Original Research Paper

Volume-9 | Issue-9 | September - 2019 | PRINT ISSN No. 2249 - 555X | DOI : 10.36106/ijar

Gastroenterology

GASTRIC – T CELL LYMPHOMA ASSOCIATED HEMOPHAGOCYTIC LYMPHOHISTIOCYTOSIS.

Senthamizhselvan K* Department of Medical Gastroenterology, JIPMER, Puducherry, India. *Corresponding Author

Mohammed A Department of Medical Gastroenterology, Madras Medical College, Chennai

ABSTRACT **Background:** Hemophagocytic lymphohistiocytosis (HLH) is a rare entity in clinical practise. It can occur in the setting of infection, malignancy, autoimmune disease and immunodeficiency.

Case report: We present a case of 18 years old male who had fever, rapid weight loss and upper gastrointestinal bleeding during the past 1 month. Gastroscopy showed an ulcerated lesion in stomach, histopathology and immunohistochemistry was suggestive of gastric T-cell lymphoma (NHL). Patient had persistent fever and drop in cell counts of all 3 lineages. Bone marrow examination revealed hemophagocytosis secondary to gastric T-cell NHL. His general condition worsened rapidly and he succumbed to his illness, before any definitive therapy could be initiated.

Conclusion: One should have a high index of suspicion to diagnose HLH, so as to initiate early treatment and improve survival.

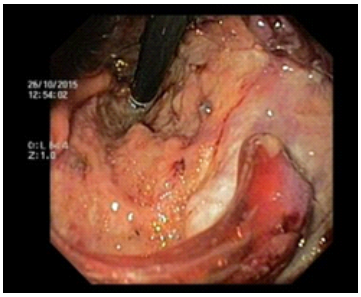
KEYWORDS : Hemophagocytic lymphohistiocytosis, Lymphoma, Ulcer, Gastroscopy

INTRODUCTION:

Hemophagocytic lymphyohistiocytosis (HLH) is a life threatening condition caused by excessive immune activation. HLH can be primary or secondary to triggers like infection, malignancy, autoimmune disease and immune deficiency status. Malignancy associated HLH may constitute upto 20% of secondary HLH [1], of them hematological malignancies constitute a major proportion [2]. They carry a grave prognosis inspite of an aggressive management [3]. Here we report a case of secondary HLH due to gastric T-cell lymphoma. Gastric T-cell lymphoma presenting as gastrointestinal bleed and developing HLH, has not been reported in literature.

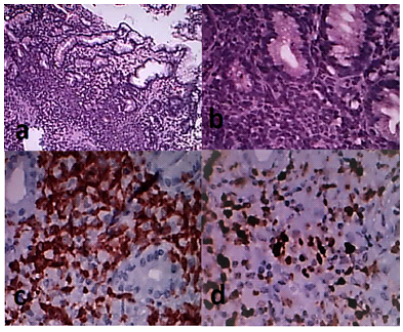
CASE REPORT:

An 18 year old male presented with fever for the past 1 month. It was intermittent and of high grade without rigors, arthralgia, myalgia and night sweats. He had easy fatiguability, decreased appetite and lost 8 kgs of weight. He had melenic stools during the past 1 week. Few hours before presentation he had hemetemesis, thrice, each bout around 250ml of fresh bleed. After that he developed orthostatic giddiness and palpitation. He did not have jaundice, abdominal distension, leg swelling and altered sensorium. There were no significant medical ailments in the past. He is the elder of the two siblings with no family history of gastrointestinal diseases. On examination he was pale and drowsy and his pulse rate was 106/min, blood pressure was 90/60mm of Hg. Per abdomen: liver was palpable 4cm below right subcostal margin and spleen was palpable 8 cm below left subcostal margin and both were firm and non-tender. Blood investigation on admission revealed severe anemia. He was stabilized with two units of packed red blood cells and an emergency gastroscopy was performed which showed an ulcerated lesion in the lesser curvature of the stomach [Figure-1].



[Figure-1: Gastroscopy image showing an ulcerated lesion in stomach]

Multiple biopsies were taken from the lesion and histopathology revealed lymphomatous cellular infiltration with atrophy of gastric glands [Figure-2a, 2b]. The immunohistochemistry panel revealed CD-3 positive cells [Figure-2c], with ki 67 index >20 % [Figure-2d] and markers like CD-10, CD-20, CK-7, Cyclin D1 and myeloperoxidase were negative.



[Figure -2 Histopathology images: a) Low power microscopy showing lymphomatous cellular infiltration in gastric mucosa, b) High power microscopy showing lymphomatous cells, c) Immunohistochemistry panel showing CD-3 positive cells, d) Image showing ki 67 index >20%]

The CT scan of the abdomen showed hepatomegaly with splenomegaly and enlarged para-aortic, peri-gastric and peri- splenic lymph nodes. The CT scan of the chest did not reveal any abnormality Hence a diagnosis of Gastric T-cell Lymphoma with a high mitotic index [ki67 >20%] was made. Patient's general condition worsened rapidly. His performance status was poor [ECOG-3]. His Serum LDH level was 849 u/l and International Prognostic Index was 4/5. He had persistent high grade fever with chills. A comprehensive fever evaluation was unyielding. His serial blood count values showed continuous drop in all the three cell lineages. Peripheral Smear study showed normocytic, macrocytic, RBCs low in number, very few granulocytes and platelets. Serum ferritin level was 1850µg/l. The reticulocyte count was 0.3%. Bone marrow examination showed marrow elements being phagocytosed by macrophages. Hence a final diagnosis of Hemophagocytic lymphohistiocytosis, secondary to gastric –T cell lymphoma was made. Due to very poor performance status, cyto-reductive therapy was given. He received steroids and supportive treatment but finally succumbed to his illness.

