BAFFLED THOUGHTS
CRYPTIC CLUES

DR.S.PREMKUMAR
SOUTHERN RAILWAY HQ HOSPITAL

- 12 year old male, 2nd born of 3rd degree CM referred from Thiruvallur with
- C/O fever - 10 days
- C/O vomiting for last 7 days
- C/O headache for 5 days
- C/O ALOC for past 10 hrs.

- H/O dog bite 4 years back, cat III dog bite not received ARV.
- H/O purulent ear discharge from Right ear present on and off for the past 3 years.
- No h/o seizures.
- No h/o head injury.
- No h/o skin rash.
- No h/o recent travel.
- No h/o contact with TB.

- He had received 3 doses of iv Ceftriaxone and iv fluids.
- Immunised as per NIP. Not received special vaccine.
- Developmentally normal child .Studying 7th Std, with good scholastic performance.

General examination

- Irritable
- GCS – 11/15.
- Eye opening - spontaneous (4).
- Verbal response – inappropriate(3).
- Motor response – withdraws to pain(4).

- PERL +

Vitals

- PR - 55/min.
- RR - 28/min,regular
- BP - 100/70 mm Hg
- +++/++
- CRT- <2 sec
- Spo2-100% in room air.
- CBG – 114 mg /dl.
- Temp: 98.3*F.

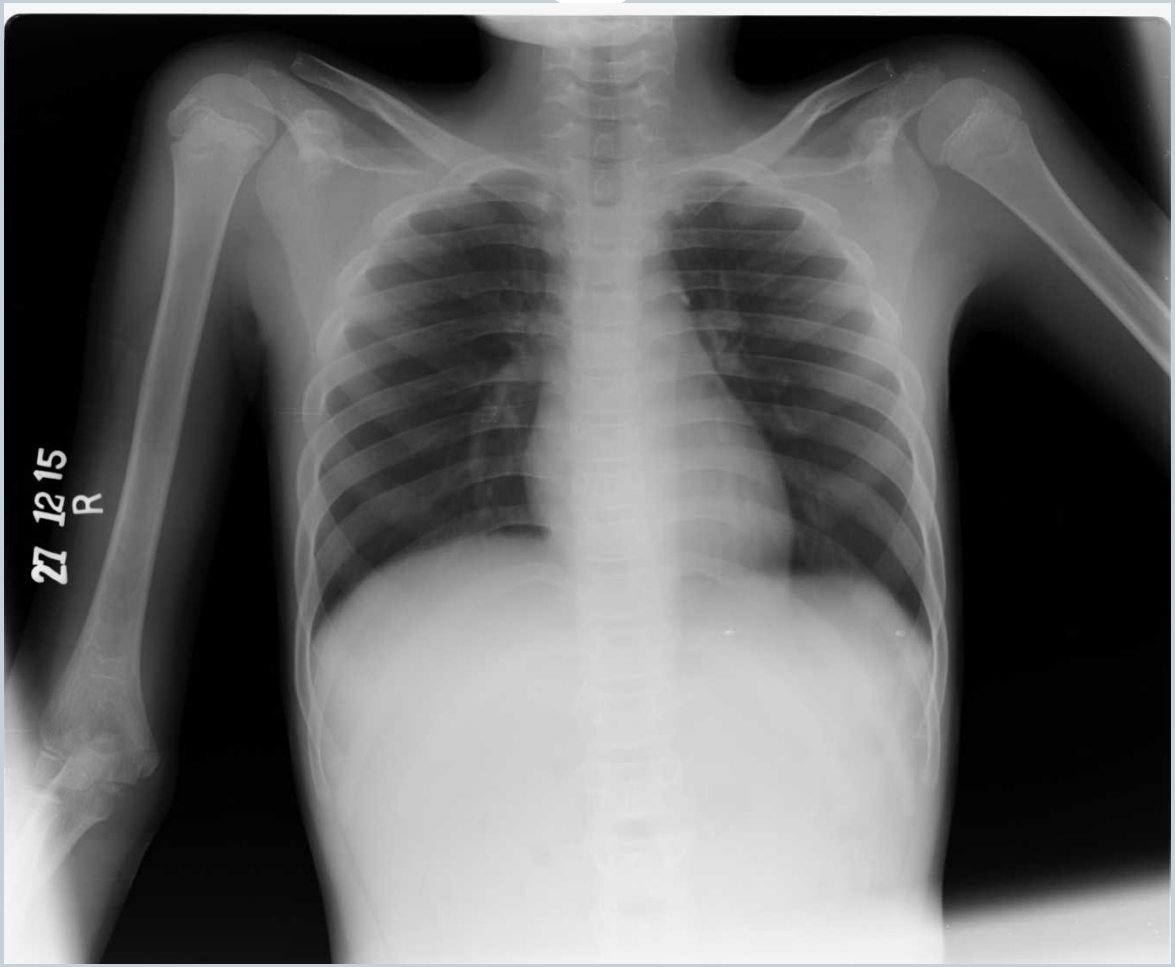
- Afebrile, hydration good.
- Spontaneous resp. effort good.
- No PICCLE.
- ENT: Right ear : Perforation in antero-inferior quadrant with purulent discharge.
- S/E:
- CVS:S1S2 +
- R/S:NVBS.
- P/A: Soft, no organomegaly.

