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ACUTE PANCREATITIS AS INITIAL PRESENTATION AND FLARE OF SYSTEMIC LUPUS ERYTHEMATOSUS: A CASE SERIES

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ABSTRACT

Acute pancreatitis (AP) is an uncommon but potentially life-threatening manifestation of systemic lupus erythematosus (SLE), occurring in approximately 0.7–4% of patients. It may appear during times of illness activity or as the first sign of SLE, posing significant diagnostic and therapeutic challenges. Early recognition is essential because its management differs from that of pancreatitis caused by more common etiologies and often requires immunosuppressive therapy. We describe two female patients with SLE-associated AP presenting in distinct clinical contexts. The first was a 25-year-old woman with no prior autoimmune disease who presented with moderate AP. Following exclusion of common causes, the development of a malar rash, arthralgia, hypocomplementemia, increased antibodies against double-stranded DNA and positive antinuclear antibodies led to the diagnosis of SLE. Class III lupus nephritis was verified by a subsequent kidney biopsy. The second patient was a 35-year-old woman with established SLE who developed AP during a disease flare characterized by reduced complement levels, deteriorating articular and cutaneous symptoms, and increased anti-double-stranded DNA titres. In both cases, imaging confirmed AP, alternative etiologies were systematically excluded, and treatment with corticosteroids and immunosuppressive therapy resulted in clinical and biochemical improvement. SLE-associated pancreatitis may happen during an aggressive disease flare-up or as the disease's first symptom. When patients have unexplained AP, especially when there are suggestive clinical or serological signs, clinicians should keep a high index of suspicion for SLE. To maximise results and detect concomitant organ involvement, prompt immunosuppressive treatment and careful monitoring are crucial.

KEYWORDS: Systemic lupus erythematosus; acute pancreatitis; lupus nephritis; disease flare; immunomodulation.

1. INTRODUCTION

The autoimmune multisystem disease known as systemic lupus erythematosus (SLE) is characterised by immune system malfunction, autoantibody production, and immune complex deposition, which lead to inflammation and progressive organ damage. SLE is more prevalent among women who are fertile and manifests a very heterogeneous clinical picture, from mild mucocutaneous symptoms to severe multisystem disease. Skin, joints, kidneys, hematological and nervous systems are the organs most commonly involved in SLE. However, almost any organ can be involved throughout the course of the disease, thus posing difficulties in diagnostics and treatment due to heterogeneity of clinical symptoms. [1,2]
GI manifestations have been noted to be a rare but well-recognized problem in patients suffering from SLE. Acute pancreatitis (AP) is one such rare but very dangerous manifestation that occurs in patients with SLE, with an incidence reported in the range of 0.7% to 4%. AP can happen at any stage of the disease's progression during periods of increased disease activity, or it can happen as the first sign of SLE prior to the disease's diagnosis. Given that abdominal pain is a symptom with multiple differentials, the diagnosis of pancreatitis associated with lupus demands the doctor to be extremely suspicious. The early distinction of pancreatitis secondary to lupus from that of other etiologies is crucial since the mechanisms involved and treatment are entirely different. [3,4]
The precise cause of SLE-related pancreatitis still lacks definition and is considered to be multifactorial. The possible pathogenic mechanisms involved include vasculitis of an immune origin, microthrombosis, immune complexes, and autoantibody-mediated damage to the pancreas. In spite of the possible mechanisms mentioned above, there is no definite proof of the cause behind the pathology. Therefore, the diagnosis of pancreatitis in patients with lupus remains largely one of exclusion where all other causes should be ruled out in order to diagnose this condition. These causes include gallstones, alcohol consumption, hypertriglyceridemia, hypercalcemia, infection, medication-induced pancreatitis, and other autoimmune pancreatitis. [5,6]

Early diagnosis of lupus-related AP is clinically important because the potential delay of diagnosis and administration of proper immunomodulators in this type of high risk patients can result into more morbidity or catastrophe. Moreover, AP may arise during flare up causing multisystem manifestations, thus driving the clinician to go for evaluation for additional systemic signs and symptoms, e.g. lupus nephritis. This case report highlights two different presentations of AP that have been found to be associated with SLE, which include AP being an initial manifestation resulting in SLE along with Class III lupus nephritis, and the other being an AP that occurred during flare of a known systemic lupus.

