

Acute Pancreatitis in the Systemic Lupus Erythematosus: A Case Series of Three Patients

Raouf Hajji^{1*}, Imed Ben Ghorbel², Mounir Lamloum², Amira Hamzaoui², Monia Khanfir²,
Mohammed Habib Houman²

¹Internal Medicine Department, Sidi Bouzid Hospital, Ibn Aljazzar Medicine Faculty of Sousse, Tunisia

²Internal Medicine Department, La Rabta University Hospital, Medicine Faculty of Tunis, Tunisia

*Corresponding author: raouf.hajji@yahoo.fr

Abstract Background: Acute pancreatitis is a rare but life threatening complication of the systemic lupus erythematosus. We report three cases of lupus-associated pancreatitis. Case reports: Two women and one man with a mean age of 28 years presented with lupus pancreatitis. In our patients, it occurred after the lupus diagnosis with a delay average of 5.3 months. It is associated in these cases with other organ involvement. Clinical, biological and abdominal Computed tomography results confirm the diagnosis. The evolution after steroids and immunosuppressive is marked in all patients with good outcomes. Conclusion: Although it is a life threatening complication, acute pancreatitis in lupus can have good prognosis provided that early diagnosis and appropriate management based on corticosteroid therapy and symptomatic treatment were established.

Keywords: *systemic lupus erythematosus, acute pancreatitis*

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1. Background

Systemic lupus erythematosus (SLE) is a chronic multisystemic, autoimmune connective tissue disease marked by a broad range of clinical and biological manifestations. Among them, acute pancreatitis is a rare but life-threatening complication. Since the first case of pancreatitis reported in 1939, less than 200 cases of SLE-related acute pancreatitis have been reported in the literature with an annual incidence varying from 0.4/1000 to 2.3/1000 [1]. Its frequency is almost between 2 to 30% of lupus patients [2].

In this article we report 3 cases of lupus-associated pancreatitis and we detail their clinical, biological, imaging features, the disease management and its outcomes

2. Case Reports

Case 1:

33-year old woman, presented in November 2009 progressively diffuse pain, fatigue and edema in lower limbs. She was admitted to the Internal Medicine Department in April 2010. On physical examination, she had myalgia, swelling lower limbs and her abdomen was painless and non-tender. The complete blood count revealed a 7 g per deciliter normocytic normochromic anemia, leukopenia (1850 per cubic millimeter),

neutropenia (950 per cubic millimeter) and lymphopenia (690 per cubic millimeter). Proteinuria was 1, 3 g/24 h with a hypoalbuminemia 15 g/l. The Antinuclear antibodies (ANA) were positive with 1/3200 titer and so was the native anti-DNA.

The imaging explorations revealed pleurisy and pericarditis. The kidney needle-biopsy (KNB) and pathology showed an extra-membranous glomerulonephritis associated with segmental and focal glomerulonephritis and vasculitis lesions. The diagnosis of lupus was retained and corticosteroid therapy was introduced. During her hospitalization, she presented with abdominal pain acute and tender epigastrium. The blood amylase level exceeds 1200 international unit per liter and the blood lipase level was 980 international unit per liter. The abdominal computed tomography (CT) had revealed pancreatitis in grade E of Balthazar's CT severity index (CTSI) without any gallstone. The patient was treated by bolus doses of methylprednisolone and cyclophosphamide with good clinical evolution, disappearance of biological and abdominal pain with normalization of pancreatic enzymes levels.

Case 2:

A 23-year-old woman, without any pathological medical background, followed-up since November 2007 for SLE. She is not smoker nor alcohol consumer. The lupus was diagnosed by the association of photosensitivity, malar rash, non-erosive polyarthritis of the knees and wrists, with hematological involvement marked by a leukopenia (4000 per cubic millimeter) and lymphopenia

(600 cubic millimeter). Both of the ANA the anti-DNA antibodies were positive.

She was treated by hydroxychloroquine for two months that she gave up by her own later. In June 2008, she had a severe flare of her disease: an important asthenia, anorexia and weight loss (10 kg in 2 months), associated with diffuse abdominal pain. On physical examination, there was a malar rash, associated with diffuse abdominal tenderness and an important lower limbs edema. The laboratory evaluation revealed normocytic normochromic anemia (hemoglobin level: 4 g per deciliter), leukopenia (3890 per cubic millimeter), lymphopenia (500 per cubic millimeter), a hyperamylasemia that is almost 25 times the normal level of blood amylase. The 24 hour proteinuria was 1, 6 g. The proteins electrophoresis had shown a hypoalbuminemia with an albumin level of 21 g per liter. Serum chemical analysis had revealed a severe renal failure with a creatinine clearance equal to 18 milliliter per minute. An active segmental and focal proliferative glomerulonephritis was found in the pathological study of the KNB. The abdominal scanner had displayed a pancreas enlargement, peripancreatic fat stranding with delayed enhancement associated with large necrotic lesions which sign an acute pancreatitis in grade E of Balthazar's CTSI. No gallstone is seen. A severe outbreak of SLE: lupus-associated pancreatitis and stage III lupus nephritis was diagnosed. Thus, the patient was treated by oral corticosteroid therapy with a daily dose of 1 mg per Kg with monthly cures of cyclophosphamide (Endoxan®: 15 mg per square meter of body surface). The disease course was marked by the disappearance of abdominal pain and the decrease of the serum amylase levels.