- CNS: GCS:11/15
- Cranial nerves :normal. Fundus-normal.
- Bulk and tone are normal.
- Superficial and DTR – normal.
- Power in both UL & LL – 4+/5.
- B/L plantar withdrawal.
- Neck stiffness present
- Kernigs and brudzinski’s sign positive

Investigations done

- CBC-TC-18,900
- DC- N88%, L5%,M-6%
- ESR- 5mm/hr
- CRP- 0.57 mg/dl
- LFT –normal.
- RFT-normal.
- S.electrolytes:Sodium-129,Potassium-3.7, Chloride-94.
- USG abdomen- Normal study.

Chest xray



COURSE IN THE HOSPITAL

Anti edema measures.

Anti inflammatory measures.

Child was empirically started on Inj.ceftriaxone , Inj. Vancomycin, Inj.Acyclovir.

After initial stabilisation his sensorium improved shifted for CT .

CT Brain plain and contrast was normal.

Proceeded with CSF analysis.

- Colour – turbid,
- Total cells -70
- PMN-30%,L 70%
- Glucose-45mg/dl(Blood glucose-139mg/dl)- 32%
- Protein- 173mg/dl.
- LDH- 52U/L
- Cl-112mMol/L
- Gram stain- no organism seen ,Ziehl Neelsen –No AFB, KOH mount- no fungal hyphae,
- Bacterial c/s and fungal c/s- no growth.

- CSF ADA- 9 U/L.
- Gene Xpert (CBNAAT)- negative.
- CSF PCR Rabies, JE, Entero virus - negative

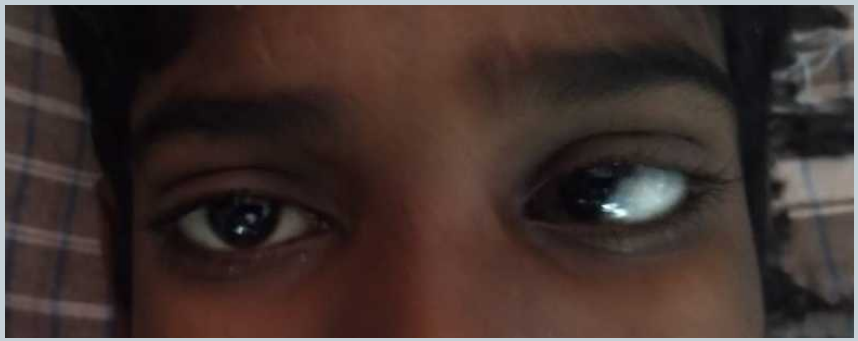
- Serum HSV1 &2 Ig M & Ig G – Negative.
- Blood c/s- no growth.
- MP card test /PS – negative.
- Mantoux 0.1ml /5 TU – negative.
- HIV- negative.
- Serum Coxsackie Ig G – Positive
- Ear discharge c/s- Aspergillus flavus.

