

## Young Male with Secondary Acute Hemophagocytic Lymphohistiocytosis

Neeraj Kumar Tulara\*

Dr LH Hiranandani Hospital, Hillside Avenue, Hiranandani Gardens, Powai, Mumbai, India

### Abstract

Hemophagocytic lymphohistiocytosis (HLH), also known as hemophagocytic syndrome (HPS), is a rare life threatening hematologic disorder manifested by clinical findings of extreme inflammation and unregulated immune activation. HLH can occur as a familial or sporadic disorder, and it can be triggered by a variety of events that disrupts immune haemostasis. Infection is a common trigger both in those with a genetic predisposition and in sporadic cases. Often the greatest barrier to a successful outcome is delay in diagnosis, which is difficult because of the rarity of this syndrome. Here we, present a case of a young male who presented with enteric fever and confirmed as acute hemophagocytic syndrome and deteriorated rapidly inspite of quick diagnosis and treatment.

**Keywords:** Hemophagocytic lymphohistiocytosis; Hemophagocytic syndrome; Enteric (Typhoid) fever

### Case Summary

39 year old male, dentist by profession, was admitted on 05/05/2015 with complaints of persistent fever on and off since last one week and severe weakness. He also had maculopapular rashes all over the body with passage of blood in stools on and off since last 3-5 days. He was admitted outside and investigated for the same found to be positive for enteric fever (blood culture positive for *Salmonella typhi*) and started on the treatment with sensitive antibiotics for the same but continue to have fever hence shifted to our centre for further management. After reviewing his reports done outside he was having pancytopenia with deranged liver functions. A suspicion of acute hemophagocytosis was made and was investigated for the same. He had past history of left leg polio but no significant family history, no h/o any consanguineous marriage, no h/o and past surgery and prolonged hospitalization, no h/o and known systemic disease. He was a nonsmoker and nonalcoholic. On admission he was fully conscious, oriented, vital parameters stable, Temp 38°C, pallor and icterus present. Systemic examination was within normal limits. He had erythroderma of entire body. He was referred to surgeon for bleeding rectum, proctoscopy was done which was s/o grade II haemorrhoids and was treated conservatively. He was also referred to dermatologist who advised symptomatic treatment for erythroderma. He was also referred to hemato-oncologist who advised to start IV steroids along with IV Cefoperazone and Sulbactam and supportive treatment. He was investigated and reports were s/o pancytopenia (all three cell lines affected), elevated AST/ALT, high bilirubin predominantly conjugated, high ferritin >2000, high triglyceride >500, high LDH >3000, high uric acid >10, with elevated creatinine and prothrombin time. HIV, HbsAG, HAV, HEV, EBV, and dengue all virus makers were negative. Repeat blood culture was negative. Typhoid IgM antibodies were positive. Ultra sonogram of the abdomen was s/o hepato-splenomegaly. Chest X ray was within normal limits. He continues to have fever spike but his vitals remained stable and he was able to take full diet orally. His Bone marrow aspiration and biopsy was done to rule out any haematological malignancy. His Bone marrow biopsy report was suggestive of acute hemophagocytosis. On day 3 of admission he suddenly became breathless and shifted to ICU where initially he was put on noninvasive ventilator (NIV) followed by mechanical ventilator in next 6 hours as he continued to deteriorate. He had multi organ failure and succumbed to death in just 6 hours of his onset of breathlessness.

### Discussion

HLH is a rare disease characterised by uncontrolled proliferation of mature histiocytes, hemophagocytosis and up-regulation of

inflammatory cytokines. The more typical findings are fever, peripheral cytopenia affecting two lineages at least, hepato-splenomegaly, hypertriglyceridemia and/or hypo-fibrinogenemia, and hemophagocytosis. Recently Histiocyte society updated its guidelines [1] where five among eight of these criteria's should be fulfilled to confirm the diagnosis. They were present in our patient, who developed high persistent fever, severe pancytopenia, hepato-splenomegaly on ultra-sonogram, high levels of ferritin, triglyceride, LDH and presence of hemophagocytes in bone marrow. Despite extensive investigations, initial blood culture positive for salmonella and presence of typhoid antibodies later was the only

