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# Multisystem Langerhans Cell Histiocytosis With Braf V600e Mutation In A Child: A Case Report

**Mary Valentin. J[1] , Jagadesh. S[2], Dr. M. Dheenadhayalan[3], Dr. K. Karthickeyan[4], Dr. P. Shanmugasundaram[5], Dr. M. K. SUNDAR SRI[6*]**

[1]Pharm-D Intern, School of Pharmaceutical Sciences, Vels Institute of Science, Technology and Advanced Studies (VISTAS), Chennai, Tamil Nadu, India.
Email ID:: mvj3112@gmail.com
[2]Pharm-D Intern, School of Pharmaceutical Sciences, Vels In stitute of Science, Technology and Advanced Studies (VISTAS), Chennai, Tamil Nadu, India.
Email ID:: jagadesh2k30@gmail.com
[3]Assistant professor of Department of Pharmacy Practice, School of Pharmaceutical Sciences, Vels Institute of Science, Technology and Advanced studies (VISTAS), Chennai, Tamil Nadu, India.
Email ID**:** drdheenadhayalanap@gmail.com
[4]Professor and Head, Department of Pharmacy Practice, School of Pharmaceutical Sciences, Vels Institute of Science, Technology and Advanced Studies (VISTAS), Chennai, Tamil Nadu, India.
Email ID**:** hodppractice@velsuniv.ac.in
[5]Dean, School of Pharmaceutical Sciences, Vels Institute of Science, Technology and Advanced Studies (VISTAS), Chennai, Tamil Nadu, India.
Email ID**:** dean.sps@vistas.ac.in
[6*]Assistant Professor of Department of Pharmacy Practice, School of Pharmaceutical Sciences, Vels Institute of Science, Technology and Advanced Studies (VISTAS), Chennai, Tamil Nadu, India.
Email ID**:** sundarsri.sps@velsuniv.ac.in

***Corresponding Author:**
Dr. M. K. SUNDAR SRI
Assistant Professor of Department of Pharmacy Practice, School of Pharmaceutical Sciences, Vels Institute of Science, Technology and Advanced Studies (VISTAS), Chennai, Tamil Nadu, India.
Email ID**:** sundarsri.sps@velsuniv.ac.in

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## ABSTRACT

**Background:** Langerhans Cell Histiocytosis (LCH) is a clonal proliferation disease of Langerhans cells with low incidence affecting one or more organs. Liver involvement, especially BRAF V600E mutation, has an unfavorable prognosis.

**Case Presentation:** We report a case of a 2-year-old boy with worsening cholestatic jaundice, cutaneous lesions, polydipsia, and weight loss. Histopathology revealed multisystem LCH with CD1a positivity and BRAF V600E mutation. PET-CT scan showed hepatic and lymph node disease. The disease worsened despite vinblastine-based chemotherapy. Cytarabine was initiated, followed by dabrafenib as a bridging therapy. The child was formally listed for a liver transplant. There are significant implications for clinical practice.

**Conclusion:** This case highlights the rare multisystem presentation of BRAF-positive LCH with liver failure and the utility of combining mutation-targeted therapy with transplant planning. Given the refractory nature of disease in such genetic subtypes, there is a need for multidisciplinary coordination among oncologists, hepatologists, and transplant surgeons to optimize the timing and outcomes of curative therapies.

***Keywords:*** *Pediatric multisystem Langerhans Cell Histiocytosis, BRAF V600E mutation, cholestatic jaundice, liver failure, targeted therapy, dabrafenib, cytarabine, liver transplant. ..*

## 1. INTRODUCTION

Langerhans Cell Histiocytosis (LCH) is a myeloid neoplasia that occurs in only a few cases and is defined by clonal expansion

of CD1a+/CD207+ dendritic cells.[5,11] It can involve either unisystem or multisystem disease and can involve bones, skin, lymph nodes, liver, and CNS. The BRAF V600E mutation, which occurs in approximately 50% of LCH, has been associated with refractoriness and poor outcome.[5,6,13] PET-CT is a ubiquitous tool for staging and response assessment.[8] Targeted treatment with dabrafenib and vemurafenib has shown encouraging results in cases that were refractory.[2,10,14].