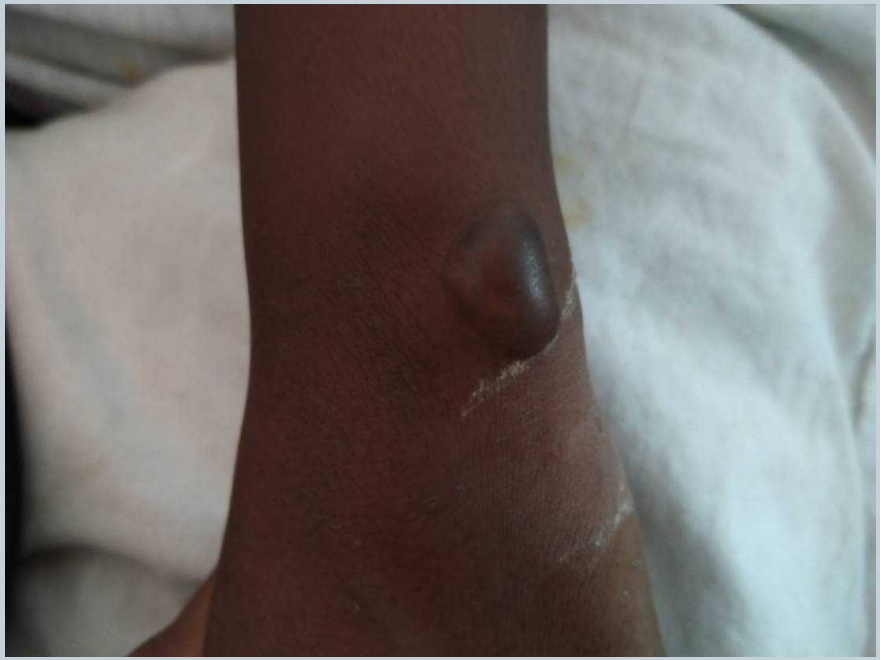
Day-1	Day-2	Day-3	Day-4	Day-5
123	126	128	128	132

Day-6	Day-7	Day-8	Day-9	Day-10
132	136	133	137	

Serum osmolality – 268mosm/kg (<280mOsm/kg)
Urine osmolality - 678 mosm/kg(>100mosm/kg)
Urine Na – 68 meq/l (>30 mEq/l).

- ON 5th day of admission he developed B/L 6th cranial nerve palsy and Right LMN 7th nerve palsy.