2. CASE PRESENTATION

2.1 Case 1

2.1.1 Clinical History

The case involved a female patient, age 25, who was sent to the emergency room and showed signs and symptoms suggestive of AP. No previous history of any autoimmune disorders or any other significant illness was present in the patient. Efforts were made to find out the underlying cause of the pancreatitis, along with taking into account the clinical history and risk factors. Details regarding the demographics of the patient, symptoms, and clinical history have been described in Table 1.

Table 1. Patient Clinical History

Parameter	Findings
Age/Sex	25-year-old female
Chief complaints	Epigastric pain (72 hours) and vomiting (24 hours)
History of present illness	Leaning forward relieves the progressive back-radiating epigastric pain, which is accompanied by nausea and two episodes of non-bilious, non-projectile vomiting
Past medical history	No history of endocrine, metabolic, or autoimmune disorders
Medication history	No chronic drug intake
History of abdominal trauma	None
Previous therapeutic interventions	None
Alcohol history	No alcohol consumption

2.1.2 Diagnostic Evaluation

During the physical examination, the patient was attentive and focused on time, place, and people. Vital signs included tachypnea (24 breaths per minute), blood pressure (124/72 mmHg), tachycardia (124 beats per minute, regular), and use of accessory muscles of breathing. There were no indications of dehydration. According to the clinical presentation and examination results, moderate AP (Day 3; BISAP score: 2) without organ failure was diagnosed.

Primary laboratory tests proved not to be striking with the exception of high levels of serum lipase and amylase (more than three times the upper normal range). Triglyceride levels in the serum were normal. As seen in Figure 1, a chest radiography also showed bilateral pleural effusions.

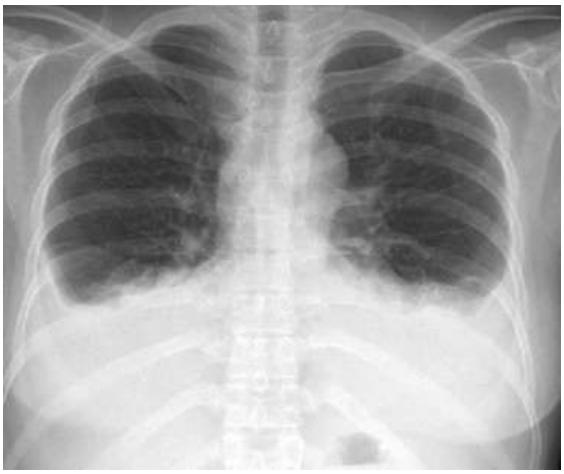

Figure 1. A chest radiograph showing pleural effusions on both sides

Whole abdominal ultrasound with Doppler imaging showed a bulked-up pancreas without any signs of gallstones, biliary obstruction, or abnormality of the blood vessels. For further investigation of the condition of the pancreas, a complete abdominal contrast-enhanced computed tomography (CECT) scan revealed acute interstitial pancreatitis, with a CT Severity Index (CTSI) of 4/10. No signs of necrosis were observed with enhancement of the pancreas and peripancreatic fat stranding (Figure 2).

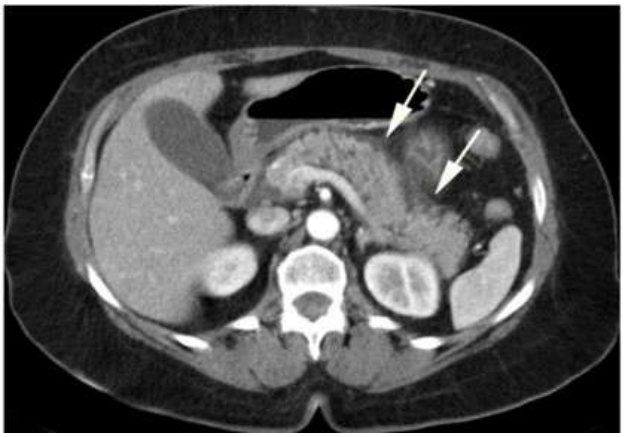

Figure 2. Contrast-enhanced CT of the abdomen demonstrating acute interstitial pancreatitis with preserved pancreatic enhancement and mild peripancreatic fat stranding (arrows). CT severity index (CTSI): 4/10

