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*Case Report*

# Macrophage Activation Syndrome complicated with acute pancreatitis as the first presentation of Systemic lupus Erythematosus

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**Abstract**

Hemophagocytic Lymphohistiocytosis (HLH) is a severe hyperinflammatory syndrome induced by aberrantly acquired macrophages and cytotoxic T cells. The primary form is called the Genetic form where as the secondary acquired form is most common in adults. Secondary HLH induced by autoinflammatory or autoimmune disorders is called Macrophage activation syndrome (MAS or MAS-HLH). Here we present a case of Systemic lupus Erythematosus presenting for the first time with MAS-HLH associated with acute pancreatitis, emphasizing the challenges in early detection and the need for prompt treatment, given the high mortality associated with MAS-HLH.

**Key Words**

Macrophage activation Syndrome, SLE, Pancreatitis

## Introduction

Macrophage Activation Syndrome (MAS) is a life-threatening disorder, first described by Hadchouel et al in 1985(1).It belongs to the hemophagocytic lymphohistiocytosis (HLH) group of diseases, which includes Primary HLH and secondary HLH. Primary is the genetic form caused by the mutations affecting lymphocyte toxicity and secondary HLH is caused by infections/malignancies/ autoinflammatory or autoimmune disorders.

Secondary hemophagocytic lymphohistiocytosis associated with autoimmune diseases or autoinflammatory disorders is said to be Macrophage activation syndrome. As there will be overwhelming immune activation leading to cytokine storm, patients with MAS-HLH present with fever, cytopenia, liver dysfunction and a sepsis like syndrome that can rapidly progress into multiple organ failure(2)..

The incidence of MAS associated with Systemic Lupus erythematosus is re about 0.9% to 4.6%(3). Acute pancreatitis, can occur as an uncommon initial manifestation of SLE, can complicate MAS. Acute pancreatitis can be an associated or triggering factor for MAS in patients with SLE. Acute pancreatitis in SLE may arise from various causes like autoimmune inflammation, drug induced reactions or secondary to infections. We present here a case of MAS-HLH complicated with acute pancreatitis as the first presentation of SLE.

## Case presentation

A 16-year-old female patient presented with a history of high-grade fever for 10 days duration, associated with nausea and abdominal pain. There were no respiratory symptoms, and she denied joint pain or hair loss. She complained of abdominal pain in the epigastric area. Her past medical and family history was non-significant.

On presentation to the ward, she was conscious and oriented with the GCS 15/15. She was febrile, with a temperature of 39.8°C, a Pulse rate of 102 bpm regular sinus rhythm, BP 90/60mmHg, and $SPO_2$ on room air 99%. She was also pale, and oral ulcers were noted. There was epigastric region tenderness, but no organomegaly or lymphadenopathy. The rest of her examination was unremarkable. Her abdominal ultrasound was normal, without evidence of organomegaly. Her chest X-ray was normal. A blood picture revealed pancytopenia. She was given barrier nursing care and has been started on empirical broad-spectrum antibiotic meropenem based on her clinical presentation and initial investigations after taking blood and urine cultures. Despite treatment with broad-spectrum antibiotics, she continued to have a fever. Her further investigations revealed that LDH-281u/l, serum ferritin-3390ng/ml, fasting triglycerides

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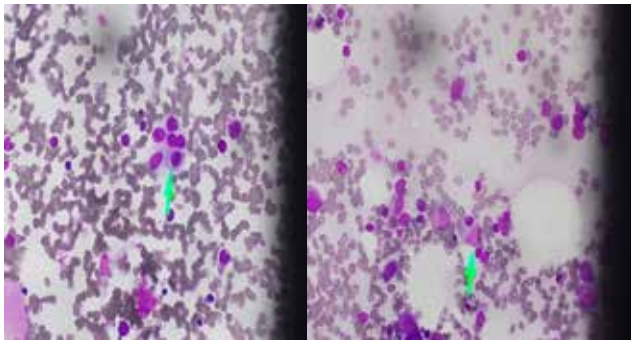
3.55U/L, and elevated liver transaminases. Viral serology for HIV and Ebstein bar virus was negative. Blood culture and urine culture showed no growth.

