LONG STORY OF A SHORT GIRL

Dr.Kiran Kumar, DNB PG

Dr.Janani Sankar's Unit

Kanchi Kamakoti CHILDS Trust Hospital

CASE HISTORY:

- 1st born, 3rd degree consanguineous parents
- Uneventful antenatal & neonatal period
- Developmentally normal
- Well till 15months of life

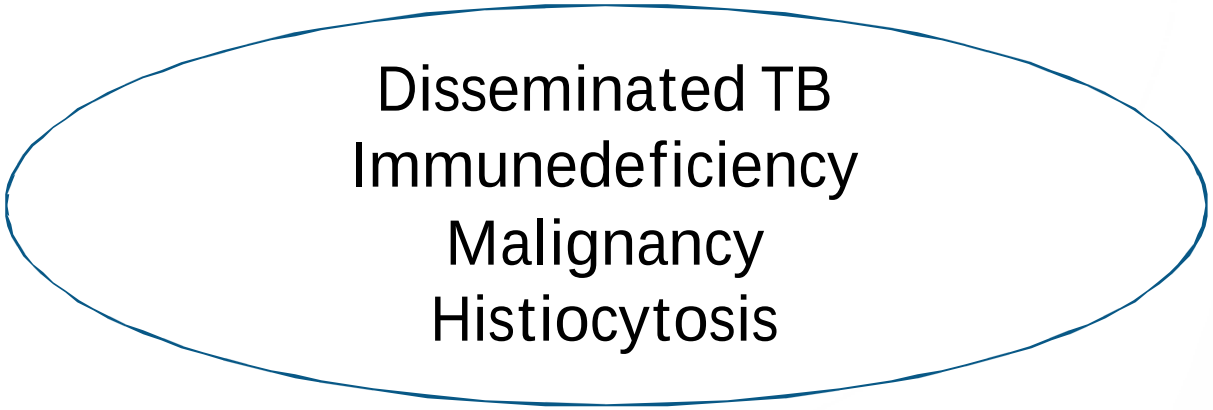
- Younger sibling – died at 20days of life ?ALF

February 2004

- 2 ½ yrs of age
- Evaluated for Recurrent fever

Hepatosplenomegaly

Anemia requiring transfusion



TC – 14000, Hb – 9 Plat – 3lakhs ESR – 90mm/hr Mantoux – 10mm CXR – opacified minor fissure HIV ELISA – non reactive Ig profile – high IgG Flow cytometry - N Bone marrow – reactive Liver Biopsy – granuloma	Started on Empirical ATT

Persisting symptoms

- Recurrent fever, high inflammatory markers, hypergammaglobulinemia, Normal T & B cell markers
- Recurrent lower respiratory infections – requiring antibiotics
- Hepatosplenomegaly

"NBT – moderate impairment"

"PROBABLE CHRONIC GRANULOMATOUS DISEASE"

Itraconazole & cotrimoxazole prophylaxis

Recurrent infections

October 2005	Pneumonia
January 2007	Posterior mediastinal mass
January 2008	Left lower lobe pneumonia with effusion
February 2008	Left paraspinal abscess
June 2008	Granulomatous spondylitis with epidural abscess
October 2009	Suppurative cervical adenitis/abscess
November 2009	Left preauricular abscess
August 2010	Interscapular abscess
February 2012	Pneumonia
August 2015	Intracranial granuloma

January 2007

- Presented with Fever, Respiratory distress
- Chest x-ray & CT chest – posterior mediastinal mass
- Thoracotomy – mediastinal node; HPE showed granuloma
- Given ATT

June 2008

- Presented with back pain
- Tender Right paraspinal swelling
- X-ray DL spine – wedge compression of D12
- MRI spine - Granulomatous spondylosis-D12

  - Epidural soft tissue lesion D11-L1

  - Cord compression

Costotransversectomy of D11-12 & drainage of epidural abscess – ASPERGILLUS isolated