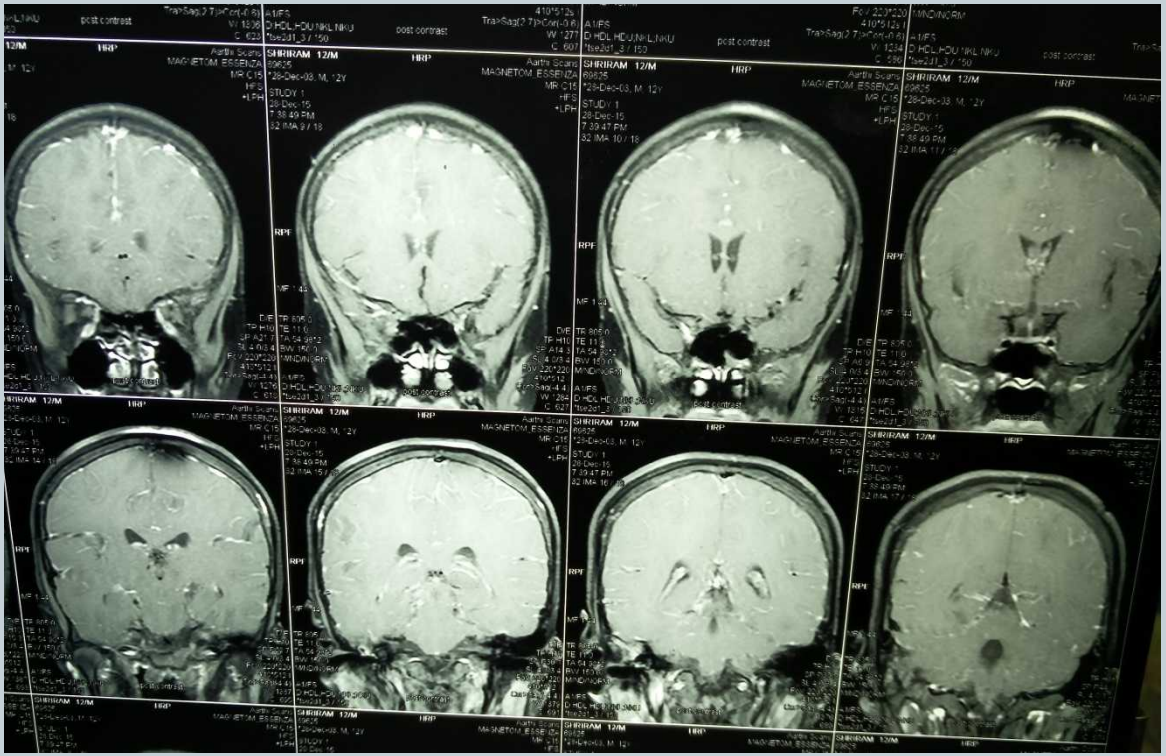




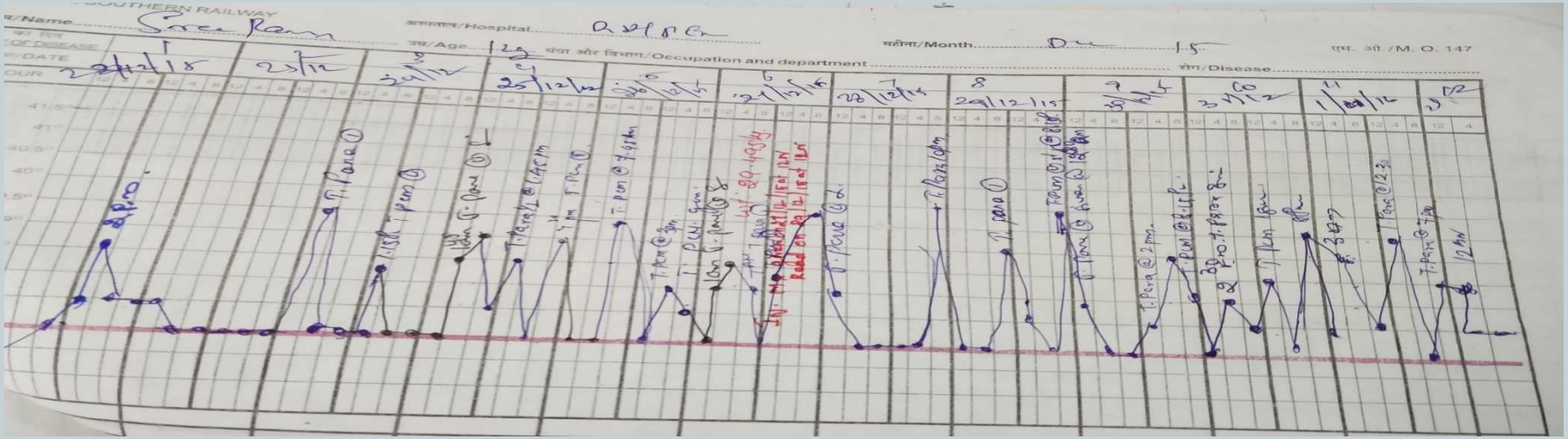
Armingaud P, Arsac P, Kerdraon R, Esteve E. Localized bullous eruption after intravenous injection of aciclovir: Toxic or immunoallergic mechanism. Ann Dermatol Venereol. 2000;127:496–498

MRI brain

- Diffuse abnormal leptomeningeal enhancement in B/L fronto temporal and parieto-occipital lobes.



FEVER CHART



Repeat LP

- CSF colour – turbid
- Cells-600 cells
- DC- PMN95%, L 4%.
- Glucose- 53mg/dl(Blood glucose- 154mg/dl)-34%
- Protein- 64mg/dl.
- LDH- 65U/L
- Chloride- 110mMol/L(116-127mMol/L)

- Gene Xpert- MTB detected.
- S.ADA- 43U/L (upto 18)
- CSF ADA- 11 U/L.(cut off 11.3 U/L)
- CSF c/s for AFB – no growth.
- Latex agglutination – Negative.

