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Case Report

Adult-onset Still's disease presenting with acute liver failure caused by haemophagocytic lymphohistiocytosis: a case report

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Introduction

Adult-onset Still's disease (AOSD) is an idiopathic inflammatory disorder with multiorgan involvement and is a diagnosis of exclusion, requiring exclusion of autoimmune, infective and malignant disorders. Haemophagocytic lymphohistiocytosis (HLH) is an immune-mediated condition with both infectious and non-infectious triggers and is a rare, but serious, complication of AOSD. Systemic lupus erythematosus and AOSD are the leading autoimmune causes of HLH. Acute liver failure is defined as acute (within 4 weeks) derangements of liver functions with coagulopathy and an altered level of consciousness without background chronic liver disease (1). Acute liver failure is a rare association of HLH.

Case Presentation

A 19-year-old, unmarried female presented with fever, arthritis and a rash of three weeks duration. On admission, she had yellowish discolouration of the eyes, drowsiness and an inverted sleep-wake pattern, with epistaxis and haematuria. On examination, she was febrile and drowsy with moderate icterus and mild pallor. There was a maculopapular, non-evanescent, salmon- coloured rash over the trunk and limbs. Apart from mild pharyngeal inflammation, there was no mucosal involvement. Abdominal examination elicited marked right hypochondrial tenderness. Musculoskeletal examination revealed large joint oligoarthritis.

Full blood count showed a neutrophilic leukocytosis with gradual development of bicytopenia. Inflammatory markers were elevated. Ultrasound abdomen revealed mild splenomegaly and increased echogenicity of the liver without bile duct dilatation. Liver functions and coagulation profile were deranged; aspartate transaminase (AST) 1850 IU/L, alanine transaminase (ALT) 615 IU/L, alkaline phosphatase (ALP) 123 IU/L, gamma-glutamyl transferase (GGT) 910 U/L , serum total bilirubin 28 mg/dl (82 % direct), international ratio (INR) 7 and activated partial thromboplastin time (aPPT) 100s. Thromboelastometry (TEM) showed a highly prolonged clot-forming

time (CFT) with normal INTEM and EXTEM clotting times, probably due to thrombocytopenia and hypofibrinogenemia. Serum ferritin level was 8453 ng/mL. The bone marrow biopsy revealed evidence of haemophagocytosis (Figure 1). Haemophagocytic lymphohistiocytosis was further evidenced by a low fibrinogen level of 128 mg/dl, hypertriglyceridaemia of 684 mg/dl and elevated lactic acid dehydrogenase (LDH) of 1200 U/L. The clinical and laboratory evaluation was consistent with the Yamaguchi criteria [2] for the diagnosis of ASOD. In addition, the patient fulfilled the diagnostic criteria for haemophagocytic lymphohistiocytosis [3]. Her disease activity was complicated by clinical and biochemical evidence of acute liver failure.

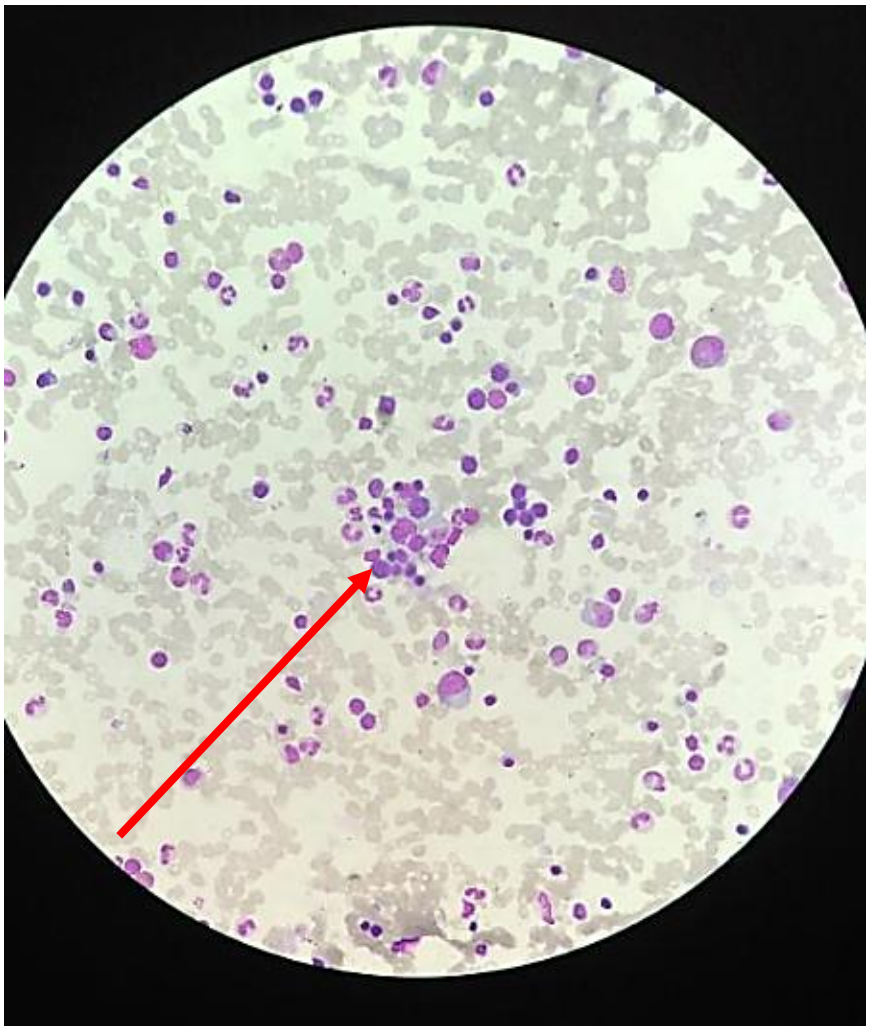

Figure 1: Large histiocytes (red arrow) engulfing red blood cells in the bone marrow biopsy.