DISCUSSION:

Hemophagocytic lymphohistiocytosis (HLH) is a syndrome of excessive cytokine storm and overwhelming inflammatory response [4]. It frequently affects very early in life, but may occur at any age. Primary or familial HLH is caused by gene mutations in a familial HLH locus. It is common in children. Secondary HLH is usually triggered by systemic infections, malignancies and rheumatologic diseases. However, 10% of adults may have underlying genetic mutations [5]. Clinical presentation of secondary HLH include fever, splenomegaly, hepatomegaly, lymphadenopathy, jaundice, skin rash, meningism and seizure. Laboratory investigations may reveal cytopenias, elevated triglycerides due to TNFα inhibition of lipoprotein lipase and elevated serum ferritin due to increased IL-1β, secreted by macrophages. Hemophagocytosis, if present is highly

pathognomonic, but it may be absent in early stages [6]. The differential diagnosis for HLH include severe sepsis, acute leukemia and thrombotic thrombocytopenic purpura. These conditions can be ruled out by thorough investigations like: chest x-ray, blood culture, urine culture, fungal culture and fungal serology, viral serology for EBV, CMV, Parvo virus, HIV and HHV-6, evaluation for lymphoproliferative disorders by pan scan, bone marrow biopsy. If there is a recent travel to endemic areas or animal exposure, evaluation for Leishmaniasis, Brucellosis, Rickettsioses and Malaria has to be done, Cryptococcosis and Toxoplasmosis has to be ruled out in immunocompromised patients. The criteria proposed by Henter et al is used widely for the diagnosis of HLH [7]. (Table – 1)

Table-1 (Diagnostic criteria for HLH)

S.No	FEATURE
1	Peak temperature >38.5 degree celsius for seven or more days
2	Splenomegaly
3	Cytopenias involving two or more cell lines
4	Hypertriglyceridemia
5	Hemophagocytosis demonstable in bone marrow, spleen or lymph node
6	Hepatitis
7	Serum ferritin level >500 µg/l
8	Low or absent NK-Cell activity
9	Soluble CD-25 >2400 u/ml

The diagnosis of HLH requires atleast five of the above criteria. Our patient has five among these namely fever, splenomegaly, cytopenia, high serum ferritin and hemophagocytosis and hence a diagnosis of HLH was made. Treatment of HLH has to be initiated promptly as a delay in therapy may lead to irreversible multi-organ failure. However the course of the illness may progress rapidly. Various treatment options include steroids, cyclosporine, chemotherapeutic agents like cyclophosphamide, doxorubicin, vincristine, etoposide, biologicals like anti – Thymocyte globulin, IL-1 receptor antagonist, anti-IL-6 and anti-TNF alfa agents, intravenous immunoglobulin, Rituximab (anti-CD 20) and Alemtuzumab (anti- CD 52). Among patients with lymphoma related HLH those with B – cell lymphomas have better prognosis, this may be due to effective chemotherapeutic drugs against them. Allogenic hematopoietic stem cell transplantation can improve survival in patients with lymphoma related HLH due to a graft versus lymphoma effect [8].

CONCLUSION:

In conclusion, HLH is a fatal syndrome which requires a high index of suspicion for diagnosis. Prompt initiation of a personalized treatment may improve the survival.

REFERENCES:

1. Li F, Li P, Zhang R, Yang G, Ji D, Huang X, et al. Identification of clinical features of lymphoma-associated hemophagocytic syndrome (LAHS): An analysis of 69 patients with hemophagocytic syndrome from a single-center in central region of China. Med Oncol 2014; 31:902.
2. Riviere S, Galicier L, Coppo P, Marzac C, Aumont C, Lambotte O et al. Reactive hemophagocytic syndrome in adults: a retrospective analysis of 162 patients. Am J Med 2014;127(11):1118–25.
3. Otrock ZK, Eby CS. Clinical characteristics, prognostic factors, and outcomes of adult patients with hemophagocytic lymphohistiocytosis. Am J Hematol 2015;90(3):220–4.
4. Larroche C, Mouthon L et al.Pathogenesis of hemophagocytic syndrome (HPS). Autoimmun Rev 2004;3(2):69–75.
5. Zhang K, Jordan MB, Marsh RA, Johnson JA, Kissell D, Meller J et al .Hypomorphic mutations in PRF1, MUNC13-4, and STXBP2 are associated with adult-onset familial HLH. Blood 2011;118;(22):5794-8.
6. Arico M, Janka G, Fischer A, Henter JI, Blanche S, Elinder G et al. Hemophagocytic lymphohistiocytosis. Report of 122 children from the international registry. FHL study group of the histiocyte society. Leukemia 1996;10(2):197-203.
7. Henter JI, Horne A, Aricó M, Egeler RM, Filipovich AH, Imashuku S et al. HLH-2004: diagnostic and therapeutic guidelines for hemophagocytic lymphohistiocytosis. Pediatr Blood Cancer 2007;48(2):124–31.
8. Hosing C, Champlin RE et al. Stem-cell transplantation in T-cell non-Hodgkin's lymphomas. Annals of Oncology: Official Journal of the European Society for Medical Oncology / ESMO 2011;22(7):1471–1477.