiparesis	Plan3
4	TB Abscess	Severe headache	Head MRI	TB Abscess	Plan4
5	Pyogenic Brain Abscess	NK, headache	Brain CT scans	Pyogenic Brain Abscess	Plan5
6	Seizure	Headache, ABM,	CT Scan, MRI	Focal Seizure	Plan6

7	Hepatomegaly	pain at URQ of the abdomen	Liver was 3.5 cm enlarged BRCM, Abdominal ultrasound (US)	Hepatomegaly	Plan7
8	Pain	Patient was complaining of pain	NK, VAS	8	Plan8

NK: Not known

Plan* 1: Continue the current treatment (TDF/3TC/EFV). In our case, the mother is poorly adhered to her medication that could also affect the adherence of her child to the medications. Careful monitoring for treatment failure, side effects, drug interactions and drug resistance should also be undertaken.

Plan* 2: Continue TB treatment (RZHE-150/75/400/275) 1tab po hs but discontinue the INH use for prophylaxis until TB treatment is completed.

Plan* 3: Forced use rehabilitation therapy should be provided

Plan* 4: Antibiotics alone are insufficient and that surgical evacuation of the abscess is essential.

Plan* 5: Antibiotics alone are insufficient and that surgical evacuation of the abscess is essential.

Plan* 6: Escalate the dose of phenytoin. Currently the child is taking 50 mg bid. It can be escalated up to 150 mg bid with slow titration

Plan* 7: Monitor liver functions tests

Plan* 8: pain management has to be modified as per the WHO pain treatment ladder

Table 4: Pharmaceutical care plan (SOAP approach).

Drug therapy problems

Drug-related needs	Categories of DTPs	Remark
Indication	Additional drug therapy	Moderate anemia? Hypokalemia? hyperchloremia
Effectiveness	Dosage too low	Phenytoin 50 mg PO BID...ABM occasionally Steroid conversion?
Safety	Dosage too high	Potential INH toxicity..... Hepatitis or Rash Pyrazinamide (47 mg/kg)... Hepatitis or Rash Ethambutol (32.4 mg/kg)... Hepatitis or Rash

Table 5: Actual or potential drug therapy problems.

Therapeutic alternatives

Therapeutic alternatives are needed for cases that the patient is not yet responding to the first line medications, or adverse reactions and drug resistance are occurring, or in case if the medication is not available in the market or other similar issues are noted [29]. Base on this we have noted some of therapeutic alternative as follows:-

Management of raised intra cranial pressure (ICP): Since vasogenic edema can be resulting from alteration in either the permeability of vasculature vessels and consequently fluid formation, which can be easily treated with steroids & osmotic agents [30]. Hence we can keep this medication as alternative. Dexamethasone 0.15 mg/kg/dose Q 6 hrs. Mannitol: 0.25-1.50 g/kg/dose (not mg) Q 1-4 hrs. Acetazolamide 10-25 mg/kg/d and Furosemide 1 mg/kg/d.

Pain management: Morphine 0.05 mg/kg IM, IV, or subcutaneously every 4 to 8 hours titrating carefully to effect [31] or fentanyl for moderate to severe chronic pain as a transdermal patch. Opioid-tolerant children greater than or equal to 2 years receiving at least 60 mg oral morphine equivalents per day: Initial dose 25 mcg/hour system or higher, based on conversion to fentanyl equivalents and administration of equianalgesic dosage [32].

Seizure control treatment: Carbamazepine initial dose, 100 mg orally 2 times a day (immediate or extended release tablets) or 50 mg orally 4 times a day (suspension). Increase dose at weekly intervals in 100 mg per day increments using a 2 times a day regimen of extended release or a 3 times a day or 4 times a day regimen of the other formulations. Maintenance dose: 400 to 800 mg per day. Maximum dose: 1000 mg per day [33]. Valproic acid for complex partial seizures, initial dose: 10 to 15 mg/kg orally or intravenously per day as an IV infusion in divided doses, increased by 5 to 10 mg/kg per week if necessary according to clinical response. Maintenance dose: 10 to 60 mg/kg per day in divided doses. Maximum dose: 60 mg/kg per day [34].

Management of TB/HIV co-infections: AZT/3TC/ABC and AZT/3TC/EFV can be alternative combinations but the patient has to be cured from the current moderate anemia before initiating AZT.

Drug-drug interactions

Two serious drug interactions requiring alternative therapy, 29 moderate-requiring close monitoring and 19 minor drug interactions were identified using MedScape multiple drug interaction checker [35].

Serious→use alternative

Rifampin+dexamethasone: rifampin will decrease the level or effect of dexamethasone by affecting hepatic/intestinal enzyme CYP3A4 metabolism. Avoid or Use Alternate Drug.

