

Young Male with Secondary Acute Hemophagocytic Lymphohistiocytosis

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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 hemostasis. 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.

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Key words: Hemophagocytic Lymphohistiocytosis(HLH); Hemophagocytic syndrome (HPS); Enteric (Typhoid) fever

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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 consanguinous marriage, no h/o and past surgery and prolonged hospitalization, no h/o and known systemic disease. He was a non smoker and non alcoholic.

On admission he was fully conscious, oriented, vital parameters stable, Temp 38 degree C, pallor and icterus present. Systemic examination was within normal limits. He had erythoderma of entire body.

He was referred to surgeon for bleeding rectum, proctoscopy was done which was s/o grade II hemorrhoids and was treated conservatively. He was also referred to dermatologist who advised symptomatic treatment for Erythoderma. He was also referred to hematologist who advised to start IV steroids along with IV Cefaperazone 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 markers were negative. Repeat blood culture was negative. Typhoid IgM antibodies was positive. Ultrasonogram of the abdomen was s/o hepatosplenomegaly. Chest X ray was within normal limits.

He continue 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 hematological malignancy. On day 3 of admission he suddenly became breathless and shifted to ICU where initially he was put on non invasive ventilator (NIV) followed by mechanical ventilator in next 6 hours as he continued

to deteriorate. He had multiorgan failure and succumbed to death in just 6 hours of his onset of breathlessness. His Bone marrow biopsy report which came next day was consistent with Acute Hemophagocytosis.

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, hepatosplenomegaly, hypertriglyceridemia and/or hypofibrinogenemia, and hemophagocytosis. Recently Histiocyte society updated its guidelines^[1] where five among eight of these criteria should be fulfilled to confirm the diagnosis. They were present in our patient, who developed high persistent fever, severe pancytopenia, hepatosplenomegaly on ultrasonogram, high levels of ferritin, triglyceride, LDH and presence of hemophagocytes in bone marrow.

Despite an extensive investigations, initial blood culture positive for salmonella and presence of typhoid antibodies later was the only 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 leukemia, 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.

CONCLUSIONS

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.

CONFLICT OF INTEREST

There are no conflicts of interest.

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	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.Protein	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

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