DOI: http://dx.doi.org/10.47746/FMCR.2023.4603

Acute Pancreatitis in Systemic Lupus Erythematosus: A Series of 27 Cases

BELLAMINE Hind* | BARAKAT Leila | BENZAKOUR Meryem | MOUDATIR Mina | ECHCHILALI Khadija | ELKABLI Hassan

***Correspondence:** BELLAMINE Hind

Address: Department of internal medicine, university hospital center, Casablanca, MOROCCO

E-mail ✉: hindbellamine@gmail.com

Received: 11 December 2023; **Accepted:** 26 December 2023

ABSTRACT

Acute pancreatitis is a rare and potentially fatal complication of systemic lupus erythematosus (SLE). This study aimed to describe the epidemiological, clinical, radiological, and evolutionary characteristics of acute pancreatitis (AP) in patients with systemic lupus erythematosus. Data from patients who met the revised ACR EULAR criteria for the diagnosis of LES were analyzed retrospectively. SLE activity was assessed according to the SLEDAI activity index, with a mean estimate of 14.

This study included 400 patients with LES admitted between January 2010 and December 2022, of whom 27 patients were diagnosed with pancreatitis. The prevalence of pancreatitis in patients with SLE was 6.75% (27/400). Acute pancreatitis occurred mainly during active SLE, and involved more organs. The outcome was good in 60% of cases, with a 40% mortality rate in lupus-associated AP.

After ruling out other causes, acute pancreatitis can be associated with SLE, if it occurs concomitantly with other signs of lupus flare-up. The diagnosis is made when the symptoms improve with specific treatment. The aim of our work is to describe the epidemiological profile, modes of presentation of lupus pancreatitis, therapeutic features and evolutionary profile of patients.

Keywords: *Pancreatitis, Lupus Pancreatitis, Systemic Lupus Erythematosus*

Introduction

Systemic lupus erythematosus (SLE) is a multisystemic inflammatory disease characterized by the presence of autoantibodies and immune complex formation. The occurrence of acute pancreatitis (AP) during systemic lupus erythematosus (SLE) is known but rare, and exceptionally revelatory. The objective of our work is to describe epidemiological, clinical, radiological and evolutive characteristics of lupus pancreatitis in a Moroccan series.

Materials and Methods

Twenty-seven observations of lupus pancreatitis were retrospectively collated in the Casablanca internal medicine department, from 400 exploited cases of systemic lupus erythematosus meeting ACR criteria, over a 12-year period from January 2010 to December 2022. The diagnosis of lupus pancreatitis

DOI: http://dx.doi.org/10.47746/FMCR.2023.4603

was retained in the absence of other causes of pancreatitis: biliary lithiasis, toxic (drugs or ethyl intoxication), traumatic and neoplastic, as evaluated by the Balthazar score.

Results

Of the 400 SLE cases analyzed, 27 patients had lupus PA, a frequency of 6.75%. These included 25 women and 2 men, with a mean age of 31 years (15 to 52 years). Pancreatic involvement was revelatory of lupus in 8 cases, and observed during a relapse of the disease in 19 patients, with a diagnostic delay of 26 months. The revealing clinical symptoms were abdominal pain, epigastralgia and vomiting in 22 patients (81.4%), diarrhoea in 2 cases (7.4%), fever in 7 patients (26%), and two patients were asymptomatic (7.4%). Biologically, lipaemia was greater than 3 times normal in all patients, 62.9% of cases presented an inflammatory syndrome at the time of pancreatitis, hepatic function tests were perturbed in 8 patients, and lipid profiles were abnormal in 6 patients. Abdominal CT scans showed Balthazar grade A pancreatitis in 6 cases (22%), grade B in 11 cases (40.7%), grade C in two cases (7.4%), grade D in three cases (11%), and grade E in five cases (18.5%). Systemic manifestations associated with AP included hematological involvement in 25 cases, renal involvement in 10 cases, neurological involvement in 10 cases, cardiac involvement in 2 cases, and ocular involvement in only 1 case. SAPL associated with LES was found in 2 patients. The mean calculated SLEDAI was 14. All our patients were receiving hydroxychloroquine 400mg/d, and most of them were already being treated for other systemic disorders, notably corticosteroids in 18 patients, immunosuppressants such as mycophenolate 2g/d in 3 patients, azathioprine 150mg/d in 9 patients and cyclophosphamide in 6 patients. Treatment of AP was based on digestive rest, bolus corticosteroid therapy of 500mg-1g/day for 3 days in 12 patients, immunosuppressive cyclophosphamide 1g in 8 patients, and azathioprine in 3 patients. Evolution was good in 59.2% of cases, with improvement of the digestive tract and normalization of lipemia at D15 of treatment. Two patients were complicated by macrophagic activation syndrome. Both had renal involvement, and one had additional cardiopulmonary involvement. We noted one case of gayet wernick complicating acute pancreatitis (AP). Eleven deaths were unfortunately reported, of which four were directly related to pancreatitis, and the rest to renal damage and infections.