The infectious causes such as viral hepatitis, cytomegalovirus infection, and Epstein-Barr virus infection were ruled out due to the presence of negative results in serological tests. The endocrine causes such as hyperparathyroidism were also ruled out due to normal serum calcium and parathyroid hormone. However, despite treatment with intravenous fluids and other conservative measures, persistent symptoms, including low-grade fever, arthralgia, and a malar rash, prompted further evaluation for SLE.

Additional testing for autoimmune disorders revealed low complement levels (C3, C4), elevated anti-double-stranded DNA (anti-dsDNA) antibodies, and a positive antinuclear antibody (ANA) test result (2+, titer 1:640, speckled pattern). Mixed Connective Tissue Disease (MCTD) panel was negative. There was presence of proteinuria (1012 mg/24 hours). Based on these investigations, the diagnosis of SLE was made, and renal biopsy was performed. Histopathology showed hypercellular mesangium with immune complexes deposition which indicated Class III (focal) lupus nephritis. Hence, the diagnosis was made of SLE with Class III lupus nephritis and lupus connected AP.

2.1.3 Management and Follow-up

The patient was first treated using intravenous fluids and other conservative treatments of AP. After the diagnosis of SLE with involvement of major organs, Hydroxychloroquine (200 mg/day) with pulse-dose corticosteroids (1 g/day for three days) were used, then mycophenolate mofetil and oral prednisone.

Symptoms improved after two weeks of therapy, along with normalization of serum amylase, lipase, and proteinuria levels. After that, the patient was released on oral prednisone, hydroxychloroquine, and mycophenolate mofetil; routine outpatient monitoring was recommended.

2.2 Case 2

2.2.1 Clinical History

A female patient, age 35, with a pre-existing condition of SLE was taken to the emergency room due to symptoms of AP. This case was different from the first one because pancreatitis developed in the context of existing SLE, thereby suggesting a flare-up of the disease. The demographic information, presentation, medical history, and background of the patient are presented in Table 2.

Table 2. Patient Clinical History

Parameter	Findings
Age/Sex	35-year-old female
Chief complaints	Severe epigastric pain (24 hours)
History of present illness	Severe back-radiating epigastric pain without accompanying nausea or vomiting
Past medical history	Known case of SLE for 3 years with cutaneous lupus, photosensitive rashes, and intermittent arthralgia
Current medications	Hydroxychloroquine and low-dose prednisone
History of abdominal trauma	None reported
Alcohol history	No alcohol consumption

2.2.2 Diagnostic Evaluation

Physical examination revealed that the patient was afebrile but seemed distraught as a result of abdominal pain. The vital signs revealed slight hypotension (blood pressure: 100/60 mmHg) and tachycardia (heart rate: 110 beats/min). Abdominal observation showed epigastric tenderness with absence of rebound tenderness and guarding. An initial diagnosis of mild AP on Day 1 (BISAP score: 0) and the absence of target organ damage was based on the clinical picture and examination results.

The baseline lab tests showed slightly increased liver enzymes (under two times upper normal limit), slightly increased creatinine and urea (1.2/65) and slight leucopenia (3500/ uL). The concentration of lipase and serum amylase was high

(more than three times the upper normal limit). The level of serum triglycerides, serum calcium and intact parathyroid hormone was normal. The chest radiography was not noteworthy, and the ultrasound of the entire abdomen did not indicate gallstones or obstruction of the biliary.
In an attempt to assess the involvement in the pancreas further, contrast-enhanced computed tomography (CECT) of the entire abdomen was done. The scan showed the existence of mild diffuse pancreatic enlargement with unclear boundaries, pancreatic enhancement, and no foci of glandular necrosis, and the CT severity index (CTSI) is 4/10 (Figure 3).