Treated with Amphotericin B, followed by oral voriconazole

Kyphoscoliosis/gibbus

Parents deferred reconstructive surgery

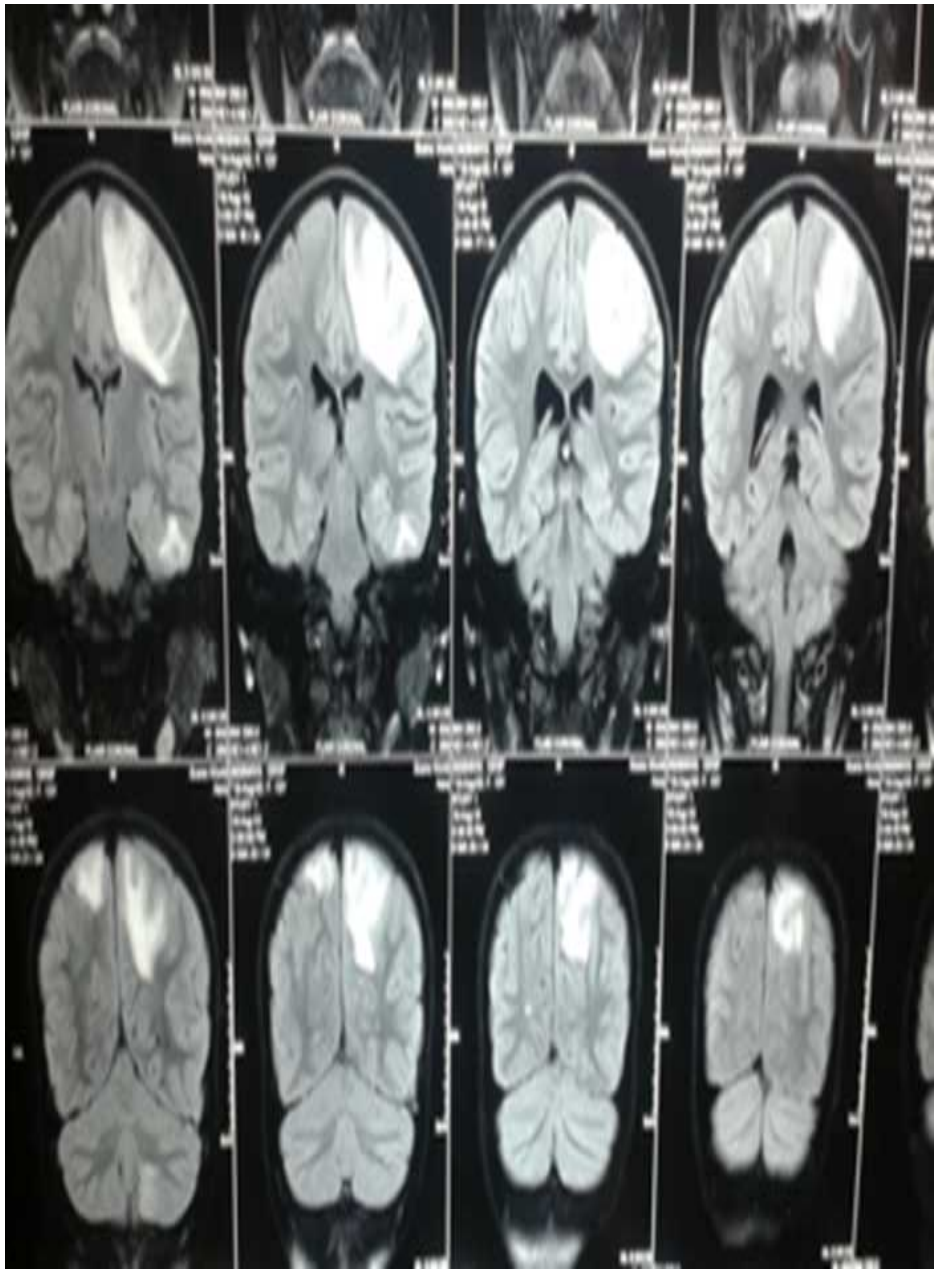
WBC Subpopulation	NBT % positive	Normal Range
Neutrophils	0%	95 – 100%