**Table 1: Investigation**

| Investigation | On admission |
|---|---|
| WBC | 0.74 * $10^9$ |
| Neutrophil | 0.21 * $10^9$ |
| Lymphocyte | 0.48* $10^9$ |
| Hemoglobin | 9.2g/dl |
| MCV | 84fL |
| MCH | 29pg |
| Platelet | 119 * $10^9$ |
| LDH | 2815u/l |
| Ferritin | 3000 ng/ml |
| Fasting Triglyceride | 309 mg/dl |
| ESR | 14 mm in first hour |
| CRP | 4.6mg/l |
| Serum amylase | 1940u/l |
| Sodium | 128 mmol/l |
| Potassium | 4.2mmol/l |
| Serum Creatinine | 48 micromol/l |
| AST | 296u/l |
| ALT | 172u/l |

On the 3rd day of admission, she complained of worsening abdominal pain mainly epigastric pain radiating to the back which was unrelated to meals. There was severe tenderness noted in the epigastric region. Blood was taken for serum amylase, and it was elevated at 1940u/l. A clinical diagnosis of acute pancreatitis was made. She was given intravenous fluid, and continued antibiotics, and analgesics. After 2 days her abdominal pain improved, and her general condition got better.



Figures 1 and 2- Bone marrow biopsy showing evidence of prominent histiocytes with hemophagocytic activity

In the meantime, her bone marrow biopsy showed evidence of prominent histiocytes with hemophagocytic activity as shown in Figures 1 and 2. Together with other clinical and biochemical parameters, she met the diagnostic criteria of HLH.

Her ANA was 1:2560 with a homogenous pattern, Ds DNA was negative and complement levels were low. With these results, she met the diagnostic criteria of SLE and the diagnosis of MAS-HLH was established she was treated with methylprednisolone pulse therapy for five days followed by oral prednisolone. Her counts started to rise, her fever subsided and her general condition improved and subsequently discharged home.

**Discussion**

MAS, which is currently grouped under secondary or acquired hemophagocytic lymphohistiocytosis (MAS_HLH), is a rare and fatal disorder that results from excess activation of T-cells and macrophages (4).

Clinically, MAS is characterized by symptoms such as persistent fever, cytopenia, liver dysfunction, and elevated levels of ferritin, LDH, and triglycerides. The hallmark of MAS is hemophagocytosis observed in bone marrow, liver, or lymph nodes, where activated macrophages engulf red blood cells, white blood cells, and platelets. Diagnosing MAS is challenging due to its overlap with other inflammatory conditions and infections, especially in patients with underlying autoimmune diseases like SLE. The criteria for diagnosing MAS include clinical features, laboratory abnormalities, and histopathological evidence of hemophagocytosis. The H-score, a diagnostic tool that incorporates clinical and laboratory parameters, is often used to assess the likelihood of HLH/MAS. However, differentiating MAS from other causes of systemic inflammation can be difficult, necessitating a high index of suspicion and prompt investigation. Our patient had a fever, a history of oral ulcers, cytopenia and low C3 and C4 levels, fulfilling the SLE diagnostic criteria. The association between SLE and MAS is well-documented, with studies indicating that up to 15% of SLE patients may develop MAS during their disease course.

Acute pancreatitis, although an uncommon initial manifestation of SLE, can complicate MAS, as

highlighted in this case. However, the relationship between acute pancreatitis and HLH was first considered in 1998 by Kanaji et al, who found that HLH can be associated with fulminant ulcerative colitis and acute pancreatitis (5).

Several studies have indicated that 53% to 85% of SLE patients with pancreatitis also have MAS (6). Acute pancreatitis in SLE patients with MAS is particularly concerning due to the additional inflammatory burden it imposes. Hence, The pancreas can be the target organ in MAS in patients with SLE warranting evaluation of pancreatic enzyme**s** (7).

It is important to be aware that pancreatitis and MAS can occur concurrently, with an underlying autoimmune disease, such as SLE. As patients with MAS associated with pancreatitis have a high mortality rate, early recognition and prompt treatment help prevent complications(8).

**Conclusion**

Hemophagocytic Lymphohistiocytosis syndrome can present with a wide range of symptoms making the diagnostic approach challenging. A high degree of suspicion is required for the possibility of HLH and the early diagnosis should be done through the diagnostic criteria in addition to looking for causative factors of secondary HLH. MAS with acute pancreatitis in SLE needs early identification and prompt treatment to avoid complications and to improve the outcome

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