Case 3:

A 28-year old man was admitted in February 2011 for generalized tonic-clonic seizures, inflammatory arthralgias, an asthenia and a photosensitivity. He has no medical background. He is not smoker nor alcohol drinker. Clinical examination revealed malar rash, mouth ulcers and non-erosive polyarthritis of the wrists and elbows. The biological evaluation revealed hemolytic anemia with a positive Coombs test, leukopenia, neutropenia, lymphopenia and thrombocytopenia. The proteinuria was 3 g per 24 hours with 3 crosses of hematuria. Anti-nuclear antibodies were positive at 1/400. The anti-Sm and anti-DNA antibodies were positive. The SLE had been diagnosed and the patient was treated by hydroxychloroquine and corticosteroid therapy (1 mg per kilogram per a day) and valproic acid (Depakine®) sodium and phenobarbital. In the fifth day of corticosteroid treatment, he had complained from a very severe abdominal pain and vomiting. The abdomen was too tender. Laboratory evaluation had revealed a significant rise of the serum amylase and the lipase. Abdominal CT showed pancreatitis grade B of Balthazar's CTSI without image of hepatic calculi. The KNB revealed proliferative diffuse glomerulonephritis and thrombotic microangiopathy lesions.

Acute pancreatitis in a systemic lupus erythematosus systemic in cutaneous, articular, hematological, renal and neurological flare was adopted. The patient was treated by monthly pulses of cyclophosphamide with the dose of 15 mg per square meter of body surface associated with corticosteroids (1 mg per Kilogram per day). A clinical and biological improvement with normalization of pancreatic enzymes was obtained after one week. In 12-month follow-up visit, the evolution was marked by the standardization of the complete blood count, the reduction of proteinuria, the stabilization of the neurological state.

Table 1. The demographic characteristics, clinical features and laboratory parameters of patients with lupus-associated pancreatitis

	Case 1	Case 2	Case 3
Gender (W:Woman / M : Man)	W	W	M
Age (Years)	33	23	28
Onset date of SLE	November 2009	November 2007	February 2011
Type of organ involvement	<ul style="list-style-type: none"> ● Hematological ● Articular ● Extra-membranous glomerulonephritis ● Pleuresy ● Pericarditis 	<ul style="list-style-type: none"> ● Cutaneous, ● Hematological, ● Articular, ● Active proliferative segmental and focal glomerulonephritis 	<ul style="list-style-type: none"> ● Cutaneous ● Hematological ● Articular ● Neurological, ● proliferative diffuse glomerulonephritis and thrombotic microangiopathy lesions
Initial Treatment of SLE	Hydroxychloroquine, Corticosteroids	Hydroxychloroquine, Corticosteroids	Hydroxychloroquine, Corticosteroids
Delay between onset of SLE and acute pancreatitis (Months)	5	7	4
Biological parameters	Amylasemia >1200 U/L Lipasemia : 980 U/L	Amylasemia : 2500 U/L	Amylasemia : 259U/L Lipasemia : 436 U/L
Abdominal CT	Stage E Pancreatitis (Figure 1. A)	stage E Pancreatitis	stage B Pancreatitis
Later Treatment	Hydroxychloroquine Corticosteroids cyclophosphamide	Hydroxychloroquine Corticosteroids cyclophosphamide	Hydroxychloroquine Corticosteroids cyclophosphamide
Outcomes	<ul style="list-style-type: none"> ● Abdominal pain disappearance ● Normalization of pancreatic enzymes level ● Ad integrum restitution and regression of necrosis lesions (Figure 1. B) 	<ul style="list-style-type: none"> ● Abdominal pain disappearance ● Normalization of pancreatic enzymes level 	<ul style="list-style-type: none"> ● Abdominal pain disappearance ● Normalization of pancreatic enzymes level

