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CASE REPORT

Recurrent Episodes of Acute Pancreatitis as an Initial Presentation of Systemic Lupus Erythematosus and Autoimmune-Associated Hemophagocytic Syndrome

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Abstract

Acute pancreatitis(AP) is a rare but fatal complication of systemic lupus erythematosus (SLE). A 40-year-old male presented with high-grade intermittent fever, abdominal pain & painless oral ulcers. Investigations revealed features suggestive of AP and coexistent SLE. Based on the H score and bone marrow aspiration findings, the diagnosis of secondary hemophagocytic syndrome (HPS)/autoimmune associated HPS (AAHS)/macrophage activation syndrome (MAS) was made. Autoimmune-associated HPS, We report a 40-year-old male case of SLE who presented with features suggesting AP, developed macrophage activation syndrome (MAS) on day 7 of admission.

Key Words

Acute pancreatitis, Systemic Lupus Erythematosus, AHAS, macrophage activation syndrome

Introduction

Gastrointestinal (GI) manifestations can be present in 50% of patients with Systemic lupus erythematosus (SLE).[1] Acute pancreatitis (AP) in SLE may occur due to disease per se or as a treatment complication, with the overall incidence being in the range of 0.9-5%.[2] AP as an initial manifestation of SLE, which has been reported occasionally.[3].The incidence and prevalence of Macrophage activation syndrome (MAS) with lupus pancreatitis is unknown. We report a 40-year-old male with SLE who presented with features suggestive of AP who progressed to develop MAS on day 7 of admission

Case report

A 40-year-old male presented with complaints of high-grade intermittent fever for the last 20 days, abdominal pain for the last 2 days. There were multiple ulcers in the oral cavity with a malar rash affecting the nasal bridge. There was the presence of bilateral cervical lymphadenopathy of 2-3 cm in size, not fixed to underlying structures and no discharging sinus. Per abdominal examination revealed tenderness over the epigastric region and splenomegaly. There was no other organomegaly. Routine blood investigations on the day 1 of admission, revealed bicytopenia, deranged Renal Function Test (RFT) and elevated amylase & lipase levels of 1088 U/L & 1840 U/l respectively. Ultrasound (USG) revealed a bulky pancreas with peripancreatic fat stranding and splenomegaly. Sepsis panel revealed elevated procalcitonin (8ng/ml), ESR (130 mm in 1st hour), CRP (12.49 mg/dl), Serum Ferritin (5196 ng/ml). Infective fever panel was negative. Urine routine microscopy showed 3+ proteinuria. Sterile blood & urine

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Fig 1. CT Scan of Abdomen Showing Bulky Pancreas with Peripancreatic Fat Stranding Affecting Head, Neck, and Tail of Pancreas, Suggestive of Acute Pancreatitis.

