Republic of the Philippines
Department of Health
NATIONAL CHILDREN'S HOSPITAL
Department of Pediatrics

A CASE REPORT OF DENGUE ASSOCIATED HEMOPHAGOCYTIC LYMPHOHISTIOCYTOSIS

By Marilei C. Lozano, MD

INTRODUCTION

Dengue infection affects 390 million yearly (Kan, F. K., et al., 2020). It causes various complications; one atypical complication is Hemophagocytic Lymphohistiocytosis (Takkinsatian, P. et. al., 2020).

Hemophagocytic lymphohistiocytosis (HLH) is a rare, potentially fatal hematologic disorder characterized by hyperinflammation, uncontrolled proliferation of activated lymphocytes, prolonged fever, pancytopenia, jaundice, and hepatosplenomegaly. (Kan, F. K., et al., (2020). Acquired HLH occurs after an intense immunologic stimulation, such as an infection, autoimmune disease, or malignancy. For Infection associated HLH, the most common causative organisms are the Epstein Barr and dengue viruses (Ishak, S. H., et. Al, 2020).

However, Dengue-associated HLH may be underrecognized due to overlapping signs and symptoms of HLH and dengue. (Chaitanya, K., et. Al, 2020). Persistence of fever beyond 7 days, elevated transaminases, progressive cytopenia and organ dysfunction may alert clinicians to suspect underlying HLH (Bhattacharya, D., et. Al, 2020). Timely recognition and aggressive treatment to control the trigger of HLH with or without HLH-specific immunotherapy are important in decreasing the mortality. As Missed or delayed diagnosis of these complications might cause death.

OBJECTIVES

1. To present a case of Dengue Associated Hemophagocytic Lymphohistiocytosis (HLH)
2. To identify the criteria for the diagnosis of HLH
3. To discuss the treatment and control the trigger in HLH

CASE SUMMARY

A 1year old 10 months female from Laguna presented with fever for 10 days. History started 9 days prior, a high grade, intermittent fever, with highest temperature of 39.1C with associated periumbilical pain. No other associated symptoms were noted. Symptoms persisted until day 9 of illness now noted with generalized weakness and decrease appetite. Brought to hospital and was managed as Severe Dengue.

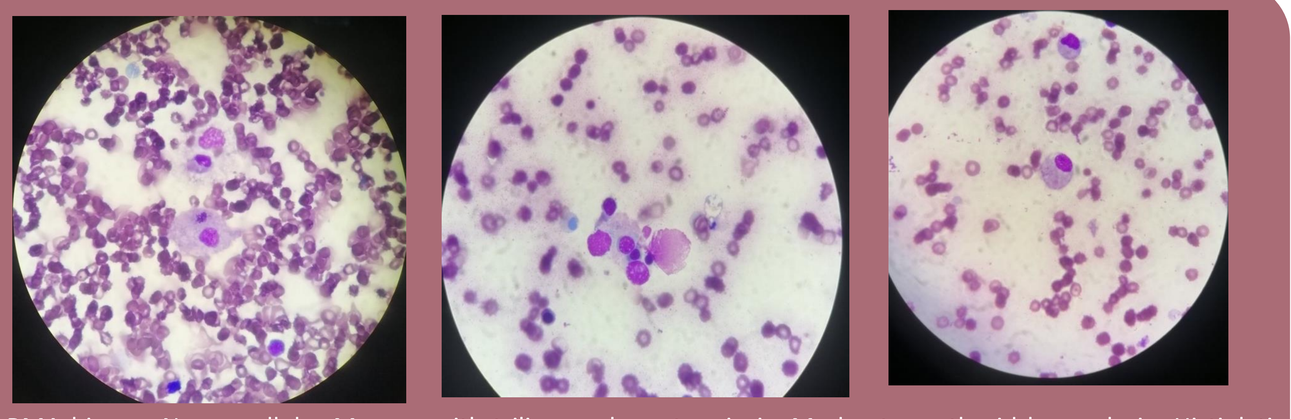
On physical examination, she was drowsy in moderate distress; with BP 90/60 CR 160 RR 48 T 39.0C , generalized pallor, blood clots per nostrils and mouth with no active bleeding; multiple palpable lymph nodes, with distended neck veins; with symmetrical chest expansion, occasional crackles, bilateral lung fields; with adynamic precordium, tachycardic, regular rhythm, no murmurs, soft non distended abdomen, with hepatomegaly 4cm below RSCM, with full and equal pulses, CRT < 2 secs, warm extremities, pale nail beds, palms and soles.