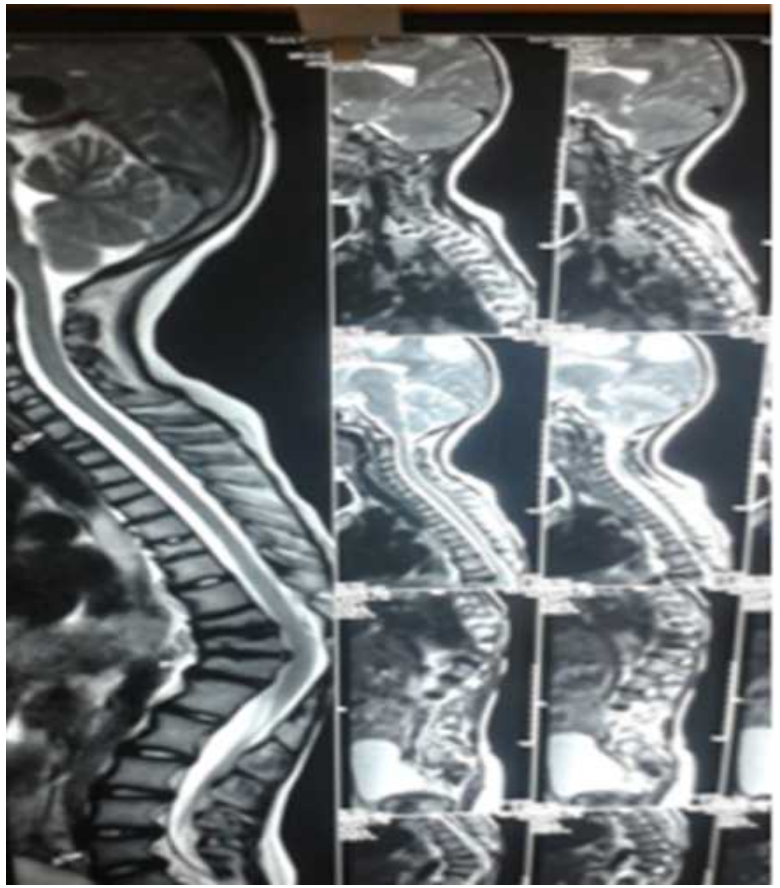
WBC Subpopulation	DHR % positive	Normal Range
Neutrophils	0%	95 – 100%

Comments: Abnormal NBT and DHR values observed. Suggestive of Chronic Granulomatous Disease (CGD).

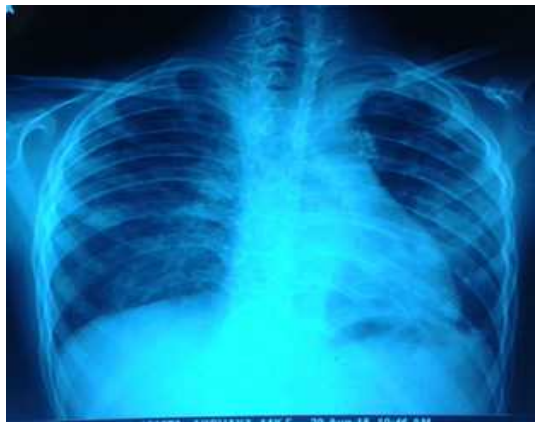
Recent admission – August 2015

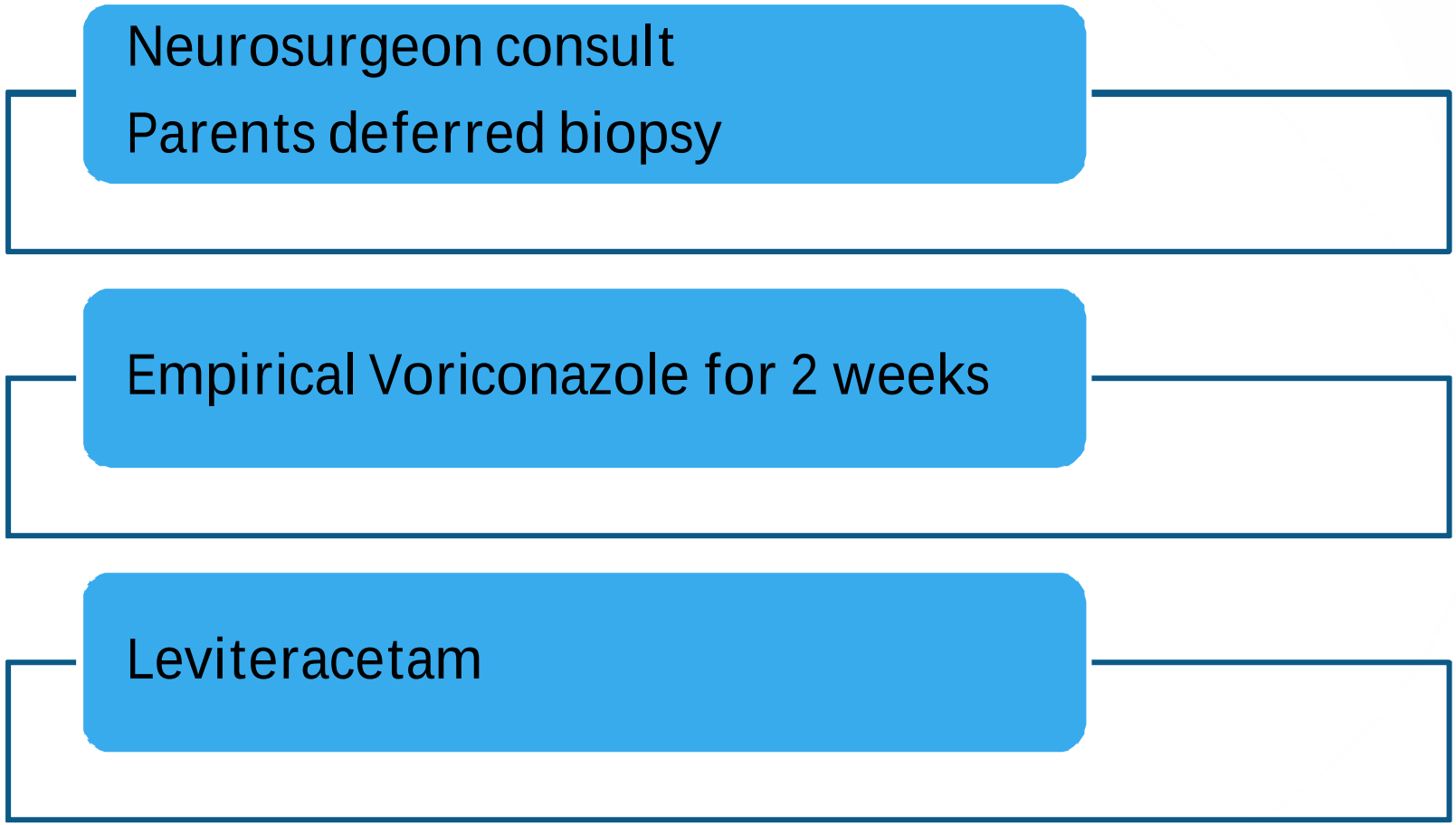
- Presented with Right upper limb weakness & partial seizures
- Headache & vomiting+
- Right monoparesis (distal weakness>proximal)
- Fundus – normal