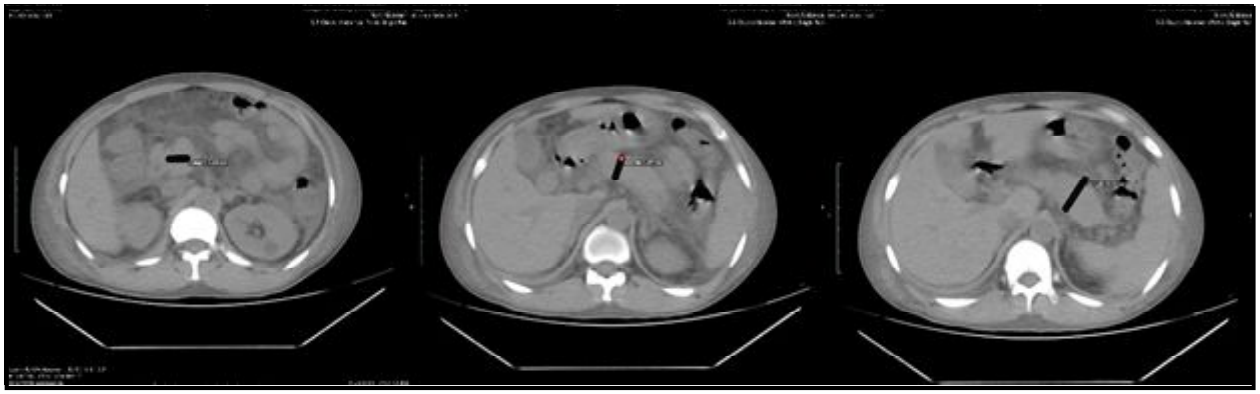
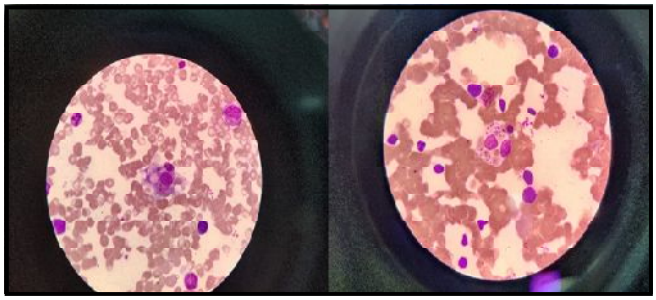


Fig 2. Bone Marrow Aspirate Showing Hypercellular Bone Marrow with Increased Hemophagocytic Histiocytes and Macrophages Engulfing both Myeloid and Erythroid cells



cultures were noted. His Liver Function Test (LFT) was deranged with SGOT of 469 IU/ml, SGPT of 234 IU/ml and serum Albumin of 1.5 mg/dl. He complained of severe calf pain associated with redness and tenderness. His Creatine Phosphokinase (CPK) levels were 4237 U/L, and d-dimer was 2 mcg/ml.

He had persistent high-grade fever. Repeat complete blood count (CBC) on day 5 of admission revealed bicytopenia worsening to pancytopenia. Anti-nuclear Antibody (ANA) profile showed high titers of Anti ds-DNA Ab, Anti SSA Ab, Anti Ribosomal Ab and Anti Ro52 Ab positivity, confirming it to be a case of SLE. He was started with Injection methylprednisolone 1 gm IV once daily for 3 days (day 5-day 8), along with Injection Human Albumin 20% in view of severe hypoalbuminemia. After pulse methylprednisolone for 3 days, the patient was started with injection hydrocortisone 50 mg QID and continued. Injection IV immunoglobulin40 gm/day was started on day 8 of admission and continued for 3 days. Hydroxychloroquine 300 mg once daily was advised.

Repeat USG on day 8 of admission, showed thickened bowel wall with narrowing of the lumen with bulky pancreas (signs of vasculitis), moderate ascites and splenomegaly. Given the evidence of ongoing vasculitis, Injection Cyclophosphamide 10mg/kg body weight and injection Mesna were administered on day 9 of admission.

Fig 3. Blood Agar and McConkey Agar of Sputum Culture Showing ElizabethkingiaMeningoseptica

Pancytopenia worsened further, Serum fibrinogen was 308 mg/dl, serum triglyceride was 292mg/dl, serum ferritin was 5196 ng/ml, and AST 92 U/L. CT scan of the abdomen on day 10 of admission revealed AP with peripancreatic fat stranding & minimal fluid collection with a CT severity index of 6 (*Fig 1*). Reactive hemophagocytic syndrome was suspected based on an H Score of 223 points (96-98% probability).Aspiration of bone marrow demonstrated hypercellular bone marrow with increased megakaryocytes and hemophagocytic histiocytes engulfing both white blood cells (WBC) and red blood cells (RBC) (*Fig 2*).

