Clinical and subclinical pancreatitis in a cohort of patients diagnosed with systemic lupus erythematosus

M.M.C. Medeiros[1], G.H. Fernandes[2], N.S.R. Pinto[2], V.A. Silveira[3]

[1]Division of Rheumatology, Department of Internal Medicine, Faculty of Medicine, Federal University of Ceará, Fortaleza, Brazil; [2]Faculty of Medicine, Federal University of Ceará, Fortaleza, Brazil; [3]Division of Rheumatology, Walter Cantídio University Hospital, Faculty of Medicine, Federal University of Ceará, Fortaleza, Brazil.

Abstract

Objectives

To evaluate amylase and lipase levels in a cohort of patients diagnosed with SLE, identify patients with subclinical and clinical pancreatitis and investigate factors associated.

Methods

Demographic, clinical and laboratory data were collected, including recent clinical symptoms possibly related to pancreatitis, use of medication, disease activity (SLEDAI-2K), and serum amylase and lipase levels. Patients with pancreatic enzyme levels ≥1.5 times in excess of the upper limit of normal and/or patients with clinical suspicion of pancreatitis were submitted to abdominal CT or US.

Results

The study included 136 SLE patients aged 33.9±11.2 years. Three patients (2.2%) were diagnosed with clinical pancreatitis and 7 (5.1%) with subclinical pancreatitis. Multiple causal factors were associated with increased enzymes levels such as activity of the disease, drug toxicity, hypertriglyceridemia and chronic kidney failure. Patients with clinical and subclinical pancreatitis (n=10) when compared with pancreatitis-free patients had more SLE active, levels were lower for haemoglobin, platelets and albumin, and higher for triglycerides and AST. Thrombocytopenia, high blood sedimentation rate and hypertriglyceridemia were the only variables associated with pancreatitis in the logistic regression model.

Conclusions

The prevalence of clinical and subclinical pancreatitis in SLE patients was low and associated with multiple potential factors. The association of thrombocytopenia and pancreatitis in SLE patients requires further studies.

Key words

systemic lupus erythematosus, clinical pancreatitis, subclinical pancreatitis

Marta M. das Chagas Medeiros, MD, PhD
Geórgea Hermógenes Fernandes, MD
Nathália Siqueira Robert Pinto, MD
Virgínia Angélica Silveira, MD

Please address correspondence and reprint requests to:
Dr M.M. das Chagas Medeiros, Federal University of Ceara, Rua Paula Ney 599/302, 60140200 Fortaleza (Ceara), Brasil CEP 60.140-200.
E-mail: mmcmedeiros@hotmail.com

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Introduction

Systemic lupus erythematosus (SLE) is a chronic autoimmune disease that can affect any organ of the body. Although the joints, skin, kidneys, lungs, heart, vessels and nervous system are the most frequently affected parts, SLE may involve the gastrointestinal tract in up to 22% of patients (1) and – though much more rarely – the pancreas (2-4). The etiology of clinical pancreatitis is usually mechanical (biliary lithiasis) or toxic/metabolic (alcohol, drugs, infection, hypertriglyceridemia). In SLE, in addition to these potential etiologies, pancreatitis has been associated with autoimmune, vascular and thrombotic mechanisms (5-13) and with toxicity induced by drugs (azathioprine, cyclosporin, corticosteroids) (14-17). The prognosis of SLE-related pancreatitis is poor, with a mortality rate of 5–27% (2-3, 18-19).

The diagnosis of pancreatitis is based primarily on the presence of highly increased serum levels of amylase and lipase, but because these enzymes may be affected in a number of other conditions unrelated to pancreatitis, the American College of Gastroenterology (ACG) (20) requires the presence of at least two of the following criteria to confirm diagnosis: 1) characteristic abdominal pain, 2) amylase and/or lipase levels in excess of three times the upper limit of normal and 3) image findings by ultrasound (US), abdominal computed tomography (CT) or magnetic resonance (MRI).

While most studies reporting pancreatic enzyme levels in SLE have been based on patients with clinical symptoms, it is believed that pancreatitis in SLE patients is most often subclinical and therefore asymptomatic. However, to our knowledge, no study has so far systematically investigated subclinical pancreatitis in SLE patients.

The objective of this study was to evaluate amylase and lipase levels in a cohort of patients diagnosed with SLE, identify patients with subclinical and clinical pancreatitis and investigate factors associated with increased enzyme levels.

Methods

Consecutive patients diagnosed with SLE according to the criteria of the American College of Rheumatology attending Walter Cantídio University Hospital (HUWC, UFC Medical School, Brazil) between March 2006 and April 2008 were invited to enroll. Following study entry, demographic and clinical data (duration of disease following diagnosis, clinical manifestations present at any time during the course of SLE, history of alcoholism, presence of pancreatitis-related disorders such as cholecystopathy, hyperparathyroidism and dyslipidemia) and laboratory findings (blood work-up, blood sedimentation rate, albumin, serum calcium levels, glycemia, total cholesterol and fractions, triglycerides, alkaline phosphatase, creatinine phosphokinase, aspartate transaminase (AST), alanine transaminase (ALT), urea, creatinine, urine analysis, serum amylase and lipase levels) were obtained from all patients. At the same time, patients were systematically evaluated for recent clinical symptoms possibly related to pancreatitis (abdominal pain, nausea, vomiting, abdominal distension, fever) and use of medication during the preceding 30 days. SLE activity was measured with the SLE disease activity index (SLEDAI-2K). Patients with pancreatic enzyme levels ≥1.5 times in excess of the upper limit of normal and/or patients with clinical suspicion of pancreatitis were submitted to abdominal CT or US. Although the findings were evaluated by different radiologists, pancreatitis was diagnosed with the same well established technical and diagnostic criteria (US: increased size and decreased echodensity as well as possible fluid collections (21); CT: diffuse or segmental enlargement of the pancreas, irregularity of the pancreatic contour with obliteration of the peripancreatic fat planes, heterogeneous appearance and areas of decreased density within the pancreas, and variable ill-defined fluid collections (22)). Patients diagnosed with pancreatitis received qualified medical treatment at the rheumatology service and the outcome was registered (cure of pancreatitis, death or complications).

