From: "ROOT" <root@sctimst.ac.in>
To: "ROOT" <root@sctimst.ac.in>
Date: 12/02/2025 08:24 AM
Subject: CPC Clinical Protocol 12.02.2025

Dear All,
The next Wednesday CPC of the session will be held tomorrow, **February 12, 2025** at **08.00 hours** (IST) in **Lecture Theatre 1**, Nehru Hospital, PGIMER, Chandigarh.

The session will also be available on the Webex platform. Kindly follow the link below to join.

https://pgitelemed.webex.com/pgitelemed/j.php?MTID=md00288711fdbf94321a0819943e426a2

In case you join in thru WebEx, kindly **ensure that your microphone and camera are switched off** and **PLEASE DO NOT SHARE YOUR SCREEN**.

The Clinical handout of the case to be discussed is attached herewith.
The clinical protocol will be discussed by ***Dr. Sanjay Verma, Department of Pediatrics.*** Radiology will be discussed by ***Dr. Chirag Ahuja.*** Autopsy pathology will be presented by ***Dr. Amanjit Bal.***

Yours sincerely,

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Regional Resource Centre, North
Department of Telemedicine
PGIMER, Chandigarh

STAFF CPC (12.02.25)

NS, 7 Years/Male	**DOA:** 25.05.2024	**Clinician in charge:** Dr Vignesh P
CR No- 201606456383 **R/O** Bilaspur, Himachal Pradesh	**DOD:** 28.06.2024 **Total stay:** 34 days	**Clinical Discussant:** Prof. Sanjay Verma **Pathologist:** Prof. Amanjit Bal **Radiologist:** Dr. Chirag Ahuja

Presenting Complaints:

- **Fever x 7 days**
- **Cough x 7 days**
- **Abdominal distention x 6 days**

History of Presenting Illness

- **Fever:** Insidious onset, documented upto 38.5 degrees Celsius, intermittent, relieved with medications, 2-3 spikes per day, no night sweats.
- **Cough:** Insidious onset, wet sounding, mainly in the morning, no postural variation, relieved by cough syrups.
- **Abdominal distension:** Diffuse, gradually progressive, associated with mild abdominal pain. No vomiting, diarrhoea, constipation, rash, jaundice, bleeding from any site, joint pain, burning micturition
- H/o Lethargy +; but No H/o Headache/ seizures/ altered sensorium

Past history:

- **1st Admission (31.12.2016 to 07.01.2017):** PDA Ligation (5 mm) with ASD (9 mm) closure was done. Then discharged on Envas, which was stopped in 2018.
- **2nd Admission - Ped Allergy Immunology (25.07.2018 to 30.8.2018):** (1st ad in AI): Admitted with a history of fever & cough from 20 days, and maculopapular rash from 1 day, O/E HSM present. Hb-**5.0**, TLC **31,300** at admission, fell to **1150** over time, TG **320** (70-150), Ferritin **>2000** (upto 400), Fibrinogen **1.48** (2-4 gm/L). CECT Chest- small patch of consolidation. FNAC Cervical LN (6.8.18)- only reactive lymphoid cells, BM (2.8.18)- Increase in histiocytes with **Hemophagocytosis** ?Infection triggered HLH
  For infectious workup, 2D Echo- Normal, urine & blood culture- sterile. Widal, Malaria, Dengue, Brucella, Kala-azar workup & Scrub IgM- Negative. HIV, Mycoplasma, and EBV serologies- Negative. CMV IgM & PCR negative. TB workup (Mx, GL AFB, family screen, CECT Chest) negative. Galactomannan Ag (upto 0.5) (8.8.18)- **1.25**. Urine for fungal smear- negative. Initially, IV antibiotics and Amphotericin (i.v.o CT chest showing consolidation and high Galactomannan) were given; plus, IVIG was given considering the possibility of KD/SOJIA for rash and fever. Later once diagnosed as HLH was made, then IV methylprednisolone and cyclosporine were given and discharged on oral prednisolone and cyclosporine.
- **3rd Admission - Ped Allergy Immunology (01/03/19 to 09/03/19):** (2nd adm in AI): Managed as a case of H1N1 pneumonia. Had HSM but no cytopenia. Ferritin 79 (upto 400), Procalcitonin 1.4 (upto 0.5), CRP-17. Cyclosporine dose was reduced and stopped in April 2019.