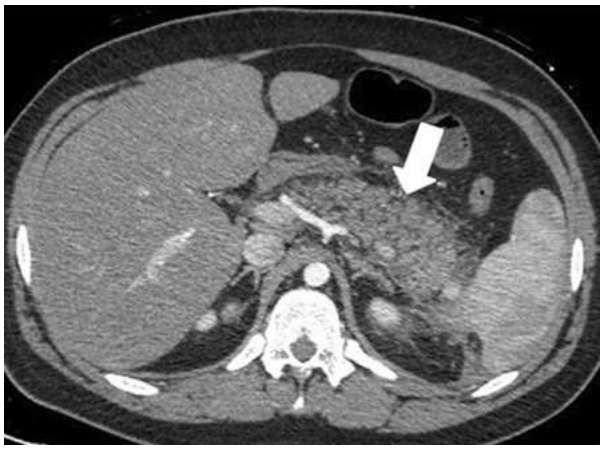

Figure 3. Contrast-enhanced CT of the abdomen demonstrating diffuse enlargement of the pancreas with poorly defined margins (arrow), preserved pancreatic enhancement, and no evidence of pancreatic necrosis. CT severity index (CTSI): 4/10

However, other causes of AP were ruled out. Tests related to autoimmune pancreatitis, which included IgG4-related disease, were negative too. Taking into account the history of SLE and the lack of alternative causes, lupus-associated pancreatitis was considered the most likely diagnosis. This episode coincided with an SLE flare, characterized by the development of a new malar rash and worsening joint pain.
Additional tests were performed and showed the positive ANA test result (2+, titer 1:640, homogeneous type), increased anti-dsDNA antibodies levels, and decreased complement C3 and C4 levels, all of which confirmed the diagnosis of SLE. There were no signs of MCTD according to the results of MCTD panel. The urine analysis did not reveal any proteinuria or hematuria. Thus, the final diagnosis was the flare-up of SLE complicated by lupus-associated pancreatitis.

2.2.3 Management and Follow-up
The patient received treatment using pulsed doses of hydroxychloroquine (200 mg/day) and corticosteroids (1 g/day for three days), along with fluid therapy and other conservative treatments for AP.
Gradual clinical improvement was observed, with tolerance to oral intake achieved after four days. Serum amylase and lipase levels normalized within the following week, accompanied by improvement in the cutaneous manifestations. With a plan for outpatient follow-up, the patient was released on oral prednisone, mycophenolate mofetil, and hydroxychloroquine.
The two cases showed differential clinical presentation of AP in association with SLE but had many common features related to diagnosis and treatment. A summary table of the two patients' demographic details, clinical presentation, diagnostic features, treatment, and outcome is provided in Table 3 below.

Table 3. Comparative Summary of the Two Cases

Parameter	**Case 1**	**Case 2**
Age/Sex	25-year-old female	35-year-old female
SLE status	Newly diagnosed SLE	Known SLE (3 years)
Clinical presentation	AP as the initial manifestation of SLE	AP during an active SLE flare
Presenting symptoms	Epigastric pain, nausea, vomiting	Severe epigastric pain radiating to the back
BISAP score	2 (Moderate AP)	0 (Mild AP)
CT findings	Acute interstitial pancreatitis; CTSI 4/10	Diffuse pancreatic enlargement without necrosis; CTSI 4/10
Common causes excluded	Gallstones, alcohol, hypertriglyceridaemia, infections, endocrine disorders	Gallstones, alcohol, hypertriglyceridaemia, infections, endocrine disorders, IgG4-related autoimmune pancreatitis
Autoimmune findings	ANA positive, elevated anti-dsDNA, low C3/C4	ANA positive, elevated anti-dsDNA, low C3/C4
Renal involvement	Class III lupus nephritis with proteinuria	No renal involvement

Treatment	Pulse-dose corticosteroids, hydroxychloroquine, mycophenolate mofetil, oral prednisone, supportive care	Pulse-dose corticosteroids, hydroxychloroquine, mycophenolate mofetil, oral prednisone, supportive care
Outcome	Clinical and biochemical recovery with proteinuria and pancreatic enzyme levels returning to normal	Clinical and biochemical recovery with improved cutaneous symptoms and pancreatic enzyme normalisation