Test Report

Patient ID: SHREE RAM
Sample ID: RX5113
Test Type: Specimen
Sample Type: CSF

Assay Information

Assay	Assay Version	Assay Type
Xpert MTB-RIF Assay G4	5	In Vitro Diagnostic

Test Result: MTB DETECTED VERY LOW;
Rif Resistance NOT DETECTED

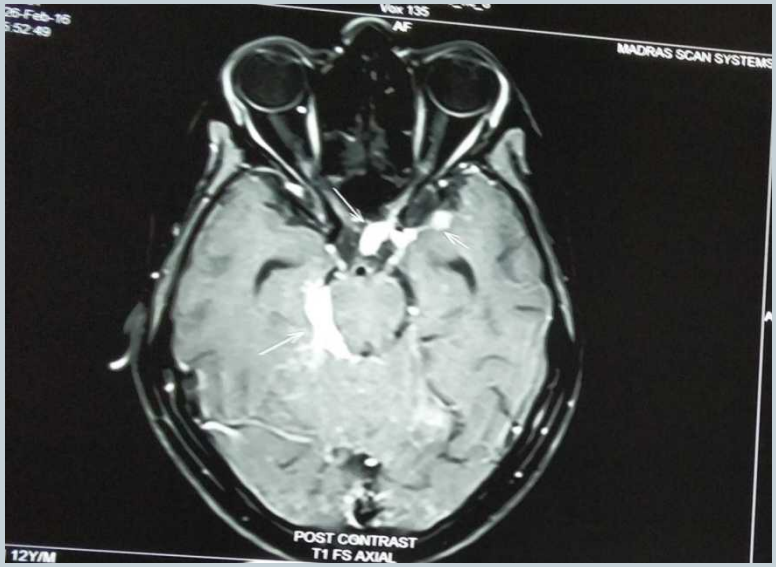
Test and Analyte Result

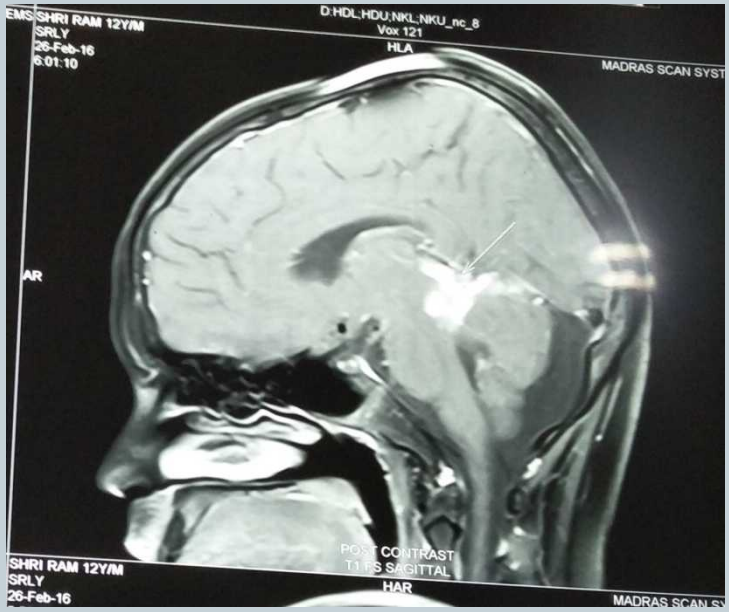
Analyte Name	Ct	EndPt	Analyte Result	Probe Check Result
Probe D	29.3	144.0	POS	PASS
Probe C	28.4	171.0	POS	PASS
Probe E	30.1	116.0	POS	PASS
Probe B	28.8	123.0	POS	PASS
SPC	24.4	214.0	NA	PASS
Probe A	28.2	110.0	POS	PASS
QC-1	0.0	0.0	NEG	PASS
QC-2	0.0	0.0	NEG	PASS

User: NIRT Chennai
Status: Done
Expiration Date*: 11/06/17
S/W Version: 4.4a
Cartridge S/N*: 247208236
Reagent Lot ID*: 31204
Start Time: 14/01/16 15:04:36
End Time: 14/01/16 16:47:26
Instrument S/N: 804977
Module S/N: 645444
Module Name: A2

Treatment

- He was started on ATT category 1 regimen along with Tab.Prednisolone.
- Over the next few days he became afebrile and he symptomatically improved.
- Neck stiffness, diplopia and headache improved subsequently.





Right side of ambient & quadrigeminal cisterns appear to be obliterated with irregular diffuse Hyperintensities extending upto right thalamus. Edema seen extending into the pontine region

ENHANCING LEPTO-MENINGITIS WITH ACTIVE EDEMA

DISCUSSION

- Tuberculosis continuous to be a significant challenge to the public health and policy makers.
- Paediatric TB poses unique challenges different from adult diseases.
- GeneXpert MTB/RIF assay is the rapid molecular method to detect MTB as well as rpoB mutation conferring rifampicin resistance .
- Line Probe Assays are emerging to identify specific type of rifampicin resistance.