Family history: One younger female sibling (born prematurely) passed away on DOL-1. Having one younger sister alive who is 1½ years old- completely well. No h/o consanguineous marriage. No family history of similar illness in any other family member

Immunization history: Immunized for age **Developmental History:** Appropriate for age

Antenatal and birth history: Noncontributory **SE history:** Lower SES, Father is a truck driver

Examination: Conscious, but there was a gradual drop in sensorium after admission. Weight: 15 kg (-2.3 Z), HR 107/min, RR 52/min, SPO2 90% on room air and 96% on nPO2. CFT <3 sec, BP 91/47 mm Hg. Pallor +, No icterus/cyanosis/clubbing/lymphadenopathy

Respiratory- Decreased air entry on the left side, no crepitations. **CVS-** S1/S2 normal, No mummer.

Per abdomen: Distended. Splenomegaly present- 7 cm palpable, firm, smooth margins. Hepatomegaly initially not detected, but later examinations mentioned a 4 cm liver below RCM.

CNS- GCS 15/15, Power, Tone, DTR – WNL, No meningeal sings, Pupils: WNL

Investigations:

	25/5	30/5	6/6	14/6	24/6
Hb	**7.9**	**7**	**7.4**	**10.5**	**8.1**
TLC	5,900	**1,380**	**880**	**11,260**	**11,100**
DLC:N/L/M/E	32/**62**/5/0	**26**/59/15/0	**3**/87/8/0	70/24/6/0	**89**/4/7/0
Platelets	**15,000**	**10,000**	**62,000**	**94,000**	**38,000**
Na/K/Cl	**129/5.4**/101	137/3.5/99	134/4.3/97	135/5.4/101	143/3.4/115
Ur/Cr	**66**/0.67	**42**/0.34	**50**/0.53	**179**/1.07	**61**/0.41
Pr/Alb	**5.3/2.2**	6/**2.3**	6.7/**3**	7.9/3.4	**5.5/2.2**
Bil-T/C	**4.2/2.5**	**3.2/1.7**	**2.55/1.09**	**5.24/2.5**	**1.4**/0.3
AST/ALT/ALP	**1207/402/361**	**226/213/354**	48/85/158	82/**156**/158	59/63/110
Ca/Phos	8.8./3.7	6.9/1.6	8.6/3.9	11.1/6.5	10.1/3.5
CRP	**117**	38	8	0.86	32

TG (70-150)	**236**			**209**	
Ferritin (<400)	**22,710**	**2,695**	149	307	
PT(11-13.5 s)	**>2 min**	22.3 sec	18.9 sec		15.7 sec
APTT (21-35 s)	**>2 min**	34.2 sec	30.3 sec		26.9 sec
INR (0.8-1.2)	-	1.88	1.59		1.33
PTI (85-100%)	-	53%	62%		86%
Fibrin (1.5-4.5)	<3.5	**0.49**	1.8		1.8
D-Dimer (<500)	**2,241**	**30,201**	**5,649**		**968**