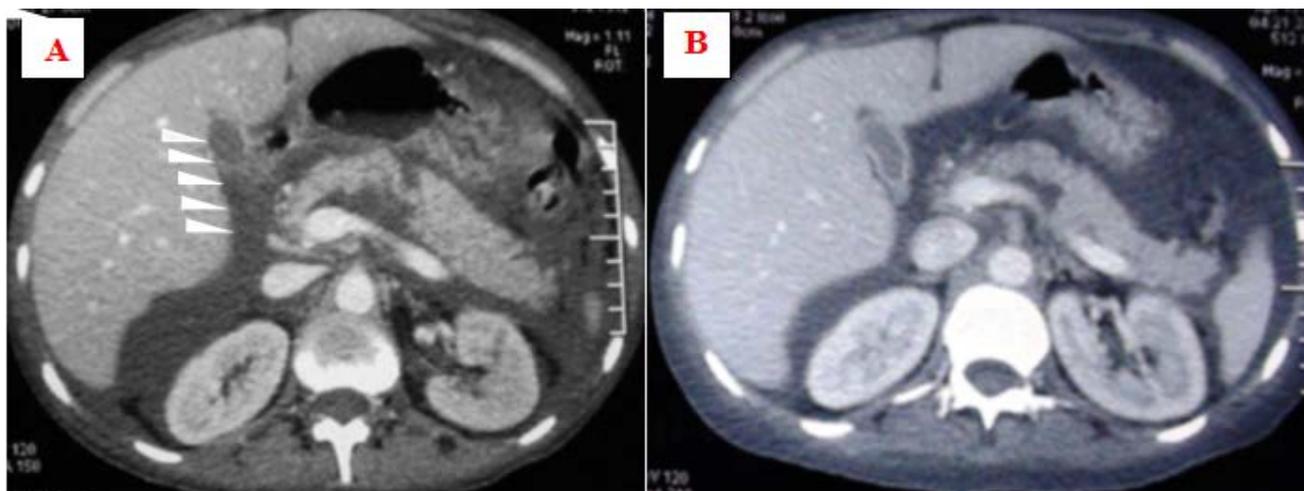


Figure 1. Abdominal CT: stage E Pancreatitis White Arrowheads indicated the swollen cholecyst with pericholecystic edema (Figure 1.A); Ad integrum restitution and regression of necrosis lesions (Figure 1.B)

3. Discussion

Acute pancreatitis is a rare and a life threatening manifestation of SLE. Its frequency ranges from 2 to 30%. [2]. Few cases have been reported in the literature: Indeed less 200 cases have been cited since 1939. This number is probably underestimated because of the existence of asymptomatic or unrecognized forms. Some authors believe that an asymptomatic hyperamylasemia is this 30, 5% of SLE patients [3,4].

The annual incidence of SLE-related acute pancreatitis ranges from 0.4/1000 to 2.3/1000 [1,5,6].

About 97% of patients are women and this is linked to the features of lupus that most of the time young women. Our 3 cases were two women and a man. Their age of onset average is 28 years.

Acute pancreatitis occurs after an average time of evolution of lupus of 3, 3 years mainly in its first 2 years. However, it may be opening in 22% of cases [3].

Our patients had pancreatitis onset after a delay average of 5.3 months.

Pancreatic impairment often occurs during an outbreak of the disease. It is associated essentially with hematological (53%), kidney (60.7%), skin (39%) and joint involvement. Two of our patients had lupus nephritis and cutaneous manifestations. The third patient had, in addition, a neurological involvement.

Abdominal pain observed in 82% of cases and fever in 24% of cases are the most common symptoms revealing. .

The acute pancreatic injury is more frequently described than chronic impairment.

Several mechanisms have been implicated. It can be ischemic phenomena such as lupus vasculitis or thrombosis in the anti-phospholipid antibody syndrome. [2,7,8,9,10,11] or drug-induced [11]. In fact, corticosteroids have long been incriminated while recently many authors refute this hypothesis. Nevertheless, the combination of corticosteroids and ischemic phenomena cannot be excluded [2,9,10,12,13].

Other drugs such as azathioprine or thiazides and some infectious agents like Mumps virus, Cytomegalovirus or Koch's Bacillus have been incriminated [14,15].

These mechanisms are added to the same causes of acute pancreatitis in non-SLE patients (Hepatobiliary disease, alcohol...).

In the last few years, autoimmune pancreatitis is discussed.

The entity of autoimmune pancreatitis, described for the first time by Sales, has received increased attention as a unique clinical entity [16,17].

Corticosteroid treatment was introduced in 65% of cases, immunosuppressive in 25% of cases and by plasmapheresis in 12% of cases. SLE-related acute pancreatitis treatment remains controversial, some authors incriminate immunosuppressive drugs and corticosteroids in the occurrence of pancreatitis however it was reported less complications and deaths in patients who have been treated with corticosteroids and immunosuppressants [6]. All of our patients have well evolved under corticosteroids and cyclophosphamide.

The evolution can be favorable in 36% of cases or progress to chronic pancreatitis in 10% with formation of pseudocysts in 8%. Its prognosis remains bad since about 50% of patients died.

4. Conclusion

The majority of SLE-related acute pancreatitis cases has been described in subjects with multiple visceral flares, as in our 3 patients. It is important to recognize suggestive clinical signs which seem nonspecific. However, a complement by a dosage of pancreatic enzymes and an abdominal CT is required. The diagnosis of lupus pancreatitis is retained after eliminating other etiologies. Rapid diagnosis and appropriate management based on corticosteroid therapy and symptomatic treatment improves greatly the prognosis of this serious condition.

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