Natural History of liver involvement in paediatric Langerhans cell Histiocytosis: Two-decade experience from a tertiary centre in southern India

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Introduction

- Langerhans cell histiocytosis (LCH) is a rare, heterogenous disorder characterized by the accumulation and clonal proliferation of the dendritic cells which is similar appearing to epidermal Langerhans cells[1].
- The prognosis of LCH depends on the organ involved ranging from a self-limiting lesion to poor outcome, especially when liver, lungs and bone marrow are involved[2].
- Hepatic LCH commonly occurs as a part of multisystemic LCH (MS-LCH), however isolated liver involvement is also known (SS-LCH) in rare instances.
- **Aim of the study**: This study aims to retrospectively analyze the hepatic LCH with respect to clinical, biochemical, imaging and disease characteristics and also attempts to assess the liver outcome and its predicting factors.

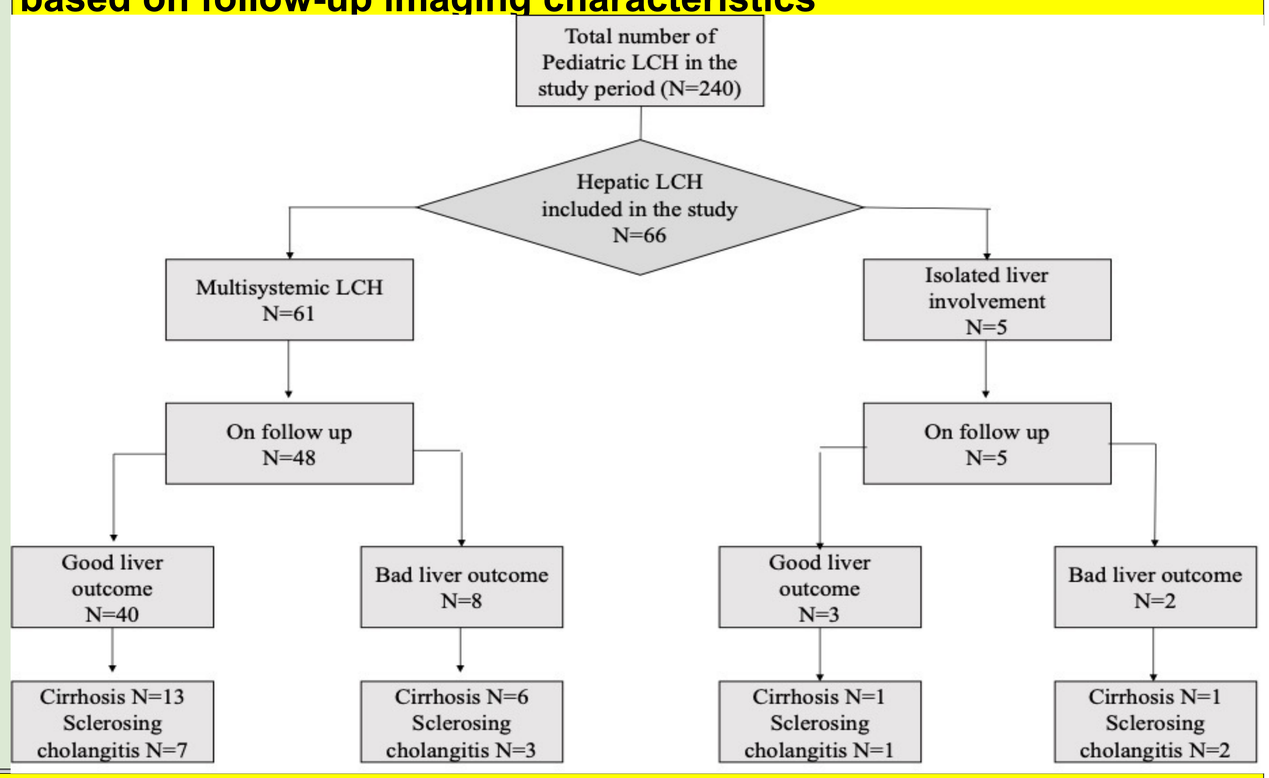
Methods

- All the children < 18 years of age, diagnosed LCH with liver involvement managed in Pediatric Hemat-oncology division of Christian Medical College, Vellore between 2004 to 2024 were included in the study
- Basic work-up done for all children. Liver function tests (LFT), ultrasound (US) abdomen in suspected liver involvement. Contrast enhanced computed tomography (CECT) done for multisystemic involvement if the liver involvement is doubtful with US abdomen.
- Magnetic resonance cholangiopancreatography (MRCP) done when sclerosing cholangitis is suspected
- Hepatic LCH is defined by European consortium for histiocytosis, if any one or more of the following is present. 1. liver enlargement of more than 3 cm below right costal margin in mid-clavicular line. 2. signs of liver dysfunction/ cholestasis 3. Imaging features or histopathology suggestive of liver infiltration.