Discussion

The occurrence of acute pancreatitis during systemic lupus erythematosus (SLE) is known but rare, its prevalence varying from 0.6 to 0.9% to 3.5% (Wang *et al*., 2016), its incidence is estimated between 0.4 and 1, 1 case per 1000 lupus per year, different rates of LES-related pancreatitis have been reported in different cohorts, 25 patients out of 2974 cases of LES (0.85%) (Derk and DeHoratius, 2004; Saab *et al*., 1998) and 63 patients out of 1811 with LES (3.5%) (Makol and Petri, 2010).

DOI: http://dx.doi.org/10.47746/FMCR.2023.4603

The median age of onset of AP in our study was 31 years, similar to most other studies (Yang *et al*., 2012; Wang *et al*., 2011), although in the largest Indian series of lupus pancreatitis, the median age of onset was 24 years (Muhammed *et al*., 2022).

A recent study of 264 cases from 11 articles observed a trend towards the onset of AP within the first 3 years of diagnosis of SLE (Alina *et al*., 2021); in our study, more than half the patients developed pancreatitis within the first year of the disease.

Pancreatic involvement is more often acute than chronic. According to various series, pancreatitis is revelatory of SLE in 22% of cases (Makol and Petri, 2010; Larino Noia *et al*., 2009; Wang *et al*., 2005; Dhir *et al*., 2011), and correlates with lupus activity; in our experience, AP was revelatory in 29% of cases, which occurred in the context of active lupus in most of our patients with SLEDAI above 4. This suggests that lupus-related autoimmunity may be the cause of AP.

Acute pancreatitis is often associated with severe visceral damage such as renal and neurological involvement (Yu *et al*., 2016), in our work, 25 patients presented with other systemic manifestations of systemic lupus erythematosus (Table 1).

Table1: Association of pancreatitis and other visceral disorders in lupus in literature series.

Visceral Damage	Ben Dhaou, *et al.* (2013)	Wang Q, et al. (2016)	Medeiros, et al. (2011)	Our series N=27
Hematological disorders	83,3%	92,3 %	50%	92,5%
Kidney damage	16,6%	80,8 %	60%	37%
Joint damage	100%	-	85,7%	82%
Neurological damage	33,3%	-	30%	37%
Pleuropulmonary disease	33,3%	67,3 %	10%	22,2%
Heart disease	50%	67,3 %	10%	7,4%
skin damage	100%	53,8%	80%	100%

The etiology of AP in a lupus patient is often difficult to determine. Its pathogenesis is multifactorial, and several etiologies are often incriminated, such as an ischemic mechanism due to vasculitis or thrombosis due to an associated antiphospholipid antibody syndrome, an autoimmune mechanism, or a drug-induced lesion related to lupus treatments such as corticoids and mycophenolate mofetil, or an intercurrent infectious disease (Ben Dhaou *et al*., 2013).

That said, the diagnosis of AP should only be made after evaluating other etiologies, such as obstructive (gallstones, pancreas divisum), toxic-metabolic (alcohol, hypercalcemia, hypertriglyceridemia)

DOI: http://dx.doi.org/10.47746/FMCR.2023.4603

or iatrogenic, given that some of the drugs associated with lupus, such as azathioprine, mycophenolate, cyclosporine or corticosteroids, may be incriminated as a cause of acute pancreatitis (Wang *et al*., 2016).

Histologically, the specimen shows inflammatory infiltrates and necrosis. Vascular lesions, including thrombosis and vasculitis, are rare (Breuer *et al*., 2006). These histopathological features are indistinguishable from pancreatitis due to other causes, but this is rarely available, and no histology was performed in our patients.

