Hemophagocytic lymphohistiocytosis as an acute febrile illness in a child with congenital HIV: a case presentation

Morgan Day DO, Lorena Galvan DO, Christal Chow MD

mlday@salud.unm.edu, logalvan@salud.unm.edu

Introduction

Little is known about the relationship between hemophagocytic lymphohistiocytosis (HLH) and renal manifestations, specifically nephrotic syndrome.

Even less is known about nephrotic syndrome in the setting of HLH and congenital human immunodeficiency virus (HIV) infection.

We report the case of a nine-year-old male with HIV and treated latent tuberculosis (TB) who presented with fever of unknown origin, was diagnosed with HLH who subsequently developed collapsing focal segmental glomerulosclerosis (FSGS).

Genetic testing revealed he was positive for two APOL1 gene mutations. APOL1 gene mutations have previously been studied in association with HIV nephropathy. Kopp et al demonstrated patients with two APOL1 gene mutations have greatly increased risk of developing glomerular disease.

Case Description

Our patient is a nine-year old HIV-positive male, adopted three years prior from Ghana. His biological family medical history is unknown. Presumptively, his HIV infection was prenatally-acquired. His antiviral medication was changed to Biktarvy (bictegravir/emtricitabine/tenofovir) seven months prior to presentation after Genosure testing demonstrated genotypic resistance.

The patient was admitted to our team with fever of unknown origin. Of note, he had a recent prior admission for the same chief complaint and was diagnosed and treated for a tick-borne illness. HLH was suspected at that time, but he did not meet criteria for HLH diagnosis.

He was noted to have a chronically elevated baseline creatinine ranging from 0.5-0.8 mg/dL.

Interventions & Timeline

On admission, echocardiogram demonstrated a diffusely dilated left coronary artery. He met criteria for incomplete Kawasaki Disease and was treated with IVIG. Persistent hypertriglyceridemia prompted re-evaluation for HLH. He met 6/8 criteria with fever (maximum temperature 39.8C), splenomegaly, hypertriglyceridemia (526mg/dL), elevated ferritin (15,425 ng/mL), hemophagocytosis on bone marrow biopsy, and elevated SIL-2R (5,734 U/mL).

Brain MRI demonstrated peripheral and subcortical white matter lesions consistent with CNS HLH involvement (see figures 1 and 2, with chevrons noting white matter lesions). PET/CT scan demonstrated findings compatible with lymphoproliferative disorder.

Our patient developed a Grade I acute kidney injury and acute nephrotic range proteinuria with urine creatinine-protein ratio of 5.26. Renal ultrasound demonstrated bilateral renal cortical echogenicity. He underwent kidney biopsy demonstrating collapsing variant of FSGS. Given he was originally from Ghana, APOL1 gene testing was performed demonstrating two different mutations of APOL1. Lisinopril was initiated and the proteinuria monitored as it down trended. He was started on steroid therapy and received intrathecal methotrexate and hydrocortisone as treatment for HLH.

Figure 1. SAG FLAIR MRI

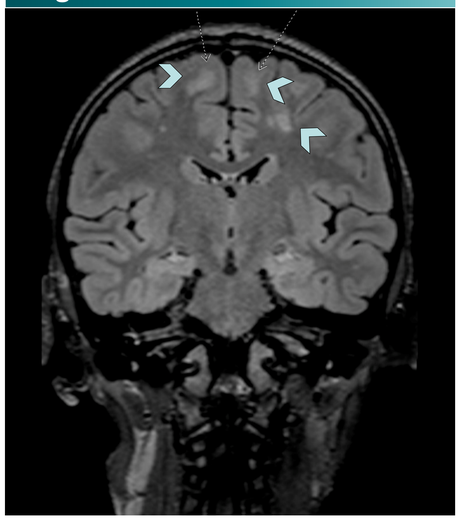
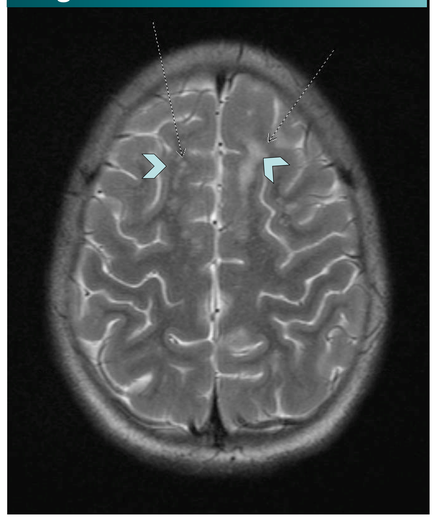


Figure 2. AXIAL T2 MRI



Discussion

HLH comes in primary and secondary forms. The secondary form develops in the setting of strong immunological activation, as seen in severe infections. (2) HLH is defined by bone marrow and organ infiltration by activated, nonmalignant macrophages, which phagocytose blood cells. (3) The most typical findings of HLH are fever, hepatosplenomegaly and cytopenias. Other common findings include hypertriglyceridemia, coagulopathy with hypofibrinogenemia, liver dysfunction, elevated levels of ferritin and serum transaminases, and neurological symptoms. (2) Though acute renal failure had previously been seen in HLH, nephrotic syndrome as a manifestation of HLH was first described by Thaunat et al in 2006. The proposed pathophysiology of HLH associated renal failure is acute tubular necrosis with or without reduction of glomerular filtration flow resulting in massive collapse of glomerular tufts, as seen in our patient. (3) As previously mentioned, HIV associated nephropathy also causes glomerular disease. (1)

Conclusion

Our case demonstrates the interesting phenomenon of glomerular disease, specifically collapsing FSGS, in a patient with known congenital HIV on immunosuppressive therapy who developed HLH. Since his HIV viral load was low, it was determined his FSGS was not secondary to HIV nephropathy, but rather HLH. Further research investigating the relationship between HLH and renal involvement is required.

References

1. Kopp JB, Nelson GW, Sampath K, et al. APOL1 genetic variants in focal segmental glomerulosclerosis and HIV-associated nephropathy. *J Am Soc Nephrol.* 2011;22(11):2129-2137. doi:10.1681/ASN.2011040388

2. Henter JI, Horne A, Aricó M, et al. HLH-2004: Diagnostic and therapeutic guidelines for hemophagocytic lymphohistiocytosis. *Pediatric Blood Cancer.* 2007;48(2):124-131. doi:10.1002/pbc.21039.

3. Thaunat O, Delahousse M, Fakhouri F, et al. Nephrotic syndrome associated with hemophagocytic syndrome. *Kidney Int.* 2006;69(10):1892-1898. doi:10.1038/sj.ki.5000352

Disclosure: Authors of this presentation have the following to disclose concerning possible financial or personal relationships with commercial entities that may have a direct or indirect interest in the subject matter of this presentation:

Morgan Day, Lorena Galvan, Christal Chow: nothing to disclose

Source of Funding: nothing to disclose