Results

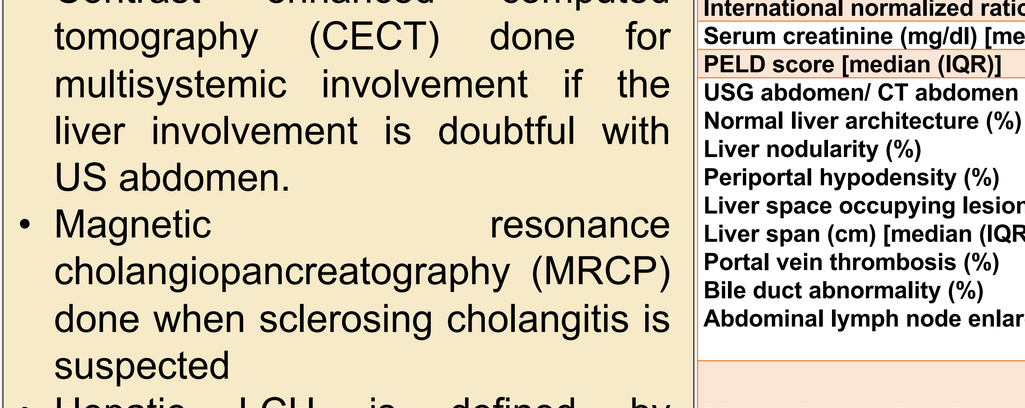
- The median age of the children was 18 (5-60) months. The boys (72.7%) were much more than the girls
- The most common symptoms of hepatic LCH were fever (93.9%), skin rash (81.8%), and abdominal distention (80.3%).
- Hepatomegaly (98.5%), splenomegaly (72.7%) and pallor (75.8%) were most common examination findings
- 59 children followed-up [median duration 24 (1-132) months)], of which treatment was ongoing for 39 children [9 (1-65) months] and treatment was completed in 20 [19 (12-48) months].

Flow-chart of the good and bad outcomes of hepatic LCH children based on follow-up imaging characteristics



Comparison of clinical, laboratory and imaging characteristics at presentation of children with good and poor liver outcomes of hepatic LCH