27.5.24	**Typhoid IgG/IgM**	Neg	**CSF Exam (20.6.24)**
24.5.24	**Widal**	Neg	Cells **102** (N93,L1,M6)
11.6.24	**HCV, HBsAg**	Neg	Protein **141**
05.6.24	**TB workup** (Mx test, GL for AFB, CBNAAT)	Neg	Sugar 72 Microscopy Occ RBC
28.5.24	**Parvo serology**	Neg	C/S Sterile
29.5.24	**EBV VCA IgM**	**Positive**	Indian Ink Negative
3.6.24	**EBV viral load**	Negative	
13.6.24	**Ceruloplasmin level**	21.7 (22-58)	
21.6.24	**Blood & urine culture**	Sterile	**Lymphocyte subset (30.5.24)**
24.6.24	**ET aspirate culture**	Sterile	Lymphocyte count 1247 [1900-3700]
25.6.24	**Beta D glucan** (<60)	**>500**	CD3 T Lymp 908 (72.8%) [1200-2600; 60-76%]
24.6.24	**NBT**	Normal	CD19+ B Lymp 245 (19.6%) [270-860; 13-27%]
03.6.24	**Ig Profile (post IVIG)**	IgG – 2,350 (771-1,771) IgA – 423 (73-209) IgM – 290 (49-206)	CD56+todim+ NK 36 (2.9%) [100-480; 4-17%]
28.5.24	**IL-6** (<7)	**12.9**	**Flow cytometry (4.8.18):** Perforin expression on CD3- CD56+ NK Cells is slightly decreased, CD 107- normal.
11.6.24	**Cyclosporine level** (50-200)	**340**	

Radiology
USG (27.5.2024,30.5.24 & 3.6 2024): Hepatosplenomegaly with moderate ascites
NCCT HEAD (18.6.2024): Hypodensity in bilateral parieto-occipital and frontal white matter: likely PRES
CEMRI BRAIN (19.6.2024): Multiple variable-sized hemorrhagic lesions in bilateral cerebral and cerebellar hemispheres with perilesional edema as described.
Possibilities are-? Atypical hemorrhagic lesions of HLH; ??Fungal abscesses

Targeted Exome Sequencing for IEI: No clinically significant variant identified

Course and management:

PICU stay (25.5.24 - 30.5.24): In PICU child was managed in line of diagnosis of HLH secondary to tropical infection with pneumonia and encephalopathy. After consultation with the AI team, Pulse methylprednisolone followed by IVIG was given. After this, encephalopathy improved significantly with GCS of 15/15. For pancytopenia, transfusions given. Workup for Malaria, Dengue, Scrub, and Typhoid was negative. Received antibiotics, once stabilized, the shifted to the ward.

Allergy immunology ward stay (30.5.24 – 28.6.24):

1) HLH- Following methylprednisolone and IVIG in the PICU, shifted to oral steroids, ferritin started to rise again and methylprednisolone was again stated which was slowly tapered. The child had improving cytopenia and decreasing ferritin gradually. Cyclosporine was started at 5 mg/kg/day with dexamethasone. Liver and spleen regressed in size and abdominal distension was seen to be decreasing.
2) CNS Symptoms- During admission, child was noticed to have an abrupt onset of altered sensorium with hyponatremia and hyperkalemia (with urine output of 2 ml/kg/day). The child had 2 isolated hypertensive BP recordings. NCCT Head was done to rule out bleeding which showed B/L post parieto-occipital hypodensities suggestive of PRES. Antihypertensives were optimized and sodium was corrected. Cyclosporine trough levels were also elevated. MRI later revealed multiple variable-sized hemorrhagic lesions in bilateral cerebral and cerebellar hemispheres with perilesional edema- Neuro HLH vs fungal brain abscess. Since child was deteriorating, he was intubated and ventilated, and meropenem, vancomycin, and liposomal amphotericin B were given. For right-side pneumothorax on day 4 of mechanical ventilation ICDT. Medical management for raised ICP given. Brain and leptomeningeal biopsy was planned for diagnostic purposes. The child developed raised ICP refractory to medical management and on examination, brain stem reflexes were seen to be absent. After being explained about the condition and prognosis of the child, the parents opted for DNR. On day 28.6.24, the child had an episode of bradycardia which progressed to asystole.

Unit's Final Diagnosis: Primary HLH with Intracranial space-occupying lesion (fungal brain abscess vs CNS HLH) with refractory raised intracranial pressure.