Clinically, overall, around 20-50% of Lupus patients may develop gastrointestinal symptoms (Dima *et al*., 2017). The clinical manifestations of our patients are very similar to the literature, based on abdominal pain as the first complaint, reported in most patients (Arbaoui *et al*., 2020) (Table 2). Acute pancreatitis should be suspected in any lupus patient with acute abdominal pain; however, lupus pancreatitis may be clinically silent and of incidental discovery (Wang *et al*., 2016), although there are rare cases of silent pancreatitis in which imaging may reveal the diagnosis (Alibegovic *et al*., 2017).

Table 2: Comparison of clinical features of patients with lupus-associated pancreatitis with other series in the literature.

References Clinical Signs	Ben Dhaou, et al. (2013)	Wang Q, et al. (2016)	Eaker and Toskes, 2018	Our series N=27
Abdominal pain	100%	89.10%	100%	81,4%
Vomiting	50%	43.5	100%	81 ,4%
Diarrhoea	-	26.1	-	7,4%
Fever	50%	71.7	66%	26%
SLEDAI	-	17 ± 9	>14	14

SLEDAI: Systemic Lupus Erythematosus Disease Activity Index

As in their study, Medeiros, *et al*. (2011) reported an incidence of 5.1% of subclinical pancreatitis. In our series, two patients were asymptomatic (stage A).

The diagnosis of pancreatitis can be confirmed by measuring enzyme levels and imaging; in fact, 97% of cases are diagnosed on the basis of increased blood lipase or amylase levels (Yang *et al*., 2012). Serum lipase has good sensitivity and specificity in the diagnosis of acute pancreatitis (Cappell, 2008), and its measurement is recommended by the French National Authority for Health (HAS) as it attains its peak more rapidly, within 24 hours of the onset of clinical signs. A level greater than three times normal within 48 hours of the onset of clinical signs confirms the presence of pancreatitis. Lipasemia was consistently elevated in our patients. However, its elevation does not correlate with the severity of acute pancreatitis (Malka and Rosa-Hezode, 2001), and it is not a screening, monitoring or severity assessment test.

As for amylasemia, even in the presence of acute pancreatitis, values may be at the limit of normal (Derk and DeHoratius, 2004).

A variety of biological manifestations may accompany this complication, such as cytolysis and moderate cholestasis. Hematological involvement is present in 100% of cases, compared with 61% of uncomplicated lupus (Yang *et al*., 2012), often in the form of anemia and cytopenia, and thrombocytopenia, which has been reported in 48% of cases of lupus pancreatitis (Breuer *et al*., 2006); renal involvement, frequent in SLE, is another risk factor for increased pancreatic enzymes (Medeiros *et al*., 2011), but pancreatitis does not appear to have a direct effect on renal function.

It is sometimes difficult to distinguish between what is due to pancreatitis and what is due to SLE itself, especially when it comes to hematological and renal damage (Breuer *et al*., 2006).

However, it would appear that thrombocytopenia, along with hypertriglyceridemia and increased sedimentation rate, are the only parameters statistically associated with pancreatitis (Medeiros *et al*., 2011).

As for imaging, echo-endoscopy makes an important contribution to the diagnosis of pancreatitis, enabling not only visualization of the pancreatic parenchyma and the bile and pancreatic ducts, but also the performance of pancreatic biopsies. Abdominal ultrasound will show signs of enlarged pancreas, peripancreatic inflammation and increased vascularity (Johnson *et al*., 2014). It also helps identify other causes of AP such as gallstones, structural anomalies and local complications such as pseudocysts, ascites and abdominal collections.

CT is generally reserved for patients with diagnostic confusion, and better characterizes complications such as pancreatic oedema, necrosis and peripancreatic fluid collections (Johnson *et al*., 2014). The severity of necrosis on CT can predict the outcome of AP (Sahu *et al*., 2017). All our patients underwent CT scans, eight of whom were already at the stage of necrosis.

MRI is more efficient, and will better define the nature of the necrotic flows. The PAL is hyposignal T1 and hypersignal T2; after injection of gadolinium, with late enhancement of the gland. Therapeutically, there is no well-established consensus on the management of acute lupus pancreatitis. The treatment of lupus AP is similar to that of the general population: absolute diet initially, followed by early nutrition within 48 to 72 h, or enteral nutrition for severe AP to reduce the risk of infection and mortality, IV hydration and analgesia (Guyot *et al*., 2021).