	Children with good liver outcomes (n=43)	Children with bad liver outcomes (n=10)	P value
Age in months [median (IQR)]	19.0 (14.0-30.0)	22.0 (11.5-43.0)	0.776
Gender (male: female)	31:12	8: 2	0.609
Symptoms duration in months [median (IQR)]	5.0 (3.0- 8.0)	5.0 (3.0-6.8)	0.879
Presentations (%)	Jaundice 16 (37.2) Bleeding 9 (20.9) Cough/ respiratory symptoms 8 (18.6) Pruritus 2 (4.8) Abdominal distension 16(72.72) Ear discharge 18 (41.9) Breathlessness 4 (9.3) Skin rash 37 (86.0) Bony fractures 12 (27.9) Polyuria 6 (14.0) Palpable lymph nodes 9 (20.9) Ascites 2 (4.8)	Jaundice 8 (80.0) Bleeding 0 (0.0) Cough/ respiratory symptoms 4 (40.0) Pruritus 3 (30.0) Abdominal distension 8 (80.0) Ear discharge 2 (20.0) Breathlessness 3 (30.0) Skin rash 23 (74.19) Bony fractures 3 (30) Polyuria 0 (0) Palpable lymph nodes 0 (0) Ascites 1 (10.0)	**0.014** 0.112 0.328 0.014 0.948 0.777 0.082 0.058 0.928 0.230 0.948 0.510
Weight z-score [median(IQR)]	-1.6 (-3.0- -0.5)	-2.3 (-2.8- -1.7)	0.503
Height z-score [median(IQR)]	-1.9 (-3.0- -0.5)	-1.6 (-2.7- 1.0)	0.948
BMI z-score [median(range)]	-0.9 (-1.7- 0.1)	-1.1 (-2.7- -0.5)	0.503
Palpable liver below RCM (cm)	5 (4- 6)	6 (4.7-6.5)	0.445
Palpable spleen below LCM (cm) [median (IQR)]	3 (3- 4.7)	3 (3-7.8)	0.892
Hemoglobin (g/dl) [median (IQR)]	9.1 (7.2 – 10.8)	9.9 (7.5-11.5)	0.676
Total bilirubin (mg/dl) [median (IQR)]	0.6 (0.4- 2.5)	5.5 (2.2- 7.0)	**0.012**
Aspartate transaminases (IU/L) [median (IQR)]	43 (27- 69)	117 (89-222)	**0.001**
Alanine transaminases (IU/L) [median (IQR)]	22 (17- 69)	90 (69- 137)	**0.012**
Serum proteins (g/ dl) [median (IQR)]	6.7 (5.3-7.5)	5.9 (5.4- 7.0)	0.091
Serum albumin (g/dl) [median (IQR)]	3.5 (3.0- 3.9)	2.9 (2.6- 3.4)	0.776
Alkaline phosphatase (IU/L) [median (IQR)]	460 (174- 989)	1147 (817- 2854)	0.068
International normalized ratio [median (IQR)]	1.1 (1.0- 1.2)	1.21 (1.2- 1.4)	0.369
Serum creatinine (mg/dl) [median (IQR)]	0.3 (0.2- 0.4)	0.3 (0.2- 0.5)	0.894
PELD score [median (IQR)]	0.0 (0.0- 6.9)	11.5 (5.8- 17.2)	0.068
USG abdomen/ CT abdomen findings			
Normal liver architecture (%)	22 (51.2)	2 (20.0)	0.075
Liver nodularity (%)	5 (11.6)	5 (50.0)	**0.047**
Periportal hypodensity (%)	15 (34.9)	6 (60.0)	0.076
Liver space occupying lesions (%)	14 (32.6)	0 (0.0)	0.035
Liver span (cm) [median (IQR)]	10.8 (9.0- 12.0)	11.25 (9.8-12.4)	0.456
Portal vein thrombosis (%)	1 (2.3)	1 (10.0)	0.532
Bile duct abnormality (%)	2 (4.7)	2 (20.0)	0.098
Abdominal lymph node enlargement (%)	11 (25.5)	0 (0.0)	0.058
Biopsy sites yielding diagnosis (%)	Bone marrow 1 (2.3) Skin 30 (69.7) Lymph node 4 (9.3) Liver 5 (11.6)	Bone marrow 0 (0) Skin 7 (70) Lymph node 2 (20) Liver 1 (10)	0.778
Follow-up duration (months) [median(IQR)]	26 (12- 56.5)	6.0 (3.8- 25.0)	0.154
Treatment status on last follow-up (%)	Treatment not started 2(4.7) Treatment completed 15 (34.9) Treatment on going 17 (39.5) Disease recurrence with ongoing treatment 5 (11.6) Disease recurrence treatment completed 4 (9.3)	Treatment not started 0 (0) Treatment completed 1 (10) Treatment on going 8 (80) Disease recurrence with ongoing treatment 1 (10) Disease recurrence treatment completed 0 (0)	0.207
LCH disease status at follow-up (%)	Nonactive 18 (41.9) Regressive 2 (4.7) Stable 12 (27.9) Progressive 11 (25.6)	Nonactive 0 (0) Regressive 0 (0) Stable 1 (10) Progressive 9 (90)	**0.002**
Imaging features showing SC at follow-up	8 (18.6)	5 (50)	0.039
Imaging features showing cirrhosis at follow-up (%)	14 (32.6)	7 (70)	**0.034**



Conclusion

- Liver involvement of LCH is commonly seen as a part of the MS-LCH, however, isolated liver involvement is also possible.
- Fever, hepatomegaly and splenomegaly were the most common presentations of the disease.
- Presence of jaundice, elevated transaminases, liver nodularity and progressive disease predict poor liver outcomes.

References

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Conflict of interest

None