TC – 11900 Hb – 9 Platelet – 5.3lakhs	USG Abdomen – HSM
CRP – 85.1mg/L	Serum galactomannan antigen – negative
ESR – 111 mm/hr	




Neurosurgeon consult
Parents deferred biopsy
Empirical Voriconazole for 2 weeks
Leviteracetam

CGD – DIAGNOSTIC APPROACH

Clinical information

1. Severe, recurrent pulmonary and hepatic infections including abscess formation
2. Specific etiologic pathogens such as B. cepacia, Nocardia, Aspergillus etc
3. Granulomatous lesions of the GI tract or the GU system

Laboratory abnormalities

1. Anemia
2. Polyclonal hypergiobulinemia
3. Elevated acute phase reactants such as ESR or CRP
4. Normal studies of T and B lymphocyte immunity

Diagnostic test

1. NBT test (no longer used)
2. DHR

Molecular tests

1. Immunoblotting or flow cytometry
2. Molecular techniques including gene sequencing and mutational analyses for subtype

TREATMENT OPTIONS

Prophylaxis of Infection	
Antibacterial therapy	Trimethoprim-sulfamethoxazole (TMP-SMX) 5 mg/kg/day (based upon the TMP component, maximum dose 320 mg P.O in two divided daily doses) [187]
Antifungal therapy	Itraconazole 5 mg/kg [85] (maximum dose 200 mg orally daily)
Immunomodulatory therapy	Interferon-gamma (IFN-γ) [85,137] 50 μg/m^2 (subcutaneous) three times a week 1.5 μg/Kg (subcutaneous) three times a week for children <0.5 m^2

Management of Infection	
Empirical treatment	TMP-SMX/Fluoroquinolone/Antifungal (Voriconazole) • *Burkholderia, Serratia* species: TMP-SMX • *Nocardia* species: TMP-SMX and/or Cabapenem • *Staphylococcaus aureus*:TMP-SMX or Vancomycin • Fungal infection: Antifungal agent ±Steroid
Liver abscess	Surgical excision [111]; IFN γ [108,120]
Granulocyte Transfusion	Unirradiated white blood cells [183,184]
Definitive treatment	
Stem cell transplant	HLA identical sibling umbilical cord stem cell transplantation (UCSCT) after myeloablative conditioning (Stem cell transplantation from a HLA-identical donor may, at present, be the only proven curative approach to CGD) [185-187]
Gene therapy	Still experimental [188-192]

Review of Literature:

REVIEW

Central nervous system aspergillosis in children: a systematic review of reported cases☆

John Dotis, Elias Iosifidis, Emmanuel Roilides*

Third Department of Pediatrics, Aristotle University, Hippokration Hospital, Konstantinoupolecs 49, GR 54642 Thessaloniki, Greece


THANK YOU
for listening!