Although corticosteroids and immunosuppressants have been implicated in the occurrence of fatal haemorrhagic pancreatitis in SLE (Reynolds *et al*., 1982), although this condition is generally corticosteroid-sensitive, they usually allow the vasculitis to heal (Eaker and Toskes, 2018). The occurrence

of pancreatitis in the course of SLE should not, therefore, lead to the discontinuation or reduction of corticosteroid therapy, unless its responsibility in the occurrence of pancreatitis is formally established. In our 27 observations, the introduction of high-dose corticosteroids improved the clinical and laboratory symptoms of 16 patients.

In a review of the literature by Breuer, *et al*. (2006), based on a series of 77 lupus patients, treatment of acute lupus pancreatitis included corticosteroid therapy in 83% of cases, combined with immunosuppressive therapy with azathioprine in 10% and cyclophosphamide in 7%. Six patients (7%) were treated with plasmapheresis and two with intravenous gamma globulin. The course of lupus pancreatitis is generally good, but the severity of the initial presentation and/or delay in diagnosis could lead to early mortality. Although pancreatic involvement is only rarely observed in SLE, it is one of the most severe clinical situations (Wang *et al*., 2016). The mortality rate appears to be higher than in lupus without pancreatic involvement (Alina *et al*., 2021), which is also attributable to other associated systemic disorders, as in our study, where we observed eleven deaths, two of which were complicated by MAS, and one by Gayet Wernick syndrome. In order to avoid such major complications, some authors insist on the importance of systematic screening for acute pancreatitis (AP), for early diagnosis and treatment (Makol and Petri, 2010; Breuer *et al*., 2006).

Conclusion

Acute pancreatitis is a relatively rare complication of SLE, usually occurring in the course of severe, relapsing lupus disease and associated with severe visceral damage such as renal and neurological involvement. Lupus etiology is difficult to prove. Improvement under specific treatment is the key to incriminating lupus. The disease is generally corticosteroid-sensitive, but the severity of the initial symptoms can lead to early death.

Conflicts of Interest: The authors declare that they have no ties of interest.

References

Alaoui M, Ammouri W, Bourkia M, Khibri H, Mouatassim N, Maamar M, Harmouche H, Mezalek ZT, Adnaoui M. La pancréatite aigüe lupique: À propos de 18 cas. *La Revue de Médecine Interne* 2018; 39: A57-A58.

Alibegovic E, Kurtcehajic A, Hasukic I, Hujdurovic A, Fejzic JA, Kurtcehajic D. Silence pancreatitis in systemic lupus erythematosus. *Intractable Rare Dis Res* 2017 May;6(2):141-144.

Alina D, Daniel VB, Ciprian J, Mariana J. Systemic lupus erythematosus-related acute pancreatitis. *Lupus* 2021; 30: 5–14.

Arbaoui I, Somaï M, Rachdi I, Daoud F, Zoubeidi H, Dhaou BB, Aydi Z, Boussema F. Pancréatite lupique aiguë: étude de 5 cas. *La Revue de Médecine Interne* 2020; 41: A139.

Ben Dhaou B, Aydi Z, Boussema F, Ben Dahmen F, Baili L, Ketari S, Cherif O, Rokbani L. Lupus pancreatitis: A case series of six patients. *Rev Med Interne* 2013; 34: 12-16.

Breuer GS, Baer A, Dahan D, Nesher G. Lupus-associated pancreatitis. *Autoimmun Rev* 2006; 5: 314–318.

Cappell MS. Acute pancreatitis: etiology, clinical presentation, diagnosis, and therapy. *Med Clin N Am* 2008; 92: 889-923.

Derk CT, DeHoratius RJ. Systemic lupus erythematosus and acute pancreatitis: a case series. *Clin Rheumatol* 2004; 23: 147–151.

Dhir V, Misra R, Agarwal V, Lawrence A, Aggarwal A. Lupus pancreatitis: early manifestation of active disease. *Lupus* 2011; 20: 547–548.