Gene Xpert MTB/RIF

- Molecular beacons target rpoB gene that covers mutation in >99.5% of RIF resistant isolates.
- -Sensitivity in gastric aspirate- 74%
- Specificity- 98%
- Good in Extrapulmonary specimens
- Now recommended by WHO as a preferred diagnostic test in children

Xpert MTB/RIF: The first automated diagnostic test for TB (photo: Foundation for Innovative New Diagnostics)

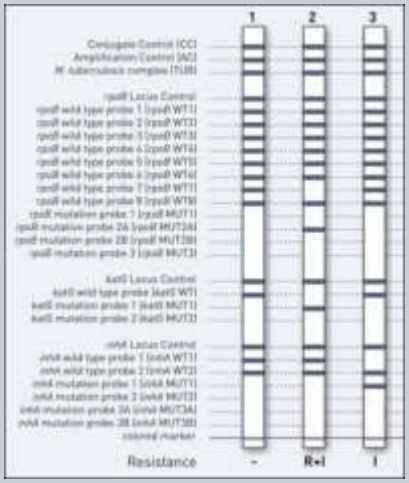
Additional gain versus smear microscopy

Type of specimens	Specimens treated	Xpert positive	%	Smear positive	%	Additional gain(fold)
Sputum	4255	258	6.2%	127	3.1%	2.0
Gastric lavage	2595	170	6.6%	40	1.5%	4.3
CSF	561	46	8.2%	2	0.4%	23.0
BAL	210	31	14.8%	3	1.4%	10.3
Pleural fluid	195	5	2.6%	4	2.1%	1.3
Pus	72	28	38.9%	6	8.3%	4.7
FNAC	70	32	45.7%	4	5.7%	8.0
Ascitic fluid	45	0	0.0	0	0.0	0.0
Others	55	12	21.8%	4	7.3%	3.0
Total	7958	582	7.3%	130	2.4%	3.1

Patel VB, Theron G, Lenders L, Matinyena B, Connolly C, Singh R, et al. (2013) Diagnostic Accuracy of Quantitative PCR (Xpert MTB/RIF) for Tuberculous Meningitis in a High Burden Setting: A Prospective Study. PLoS Med 10(10): e1001536. doi:10.1371/journal.pmed.1001536

Line Probe Assays for MTB Drug Susceptibility Testing

- Geno type MTBDRplus
- DNA or RNA amplified and hybridized onto nitrocellulose strip for detection of MTB resistant mutations.
- Identifies most common INH(inhA & katG:92-99% sensitivity) or RIF (rpoB:96-100%)
- Directly from clinical samples in 2-4 hours.
- 2nd line testing also available now.



WHO Recommendation

- Xpert MTB/RIF may be used rather than conventional microscopy and culture as the initial test in all children suspected of having TB.
- In young children Tb is usally paucibacillary disease, meaning that culture is much more likely than microscopy to yield a positive diagnosis.
- In addition, culture differentiates MTB from other non tuberculous mycobacteria and allows drug susceptibility testing.
- For CSF specimens, Gene Xpert should be preferentially used over culture if the sample volume is low or additional specimens cannot be obtained, in order to reach quick diagnosis

- High index of suspicion- extra pulmonary TB→

Gene xpert test negative → subsequent diagnostic testing negative →suspicion persists →Initiation of treatment.

Automated real-time nucleic acid amplification technology for rapid and simultaneous detection of tuberculosis and rifampicin resistance: Xpert MTB/RIF system for the diagnosis of pulmonary and extrapulmonary TB in adults and children. Policy Update. Geneva, World Health Organization, 2013.

Take home message

- Every effort must be made to confirm the diagnosis in children suspected to have tuberculosis.
- Therapy must not be started on an emperical or trial basis.
- Confirmation of diagnosis requires efforts to isolate / identify Mycobacteria from biological specimens examined on multiple occasions.
- Drug resistant Mycobacteria are emerging as a significant public health problem.
- Gene Xpert is emerging as a powerful molecular tool diagnosing TB and determine rifampicin resistance but should not be used indiscriminately.

THANK YOU