3. DISCUSSION

AP is an infrequent but clinically significant manifestation of SLE and may happen during an SLE flare-up or as the disease's first symptom. This case series illustrates both clinical presentations. In the first case, AP led to the diagnosis of SLE with concurrent Class III lupus nephritis, whereas the second case developed AP during an active SLE flare. It is important to note the different presentations, as they are relevant to the diagnosis, assessment of disease activity and management of the condition. The exact cause of SLE-related pancreatitis has not been completely elucidated and is thought to be due to multiple mechanisms including immune-mediated vasculitis, autoantibody-mediated pancreatic injury and microvascular thrombosis. However, a specific pathogenic mechanism for this process has not been confirmed.[5] The response seen in both patients to immunosuppression using steroids suggests an immune-mediated mechanism of the pancreatic involvement.

AP has been described in about 0.7 to 4% of SLE patients. [6,7] In general, pancreatic involvement occurs during episodes of SLE activity. [3] While the manifestations of pancreatitis in association with lupus are similar to those of pancreatitis from other causes, high serum amylase can be found in SLE patients even in the absence of pancreatic inflammation. [5] Hence, diagnosis relies not only on laboratory findings but should include clinical and radiologic evaluation.

Drug-induced pancreatitis is another possible diagnosis to consider when dealing with patients who have SLE. One of the possible drugs that could potentially be responsible for inducing pancreatitis is azathioprine; yet it is quite rare, and before making this conclusion, one needs to eliminate all other possible causes of this disorder. [8] In another study comprising 35 patients with SLE and 49 cases of AP, SLE emerged as one of the significant causes of pancreatitis once other established causes were excluded, along with affecting disease prognosis. [9] In the present cases under discussion, gallstones, hypertriglyceridemia, endocrine problems, infections, and IgG4-related autoimmune pancreatitis, where relevant, were also ruled out.

Lupus nephritis, which can occur in as high as 60% of SLE cases, continues to be a critical factor affecting the prognosis. [10] The first case was associated with Class III lupus nephritis and required prompt immunosuppressive therapy while the second one showed pancreatic manifestations of active disease without any renal involvement. Recent studies have emphasized the fact that AP in SLE patients is either an early presentation of lupus or disease flare-up and the condition becomes favorable under early immunosuppressive treatment. [3,4] These cases underscore the point that SLE must be suspected in AP patients, especially in those where other causes have been ruled out and where clinical and/or serological evidence suggests this diagnosis. Early recognition, prompt immunosuppressive therapy, and detection of organ involvement are all key aspects for successful treatment. Although this case series suffers from the small number of cases, the cases presented show two distinct clinical presentations of lupus-associated pancreatitis. Further multicentre studies and larger case series are needed to better define the clinical spectrum and optimize the management of this uncommon manifestation.

4. CONCLUSION

AP is a rare but clinically important manifestation of SLE that may occur either as the initial presentation of the disease or during an active disease flare. The two cases presented in this series highlight the diverse clinical spectrum of lupus-associated pancreatitis and emphasize the status of considering SLE in patients with unexplained AP, particularly when accompanied by suggestive clinical or serological features. Before attributing pancreatitis to SLE, common etiologies such as gallstone disease, alcohol use, metabolic abnormalities, infections, and drug-induced pancreatitis should be systematically omitted. Early recognition and timely initiation of immunosuppressive therapy, together with appropriate supportive management, are essential for achieving favorable clinical outcomes and preventing disease progression. These cases also underscore the importance of evaluating patients for concurrent systemic involvement, as AP may coexist with manifestations such as lupus nephritis or indicate active disease. Although limited by the small number of cases, this case series adds further clinical evidence regarding the variable presentation of lupus-associated pancreatitis. Careful long-term follow-up remains essential for monitoring disease activity, identifying subsequent organ involvement, and optimizing long-term patient management.

Ethics Statement: Consent for publication of the clinical details and accompanying images was obtained from both patients. Patient confidentiality and anonymity have been maintained throughout the manuscript.

Funding: This study received no external funding.

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