The initial management was for acute liver failure with hepatic encephalopathy and coagulopathy. Bleeding was managed with; local measures-gentle nasal suction, anterior nasal packing and elevated head position; systemic treatment - IV vitamin K 10mg daily for 3 days, IV tranexamic acid 500mg tds and transfusion of 1 unit of

packed red blood cells, 10 units of cryoprecipitate and 6 units of platelets. To treat the hepatic encephalopathy, the patient was kept in a quiet environment in a raised head end position, without sedation. Lactulose was titrated to promote laxation and suppress straining. Liver protective treatment with N-acetyl cysteine (NAC) was prescribed along with rifaximin, a broad spectrum, non-absorbent antibiotic. During this period water-electrolytes, acid-base and metabolic equilibrium were maintained. HLH, the culprit for the acute liver failure, was treated with methylprednisolone pulses, 1g daily for 3 days followed by a tailing-off regime of oral prednisolone. Once the patient recovered from the acute liver failure and encephalopathy, steroid-sparing immunomodulatory treatment with oral ciclosporin 100 mg/daily along with NSAIDS commenced. The patient had a complete recovery and is now on routine clinic follow up with regular monitoring.

Discussion

Adult-onset Still's disease is a cytokine-mediated inflammatory disorder with interleukin 6 (IL-6), tumour necrosis factor (TNF-α), and interferon-γ (IFN-γ) involved in disease activity [4]. Our patient fulfilled all major and minor Yamaguchi criteria [2] and the evaluation excluded infections, malignancies and other autoimmune diseases. Haemophagocytic lymphohistiocytosis is a type of histiocytic disorder related to macrophage activation. HLH is triggered by infections, autoimmune disorders and malignancies. The cytokine storm along with the accumulation of lymphocytes and mature macrophages in the lymphoreticular system is believed to be responsible for target organ damage in HLH. Further tests for the diagnosis of HLH including NK-cell activity and soluble CD25 assays are not available in our set up. Our patient fulfilled all the other available criteria. Acute liver failure is a dreaded complication of HLH with a high mortality. HLH mediated liver injury is an area of much debate. One hypothesis is that cytokine activation in HLH results in hepatic endothelial disruption and TNFα mediated activation of Kupffer cells inducing apoptosis [5]. Our patient had HLH induced acute liver failure and the diagnosis of HLH in the background of AOSD was a challenge as many features such as hyperferritinaemia, transaminitis, deranged coagulation, cytopaenia and organomegaly were non-specific and seen in both HLH and AOSD. But a high degree of clinical suspicion led to early diagnosis and prompt treatment with an excellent outcome.

Conclusions

Adult-onset Still's disease is a diagnosis of exclusion and is occasionally accompanied by haemophagocytic lymphohistiocytosis. Acute liver failure is a dreaded complication of HLH. A high degree of clinical suspicion aids early recognition and treatment.

Abbreviations

AOSD	adult-onset Still's disease
HLH	haemophagocytic lymphohistiocytosis
AST	aspartate transaminase
ALT	alanine transaminase
ALP	alkaline phosphatase
GGT	gamma-glutamyl transferase

INR	international ratio
aPPT	activated partial thromboplastin time
TEM	thromboelastometry
LDH	lactic acid dehydrogenase
NAC	N-acetyl cysteine
IL-6	interleukin 6
TNF-α	tumour necrosis factor
IFN-γ	interferon-γ

References

1. Wendon J, Cordoba J, Dhawan A. EASL clinical practical guidelines on the management of acute (fulminant) liver failure. Journal of [Internet]. 2017; https://doi.org/10.1016/j.jhep.2016.12.003
2. Efthimiou P, Paik PK, Bielory L. Diagnosis and management of adult onset Still's disease. Ann Rheum Dis. 2006 May;65(5):564-72. https://doi.org/10.1136/ard.2005.042143
3. Henter JI, Horne AC, Aricó M, Egeler RM. HLH-2004: diagnostic and therapeutic guidelines for hemophagocytic lymphohistiocytosis. Pediatr Blood Cancer [Internet]. 2007 https://doi.org/10.1002/pbc.21039
4. 4. Gerfaud-Valentin M, Jamilloux Y, Iwaz J, Sève P. Adult-onset Still's disease [Internet]. Vol. 13, Autoimmunity Reviews. 2014. p. 708-22. https://doi.org/10.1016/j.autrev.2014.01.058
5. Padhi S, Sarangi R, Patra S, Chandra Samal S. Hepatic Involvement in Hemophagocytic Lymphohistiocytosis. In: Hepatitis A and Other Associated Hepatobiliary Diseases [Working Title]. IntechOpen; 2020. https://doi.org/10.5772/intechopen.90238