Following the next 2 days (day 11- day 13), the patient improved symptomatically with subsiding fever and improvement in blood parameters, but developed a productive cough with mucoid expectoration. Sputum culture showed Elizabethkingia Meningoseptica, a gram-negative bacillus, which was treated with injection Meropenem and Clindamycin, for another 5 days, according to the sensitivity reports to which the patient responded satisfactorily (Figure 3). The patient was discharged on day 28 with oral steroids, oral antibiotics (sensitive to ofloxacin), and other supportive measures and was planned for a second dose of cyclophosphamide after 2 weeks.

Discussion

Acute abdominal pain affects 20% of SLE patients, and the most common causes are vasculitis involving the small bowel with perforation, ulceration, infarction, or sterile peritonitis.[4] Necrotizing vasculitis, occlusion of arteries and arterioles by thrombi, intimal thickening and proliferation, and immune complex deposition with complement activation in the pancreatic arterial walls have all been suggested as potential causes of AP in SLE.[5] Autoantibody production or an abnormal cellular immune response can also cause direct inflammation of the pancreatic parenchyma. Patients with chronic SLE are commonly exposed to long-term drug therapies such as glucocorticoids, diuretics, and azathioprine, all of which can cause AP.

AP is commonly seen within the first year of diagnosis of lupus. [6] The majority of cases of AP described in the literature have occurred in the context of active lupus. This may suggest that AP is caused by lupus-related autoimmunity. The development of AP as a presenting manifestation of SLE in a steroid naive patient lends credence to the significance of lupus-related AP. Furthermore, the majority of patients with AP associated with lupus are safely treated with steroids, implying that steroids might play a limited role, if any, in the development of AP. [6] Furthermore, in an Indian original article, cessation of steroids was identified as a risk factor for the development of AP. [7] AP in lupus is typically managed with immunosuppression and supportive therapy. Steroids, azathioprine, and cyclophosphamide are usually used for treatment. Untreated lupus pancreatitis is linked with a complication rate of 57% and a mortality rate up to 45%, which is significantly higher than in non-SLE patients.[7] Mortality is higher if multiple organ systems are involved.[8]

HPS is identified by histiocyte activation with predominant hemophagocytosis in the bone marrow and other reticuloendothelial systems (RES). Disorganized macrophage lymphocyte interactions associated with a cytokine surge such as TNF-alpha, M-CSF receptors, interleukin (IL)-1, IL-2, IL-6, IL-18, interferon-gamma, sIL-2R, and soluble TNF receptors (sTNFRs) derived from Th1 cells and macrophages has been hypothesized to cause a massive inflammatory reaction.[9] It has been proposed that IL-18, a strong inducer of Th1 cytokines, plays a role in autoimmune-related HPS (AAHS).[10]

The presence of bicytopenia, histiocytic hemophagocytosis in bone marrow or other RES during the active phase of the underlying autoimmune disease, and, most importantly, the exclusion of infectious aetiology are considered necessary for the diagnosis of AAHS .The goal of secondary HLH treatment is to address the underlying condition. High-dose corticosteroids and immunosuppressive agents such as cyclophosphamide, cyclosporine, and intravenous immunoglobulin (IVIG) are effective in HLH caused by SLE.There have been few reports of treatment-refractory SLE leading to HLH that was successfully treated with rituximab and infliximab.Our patient improved clinically after being treated with high-dose steroids, IV Immunoglobulin therapy and cyclophosphamide.

Conclusion

This report highlights the possibility of SLE, secondary HPS, and AP in patients with high-grade fever, severe abdominal pain, and oral ulcer as their primary complaints. The association of HPS and AP in acute SLE is extremely uncommon. Further, if unexplained cytopenia develops with an underlying autoimmune disease, the physician should be aware of the possibility of HPS/AAHS. Because the clinical features of SLE and HLH overlap, a high level of suspicion is required for prompt diagnosis and early treatment. Even with adequate treatment, HLH/AAHS have significantly high mortality, which can be curtailed if glucocorticoids and other targeted immune therapies can be started early after ruling out other causes of pancreatitis.

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