	05/05/2015	06/05/2015	07/05/2015	08/05/2015
Hb	8.8	7.5	8.6	7.5
WBC (Neu%)	2600 (21%)	800 (15%)	800 (20%)	300 (20%)
Plat	62000	47000	37000	11000
INR	1.41			2.49
AST	535		248	
ALT	399		278	
AlPhos	485		544	
GGT	222		307	
T.Bil	5.03		6.95	
Conj. Bil	4.28		4.68	
Unconj. Bil	0.00		0.44	
T. Protien	5.53		4.53	
Albumin	3.08		2.42	
Globulin	2.45		2.11	
Creat	1.63		1.18	1.94
Uric acid	10.31			
Calcium	6.89			
Pohs	2.87			
Na	131			141
K	2.87			3.77
Cl	96.90			104.60

Table 1: Investigation done for 3-5 days in individuals.

\*Corresponding author: Neeraj Kumar Tulara, Dr LH Hiranandani Hospital, Hillside Avenue, Hiranandani Gardens, Powai, Mumbai 400076, India, Tel: +91-9833552955; E-mail: [drntulara@rediffmail.com](mailto:drntulara@rediffmail.com)

Received: February 24, 2016; Accepted: March 07, 2016; Published: March 10, 2016

Citation: Tulara NK (2016) Young Male with Secondary Acute Hemophagocytic Lymphohistiocytosis. Oncol Cancer Case Rep 1: 111.

Copyright: © 2016 Tulara NK. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

positive result able to explain the initial symptoms and secondary HLH. The list of possible etiologies for secondary HLH is long and includes infections (mainly EBV, herpes simplex virus, cytomegalovirus, avian influenza) [2-4], rheumatologic diseases (rheumatoid arthritis, systemic lupus erythematosus, Kawasaki disease, adult onset still's disease) [5,6] malignancy (natural killer cell leukaemia, peripheral T cell lymphoma) [7,8] acquired immune deficiency states (after organ transplants), and drugs [9]. In patients who present with secondary HLH, treatment of the underlying cause can lead to control and resolution of HLH but our patient's case was dramatically different, with rapid evolution to a lethal multi organ failure syndrome in spite of starting treatment for the primary reason i.e. *salmonella typhi* as in our case. Our case is unique as, so far there is no case report of secondary HLH where the primary infection is bacterial mainly *salmonella typhi* (Table 1).

### Conclusion

Hemophagocytic lymphohistiocytosis with multi organ failure syndrome can be induced by the *Salmonella typhi*. Despite its rarity, clinicians should be aware of this possibility to enable early diagnosis and treatment.

### References

1. Henter JL, Horne A, Arico M, Egeler RM, Filipovich AH, et al. (2007) HLH –2004:

Diagnostic and therapeutic guidelines for Hemophagocytic Lymphohistiocytosis. *Pediatr Blood Cancer* 48: 124-131.

2. Phillips J, Staszewski H, Garrison M (2008) Successful treatment of secondary hemophagocytic lymphohistiocytosis in a patient with disseminated histoplasmosis. *Hematology* 13: 282-285.
3. Imashuku S (2011) Treatment of Epstein-Barr virus-related hemophagocytic lymphohistiocytosis (EBV-HLH); update 2010. *J Pediatr Hematol Oncol* 33: 35-39.
4. Fisman DN (2000) Hemophagocytic syndromes and infection. *Emerg Infect Dis* 6: 601-608.
5. Cortis E, Insalaco A (2006) Macrophage activation syndrome in juvenile idiopathic arthritis. *Acta Paediatr Suppl* 95: 38-41.
6. Parodi A, Davi S, Pringe AB (2009) Macrophage activation syndrome in juvenile systemic lupus erythematosus: a multinational multicenter study of thirty-eight patients. *Arthritis Rheum* 60: 3388-3399.
7. Celkan T, Berrak S, Kazanci E (2009) Malignancy-associated Hemophagocytic Lymphohistiocytosis in pediatric cases: a multicenter study from Turkey. *Turk J Pediatr* 51: 207-213.
8. Kelesidis T, Humphries R, Terashita D (2012) Epstein-Barr virus-associated hemophagocytic lymphohistiocytosis in Los Angeles County. *J Med Virol* 84: 777-785.
9. Finkielman JD, Grinberg AR, Paz LA (1996) Case report: reactive hemophagocytic syndrome associated with disseminated strongyloidiasis. *Am J Med Sci* 312: 37-39.