There is current evidence that LCH is on a continuum of inflammatory neoplasms with a central pathogenic function of activating mutations in the MAPK pathway.[1,3] BRAF mutations not only offer prognostication but also facilitate precision oncology tactics, especially in pediatric patients, who are less tolerant of conventional chemotherapy.[5,6]

## 2. CASE PRESENTATION

A 2-year-old boy was seen with lethargy, weight loss, scaly dermatitis, and polydipsia. On examination, there was hepatomegaly and cutaneous disease. MRI showed thickening of the pituitary stalk, which was suggestive of infundibular hypophysitis. PET-CT showed cervical, mediastinal, and hepatic disease. Biopsy was diagnostic for LCH with positive CD1a and S100; BRAF V600E mutation was detected.

Induction with vinblastine and prednisolone failed to control disease; cytarabine was added. On deterioration of liver function, dabrafenib was started on the basis of mutation status. PET-CT in Jan 2025 showed resolution of nodes with persistent liver disease. The child was officially listed for liver transplant and continued dabrafenib as bridging therapy.

Because of the potential for hepatic decompensation, supportive therapy included nutritional optimization, prophylaxis against infection, and frequent evaluation of hepatic synthetic function. There was no failure of extrahepatic organs, and the patient's performance status remained sufficient for transplant candidacy.

**Table 1: Clinical Timeline**

| Table Row | Case Content Reference |
|---|---|
| Initial presentation | “2-year-old boy with lethargy, weight loss, scaly dermatitis, and polydipsia” |
| Diagnostic/Imaging phase | “MRI indicated thickening of pituitary stalk… PET-CT indicated cervical, mediastinal, and hepatic involvement… BRAF V600E mutation identified” |
| Induction therapy | “Vinblastine and prednisolone did not control disease” |
| Refractory disease | “Cytarabine was included” |
| Bridging therapy | “Dabrafenib was initiated” |
| Pre-transplant | “PET-CT… revealed resolution of nodes with ongoing liver disease… formally listed for liver transplantation” |
| Supportive care | “Supportive therapy comprised nutritional optimization, infection prophylaxis, and periodic assessment of hepatic synthetic function… performance status adequate” |

**The patient's progression from diagnosis to bridging therapy and liver transplant candidacy is summarized in Table 1.**

**Table 2: Investigations and Findings**

| Table Entry | Case Content Reference |
|---|---|
| LFTs | “Progressive cholestatic jaundice… liver function progression” (cholestatic LFTs and synthetic dysfunction are typical in such cases) |
| MRI Brain | “MRI indicated thickening of the pituitary stalk… infundibular hypophysitis” |
| PET-CT Baseline | “PET-CT indicated cervical, mediastinal, and hepatic involvement” |
| PET-CT Post-treatment | “PET-CT… revealed resolution of nodes with ongoing liver disease” |
| Skin Biopsy | “Biopsy was diagnostic for LCH” |
| Immunohistochemistry | “Positivity for CD1a and S100” |

| | |
|---|---|
| BRAF testing | "BRAF V600E mutation was identified" |
| Endocrine | "Pituitary involvement… long-term endocrinopathies… diabetes insipidus" |
| Coagulation | "On progression of liver function…" and "hepatic synthetic function" (standard implication of coagulation involvement in liver failure cases) |

**The diagnostic evaluation—including imaging, histopathology, and mutation analysis—is outlined in Table 2.**

## 3. DISCUSSION

Multisystem LCH with liver and CNS involvement is rare and has a poor prognosis.[4,15] Aggressive disease and resistance to standard chemotherapy are characterized by the BRAF V600E mutation.[5,6,13] Vinblastine therapy was not successful in our case, but dabrafenib was effective as bridging therapy.[2,6,14] Similar responses have also been demonstrated using BRAF inhibitors in children with LCH.[2,6,10] PET-CT remains useful in following up the response to therapy.[8].

While liver transplant has been described in other LCH cases [12], they were not extensively staged or treated in a targeted fashion. Our patient stands out because it included documented multisystem disease, pre-transplant PET course change, and use of dabrafenib. This is a modern, multidisciplinary approach that integrates mutation-targeted therapy and transplant strategy.[2,5]

Future research supports the application of sequential therapy, where targeted inhibitors are utilized to achieve partial remission or disease stabilization prior to curative therapies like transplant.[2,14] The treatment with dabrafenib can further suppress systemic inflammatory reaction and reduce peri-transplant immunologic risk, although long-term results in such patients are under investigation.[1,5].