Rifampin+prednisolone: rifampin will decrease the level or effect of prednisolone by affecting hepatic/intestinal enzyme CYP3A4 metabolism. Avoid or Use Alternate Drug.

Discussion and critique of current treatment

The gradual worsening of ABM of RLE & RUE could be due to lack of appropriate titration of the dose of phenytoin. The Initial dose of phenytoin has to be initiated with 5 mg/kg/day orally in 2 or 3 equally divided doses, with subsequent dosage individualized to a maximum of 300 mg orally daily. The Maintenance dose should be 4 to 8 mg/kg and for children over 6 years old and adolescents may require the minimum adult dose (300 mg/day) [36]. In fact the brain abscess could also precipitate the seizure or my aggravate it more [37]. In this regard decompression with stereotactically guided aspiration and antibiotic therapy (both for TBA and PBA) based on results of pus culture and sensitivity is mandatory [2].

The patient received both conventional and tradition remedies that may still harm current medication if the patient relatives do not receive appropriate health education on use and impact of nonconventional therapies. Several unconventional therapies may constitute a risk to the health of children and adolescents [38].

The major drug therapy problems identified in this case are the prescription of rifampin with dexamethasone or prednisolone. Rifampin has been known to decrease the level or effect of dexamethasone/prednisolone by affecting hepatic/intestinal enzyme CYP3A4 metabolism. Hence, avoiding the use or use of alternative drug is recommended [35].

The anemia in our case was not properly addressed. The patient developed microcytic (decreased MCV), hypochromic (decreased MCH) anemia. Where in both cases iron deficiency could be the cause. Iron store and iron binding capacity was not done because of lack of availability of the tests in the setup. Hence, the clinical pharmacists recommended the provision of iron and monitor the increment in reticulocytes after one to two weeks and if an increment in one to two unit serum hgb is measured continue the treatment if not reevaluate the patient conditions. Some studies already confirmed that iron status is an important cause of anemia in HIV-infected patients [39].

A low serum potassium concentration is perhaps the most common electrolyte abnormality encountered in clinical practice. In our case the patient serum potassium was already decreased (hypokalemia) and she was needed to receive potassium rich diet and/or potassium supplements. Furthermore, she was in state of metabolic alkalosis and her serum chloride was decreased. This means the patient had excess of sodium in the serum to shift the anion-gap to more basic. The use of potassium sparing diuretics in this regard may benefit the patient to retain the loss of potassium and equilibrate the anion gap [40].

Three of the four anti TB medication (RHZ) are hepatotoxic. Hence the patient demanding more aggressive hepatic function tests [41]. In our case the patients is receiving INH for both prophylaxis and active

infection treatment, that is receiving the maximum 300 mg from the four tables for the treatment and additional 100 mg for prophylaxis. The CDC recommendations of INH dosage for active TB 10 is 15 mg/kg/day once daily (maximum dose: 300 mg/day) or 20 to 30 mg/kg/dose (maximum dose: 900 mg/day) 2 times weekly as part of a multidrug regimen [42].

Pain management is another unaddressed problem for the patient. We used visual analog pain score (VAS) that is identified working better to assess pain in children. Based on VAS the patient was categorized as having severe pain. The patient was receiving oral morphine syrup. When we compare the oral to IV opioid the potency of IV morphine is 6X more potent that the oral route of major hepatic first pass metabolism. Furthermore the frequency of administration was set as PRN where scheduled therapy is better in controlling severe intermittent pain using opioids as in our case. The 1986 WHO pain ladder (targeting specifically severe pain) has been a reference for a long time and suggested to step up from a non opioid to a "weak" opioid if the pain was not relieved and then only to a strong one if once again the pain control was not satisfactory. Nowadays, however, due to the usual high level of pain presented by palliative patients, and based on our deeper understanding of the pathophysiological mechanisms of pain as well as on the increased amount of new therapeutic formulations, we tend not to use "weak" opioids anymore [43].

Progress report

Subjective and objective evidences revealed that patient has improved a lot since after admission. Further Imaging modalities and laboratory tests are needed to continually monitor patient progress.

Patient education points

Patient education points were focused on the adherences issues; possible ADR and S/Es; the use of conventional medicine; the use of better dietary supplement to nourish the child; issues of schooling (since the child is 9 years and only grade one); on future appointment date and how to use medication properly.

Competing Interests

The authors declare that they have no competing interests.

Authors' Contributions

MT discovered the case, managed the case, and prepared the draft. MA designed the write-up; coordinated, collected the necessary information and rewrote the final manuscript; BA managed the case and reviewed the final manuscript. All authors read and approved the final manuscript.

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