Dima A, Jurcut C, Balanescu P, Balanescu E, Badea C, Caraiola S, Miler I, Ramba D, Ionescu R, Baicus C, Dan GA. Clinical significance of serum and urinary interleukin-6 in systemic lupus erythematosus patients. *Egypt Rheumatol* 2017; 39: 1-6

Eaker EY, Toskes PR. Case report: systemic lupus erythematosus presenting initially with acute pancreatitis and a review of the literature. *Am J Med Sci* 1989; 297: 38–41.

Guyot A, Lequeu JB, Dransart-Rayé O, Chevallier O, Nguyen M, Charles PE, Mouillot T, Manfredi S, Degand T. Management of acute pancreatitis. A literature review. *Rev Med Interne* 2021; 42: 625-632.

Johnson CD, Besselink MG, Carter R. Acute pancreatitis. *BMJ* 2014; 349: g4859.

Larino Noia J, Macías García F, Seijo Ríos S, Iglesias García J, Domínguez Munoz ˜ JE. Pancreatitis and systemic lupus erythematosus. *Rev Esp Enferm Dig* 2009; 101: 571–579.

Makol A, Petri M. Pancreatitis in systemic lupus erythematosus: frequency and associated factors – a review of the Hopkins lupus cohort. *J Rheumatol* 2010; 37: 341–345.

Malka D, Rosa-Hezode I. Positive and etiological diagnosis of acute pancreatitis. *Gastroenterol Clin Biol* 2001; 25: 1S153-68.

Medeiros MMC, Fernandes GH, Pinto NSR, Silveira VA. Clinical and subclinical pancreatitis in a cohort of patients diagnosed with systemic lupus erythematosus. *Clin Exp Rheum* 2011; 29: 776–782.

Muhammed H, Jain A, Irfan M, Charles S, Dwivedi P, Chavan PP, Khubchandani R, Sharma A, Phatak S, Shukla AN, Shah R, Subramanian N, Pandya SC, Singh YP, Chengappa KG, Thabah M, Rajasekhar L, Shobha V, Negi VS, Dhir V, Sharma A, Misra R, Aggarwal A; SLE-SIG of IRA. Clinical features, severity and outcome of acute pancreatitis in systemic lupus erythematosus. *Rheumatol Int* 2022; 42: 1363-1371.

Reynolds JC, Inman RD, Kimberly RP, Chijong JH, Kouacs JE, Walsh MB. Acute pancreatitis in systemic lupus erythematosus: report of twenty cases and a review of the literature. *Medicine* 1982; 61: 25–32.

DOI: http://dx.doi.org/10.47746/FMCR.2023.4603

Saab S, Corr MP, Weisman MH. Corticosteroids and systemic lupus erythematosus pancreatitis: a case series. *J Rheumatol* 1998; 25: 801–806.

Sahu B, Abbey P, Anand R, Kumar A, Tomer S, Malik E. Severity assessment of acute pancreatitis using CT severity index and modified CT severity index: correlation with clinical outcomes and severity grading as per the Revised Atlanta Classification. *Indian J Radiol Imaging* 2017; 27: 152–160.

Wang CH, Yao TC, Huang YL, Ou LS, Yeh KW, Huang JL. Acute pancreatitis in pediatric and adult-onset systemic lupus erythematosus: a comparison and review of the literature. *Lupus* 2011; 20: 443–452.

Wang F, Wang NS, Zhao BH, Tang LQ. Acute pancreatitis as an initial symptom of systemic lupus erythematosus: a case report and review of the literature. *World J Gastroenterol* 2005; 11: 4766–4768.

Wang Q, Shen M, Leng X, Zeng X, Zhang F, Qian J. Prevalence, severity, and clinical features of acute and chronic pancreatitis in erythematosus. *Rheumatol Int* 2016; 36:1413–1419.

Yang Y, Ye Y, Liang L, Wu T, Zhan Z, Yang X, Xu H. Systemic-lupus-erythematosus-related acute pancreatitis: a cohort from South China. *Clin Dev Immunol* 2012; 2012: 568564.

Yu YK, Yu F, Ye C, Dai YJ, Huang XW, Hu SX. Retrospective analysis of plasma exchange combined with glucocorticosteroids for the treatment of systemic lupus erythematosus-related acute pancreatitis in central China. *J Huazhong Univ Sci Technolog Med Sci* 2016; 36: 501-508.