soho2023
ELEVENTH ANNUAL MEETING

# Case Report: hemophagocytic lymphohistiocytosis with central nervous system involvement

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## INTRODUCTION

- Central nervous system (CNS) involvement in hemophagocytic lymphohistiocytosis (HLH) is very rare, and significantly impacts on its treatment and prognosis. Isolated CNS-HLH is a challenging condition with high morbidity and mortality. Viral infections, such as Epstein-Barr virus (EBV), are a well-recognised trigger of such cases (1) .

## AIM

Reporting the clinicopathologic findings, diagnostic difficulties, and treatment approach and outcomes of another rare case of relapsed HLH disease with CNS infiltration.

## METHOD

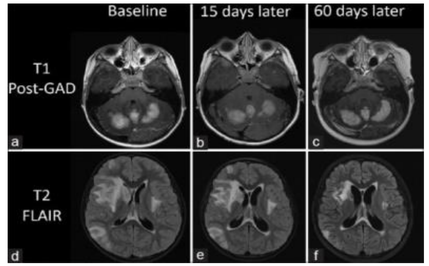
- We report a case of a 23-year-old male who attended the haematology clinic in the University College of London Hospital, United Kingdom.
- This includes history taking, physical examination, full blood count, chemistry profile and HLH profile ,Bone marrow aspiration and trephine biopsy. CSF examination including cultures, neuroimmunology and Neopterin level . Radiological testing as MRI brain and PET CT scan were used.

## RESULTS

- Our patient was diagnosed with EBV-driven HLH in 2019 after presenting with generalized lymphadenopathy, pancytopenia, fever and elevated HLH markers). He responded well to treatment with the HLH 2004 regimen .
- Two years later, he represented with dizziness, headache and ataxia. Magnetic resonance imaging (MRI) showed progressive diffuse cerebellitis with extensive supratentorial signal abnormality affecting the limbic system and acute hydrocephalus. PET/CT scan, CSF examination and neuroimmunology markers were unremarkable for any haematological malignancy.
- HLH workup was negative at presentation, and complete blood count was normal .Viral markers, including EBV PCR, CMV PCR and JC PCR, were negative. Bone marrow cytology showed no evidence of haemophagocytosis.
- The patient received 3 days of methylprednisolone (1g/day) with no improvement.CSF Neopterin level was 82.9 nmol/L(normal range 8-14.5 nmol/l) with progressive pancytopenia. Bone marrow trephine showed HLH activity with negative EBER.
- He received treatment with HLH 2004 protocol .Subsequently he showed resolution of clinical and radiological signs, normalisation of CBC indices, resolution of HLH markers, and normal MRI findings.
- The patient underwent sibling allogenic haematopoietic progenitor cell transplantation with reduced intensity conditioning (Fludarabine, cyclophosphamide and Melphalan regimen).He remains in remission 16 months later, with no evidence of recurrence.

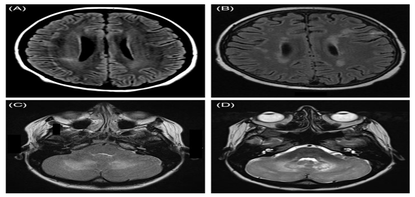
| Date | WBC (x10^3/µL) | Absolute neutrophil count (ANC) | Absolute lymphocyte count (ALC) | RBC (x10^6/µL) | Haemoglobin (g/dL) | MCV | MCH | Platelets (x10^3/µL) |
|---|---|---|---|---|---|---|---|---|
| 07/11/2021 | 4.5 | 3 | 1.5 | 5 | 11.5 | 85 | 30 | 180 |
| 14/11/2021 | 2.7 | 1.1 | 1.6 | 3.2 | 9.9 | 95 | 31 | 100 |
| 22/11/2021 | 2.2 | 1 | 1.2 | 2.9 | 8.5 | 89 | 31 | 85 |
| 14/12/2021 | 3.6 | 1.9 | 1.6 | 3.4 | 10.5 | 88 | 30 | 103 |
| 08/04/2022 | 5.2 | 4 | 0.9 | 5.2 | 12.5 | 86 | 32 | 320 |
| 12/08/2022 | 6.3 | 4.9 | 1 | 5.2 | 12.5 | 89 | 32 | 270 |

***A table demonstrating the changes in patient blood count over time***




The provided images are not out patient`s but reflects how CNS radiological changes in HLH can vary in considerable way from subtle changes , hydrocephalus , infarcts or SOLs.

**Figure(1)** : a-c) reveal post-GAD enhancement in the cerebellum, demonstrating persistent and worsening enema at 60 days. (d-f) show T2-FLAIR lesions evolution over time. Right frontal hemisphere lesion is improved (f) when compared to baseline (d). *(2)*




A) Axial MR brain FLAIR sequence from patient one at t presentation with bilateral hyper intensities in the centrum semivale of the parietal lobes. (B) FLAIR sequence demonstrating progression of bilateral supratentorial white matter hyper intensities (C) T2-weighted MRI showing bilateral cerebellar hemisphere white matter hyper intensity with local mass effect (D) T2-weighted MR brain showing progression of the bilateral cerebellar white matter , with prominent involvement of the bilateral dentate nuclei(3).

## CONCLUSIONS

- HLH with CNS involvement is very rare with high morbidity and mortality.
- CNS manifestations can precede systemic findings which makes diagnosis challenging.
- Allogenic stem cell transplant can produce durable remissions in patients with CNS-HLH, and should be considered in the treatment approach.

## REFERENCES

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## CONTACT INFORMATION

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