DISCUSSION

HLH is an acute or subacute febrile illness associated with multiple organ involvement. Diagnosis may be made in the presence of molecular diagnosis consistent with HLH and if at least 5 of 8 diagnostic criteria based on HLH-2004 protocol are met: **fever, splenomegaly, cytopenias, hypertriglyceridemia, hypofibrinogenemia, hemophagocytosis in tissue, hyperferritinemia, increase in CD25/IL-2 receptor or reduced NK cell function** (Kapdi, M, et al., 2012). Cytopenia , especially anemia and thrombocytopenia are seen in >80% of patients on presentation. A very high serum ferritin has a high sensitivity and specificity. Nearly all patient with HLH have hepatitis as manifested by elevated liver function tests including AST, ALT, LDH and bilirubin levels. Hypertriglyceremia and coagulation abnormalities are due to impaired hepatic synthetic function. Bleeding is common and is due to altered coagulation factors.

In relation to this report, patient presented with 10 days history of fever, with hepatomegaly on physical examination and is supported with laboratory findings of cytopenia – anemia and thrombocytopenia, abnormal coagulation parameters with elevated D dimer, hypertriglyceridemia, hyperferritinemia, hypofibrinogenemia, and elevated liver function tests and with histiolytic infiltrates of hemopahocytosis on bone marrow. Hence diagnosis of Dengue associated HLH was made.

The aim of management of infection associated HLH is to treat the underlying cause that triggered it. Since there is no specific treatment for Dengue, aside from fluid therapy, treatment should intend to suppress the inflammatory response and control cell proliferation. In a study by Koshi, M et al in 2016 early administration of corticosteroids and or IV Immunoglobulins or cyclosporine A seemed to be successful in suppressing hyperinflammatory state and may be adequate for less severe cases. In relation with our patient, she was given Dexamethasone and IV immunoglobulin which showed improvement. Etoposide administration was considered with our patient however weighing the risk and benefit that this may further add insult to increasing liver enzymes this was not given.



BMA biospy: Normocellular Marrow with trilineage hematopoiesis. Moderate erythroid hyperplasia. Histiolytic infiltrates with hemophagocytosis

CONCLUSION

Early diagnosis of dengue associated HLH may be crucial but should be considered in patients presenting with prolonged fever, with organomegaly and cytopenia. Early intervention and recognition of disease with appropriate therapy with steroids and IVIg are important to improve outcome. Clinician must be aware of dengue complications so as to recognized and give immediate treatment to improve outcome.

REFERENCES

- Kan, F. K., Tan, C. C., Von Bahr Greenwood, T., Khalid, K. E., Supramaniam, P., Hed Myrberg, I., Tan, L. H., & Henter, J. I. (2020). Dengue Infection Complicated by Hemophagocytic Lymphohistiocytosis: Experiences From 180 Patients With Severe Dengue. *Clinical infectious diseases : an official publication of the Infectious Diseases Society of America*, *70*(11), 2247–2255. https://doi.org/10.1093/cid/ciz499
- Kapdi, Muznah; Shah, Ira (2012). Dengue and haemophagocytic lymphohistiocytosis. Scandinavian Journal of Infectious Diseases, 44(9), 708–709. doi:10.3109/00365548.2011.652667
- Takkinsatian, P., Sowithayasakul, P., & Prommalikit, O. (2020). Dengue associated haemophagocytic lymphohystiocytosis: An often-missed complication of a common infection. *The Medical journal of Malaysia*, *75*(5), 588–590.