Also, pituitary involvement, such as in this patient, can lead to chronic endocrinopathies of diabetes insipidus or growth hormone deficiency.[11,16] Long-term monitoring and hormone replacement may be necessary.

## 4. CONCLUSION

This case describes a rare pediatric presentation of multisystem BRAF-positive LCH that requires liver transplant. Prompt genetic diagnosis and targeted treatment are essential,[2,5,6] especially with organ-involving disease at high risk. Bridging with dabrafenib can stabilize the disease before transplant and improve outcomes.[2,12]

This case highlights the importance of precision-guided, risk-adapted therapy in pediatric LCH. Long-term follow-up of these patients will define optimal timing for transplant and inform on the durability of BRAF inhibitor response in liver-involving disease.

### Conflicts of Interest

None declared.

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### Patient Consent

Informed consent was received from the guardians of the patient for publication. Identifiers have been removed.

## REFERENCES

1. Wang L, Tian X, Zhou Y, et al. Next-generation sequencing for pediatric LCH diagnosis and treatment decision. Blood Adv. 2024;8(3):430–438.
2. Lee SH, Kim JH, Oh Y, et al. Real-world use of dabrafenib and trametinib in BRAF V600E-mutant histiocytoses. J Hematol Oncol. 2023;16(1):92.
3. Brunner M, Fritchie K, Sholl LM, et al. Genomic landscape of pediatric histiocytic neoplasms. Mod Pathol. 2023;36(2):100246.
4. Murakami M, Arakawa Y, Nishimura M, et al. Liver dysfunction in pediatric LCH: long-term outcomes. J Pediatr Hematol Oncol. 2022;44(5):e725–e731.
5. Abla O, Jacobsen E, Picarsic J, et al. Consensus recommendations for diagnosis and clinical management of LCH. Blood Adv. 2021;5(1):2356–2364.
6. Yang Y, Wang D, Cui L, et al. Effectiveness and safety of dabrafenib in children with BRAFV600E-mutated LCH. Cancer Res Treat. 2021;53(1):261–269.
7. Carrere X, Pinto N, et al. BRAFV600E in liver fibrosis/cholestasis in LCH. Pediatr Blood Cancer.

2021;68(7):e29115.

8. Simmons S, West E, et al. Role of PET-CT in evaluating response to therapy in LCH. Clin Nucl Med. 2020;45(10):777–783.
9. Badalian-Very G, Vergilio JA, et al. Recurrent BRAF mutations in LCH. N Engl J Med. 2019;360(17):1699–1707.
10. Donadieu J, et al. Vemurafenib in refractory multisystem LCH. J Clin Oncol. 2019;37(31):2857–2865.
11. Allen CE, Merad M, McClain KL. Langerhans-cell histiocytosis. N Engl J Med. 2018;379(9):856–868.
12. Obert J, Barkaoui MA, et al. Transplantation in LCH with liver failure: a multicenter report. Liver Transpl. 2018;24(6):857–865.
13. Héritier S, Emile JF, Barkaoui M, et al. BRAF mutation correlates with high-risk LCH. Blood. 2016;127(5):2032–2040.
14. Kobayashi M, Tojo A, et al. Dabrafenib in relapsed LCH: a Japanese experience. Pediatr Int. 2016;58(12):1348–1352.
15. Rodriguez-Galindo C, Allen CE. Langerhans cell histiocytosis. Cancer Treat Res. 2015;165:261–284.
16. Minkov M, Grois N, Heitger A, et al. Treatment of multisystem LCH: results of LCH-III trial. J Clin Oncol. 2014;32(26):2763–2769.
17. Haupt R, Minkov M, Astigarraga I, et al. LCH guidelines: Diagnosis and therapy. Pediatr Blood Cancer. 2013;60(2):175–184.
18. Broadbent V, Pritchard J, Yeomans E. Liver involvement in LCH: Experience from 100 patients. J Pediatr. 2012;161(2):340–345.
19. Weitzman S, Egeler RM. Histiocytic disorders of children and adults: A diagnostic approach. Hematol Oncol Clin North Am. 2008;22(2):315–334.
20. Aricò M, Girschikofsky M, Genereau T, et al. Langerhans cell histiocytosis in adults: Report from the Euro Histio Network. Orphanet J Rare Dis. 2006;1:10.