Following ACG guidelines (20), patients were diagnosed with clinical pancreatitis when presenting at least

two of the following: 1) characteristic abdominal pain, 2) amylase and/or lipase levels in excess of three times the upper limit of normal and 3) image findings. Patients not meeting the ACG criteria for clinical pancreatitis but with amylase and lipase levels twice the upper limit of normal were diagnosed with subclinical pancreatitis.

Serum levels of amylase and lipase were measured at the HUWC laboratory using a Roche/Hitachi 917 analyser for enzymatic colorimetric assays. The normal reference values were 28-100 U/L for amylase and 13-60 U/L for lipase.

Statistical analysis

Findings were analysed with the software STATA v. 7.0. Average and median values, standard deviations and percentages are presented in the tables. Intergroup differences in percentages and average values were analysed with the Chi-square test and the Mann-Whitney test. Logistical regression was used to identify factors independently associated with clinical and subclinical pancreatitis.

Results

The study included 136 SLE patients aged 33.9±11.2 years, the vast majority of whom were women (94.8%). The average duration of disease following diagnosis was 81.1±67.5 months. The most frequent manifestations were musculoskeletal (85.7%), cutaneous (75.6%) and renal (53.6%). APS (phospholipid antibody syndrome) was observed in 12.5% of the patients. The average SLEDAI was 6.7±8.0. The average levels of haemoglobin and hematocrits were 11.6±2.1 g/dL and 34.8±6.4%, respectively. The average levels of leukocytes and platelets were 7,130±3,947 cells/mm^3 and 242,000±90,180 cells/mm^3, respectively. The average level of creatinine was 1.18±1.56 mg/dL and the blood sedimentation rate during the first hour was 45.6±30.1 mm. Based on ACG diagnostic criteria of pancreatitis, only 3 patients (2.2%) were diagnosed with clinical pancreatitis and 7 (5.1%) were diagnosed with subclinical pancreatitis (lipase and/or amylase >2x in excess of the upper limit of normal). Table I shows the demographic and clinical characteristics of patients with and without pancreatitis.

Fifteen (11%) and fourteen patients (10.3%) presented serum lipase and amylase levels ≥1.5 times in excess of the upper limit of normal, respectively. Four patients (2.9%) had lipase levels 3x in excess of the upper limit of normal (Table II).

Table I. Demographic and clinical characteristics of patients diagnosed with systemic lupus erythematosus with and without clinical and subclinical pancreatitis.

Characteristics	SLE patients with clinical and subclinical pancreatitis (n=10)	SLE patients without pancreatitis (n=126)	*p*-value
Age:			
Average ± SD	30.3 ± 10.3	34.3 ± 11.3	NS
Median (range)	27.5 (22-40)	33 (26-41)	
Female (%)	100	94.4	NS
Caucasian (%)	20	37.3	NS
Time since diagnosis (months)			
Average ± SD	51.2 ± 45.9	84.2 ± 68.5	NS
Median (range)	42 (7-96)	72 (36-108)	
Clinical manifestations present at any time during the course of SLE (%)			
Joints	90	83.3	NS
Skin	80	73.8	NS
Serositis	10	26.2	NS
thrombocytopenia	50	11.1	0.001
Central nervous system	30	15.0	NS
Vasculitis	0	10.3	NS
Nephritis	60	52.4	NS
Phospholipid antibody syndrome	10	12.7	NS
Comorbidities (%)			
Cholecystopathy	20	4.7	0.04
Dyslipidemia	10	7.1	NS
Hypothyroidism	0	4.7	NS
Systemic arterial hypertension	40	35.7	NS
Diabetes mellitus	0	3.2	NS
Recently used drugs (% patients/cumulative average dose ± SD over preceding 30 days)			
Oral prednisone (mg)	90/ 439.5 ± 403	88.1/ 435.3 ± 530.1	NS
Oral azathioprine (mg)	20/ 2650 ± 494.9	20.6/ 4234.6 ± 5866	NS
IV pulse cyclophosphamide (mg)	0	6.3/ 837.5 ± 245.1	NS
Oral methotrexate (mg)	0	5.5/57.1 ± 37.2	NS
Ingestion of alcohol (%)			
Never	60	53.2	NS
Presently	10	8.7	NS
Previously	30	38.1	NS
SLEDAI-2K			
Average ± SD	11.1 ± 8	6.3 ± 7.9	0.05
Median (range)	12 (5-17)	3 (0-11)	

IV: intravenous; NS: non-significant *p*-value.

Table II. Increased amylase and lipase levels in a sample of 136 patients diagnosed with systemic lupus erythematosus.

	Increased amylase* (n / %)	Increased lipase** (n / %)
>1.5 times in excess of the upper limit of normal	14 / 10.3	15 / 11.0
> 2.0 times in excess of the upper limit of normal	5 / 3.7	8 / 5.9
> 3.0 times in excess of the upper limit of normal	0	4 / 2.9

* reference value: 28-100 U/L; ** reference value: 13-60 U/L.

Table III. Characteristics of SLE patients with clinical and subclinical pancreatitis.

Age	Duration of SLE	Manifestations of SLE	SLEDAI score	Abdominal symptoms	Probable causes of increased enzyme levels	Image analysis	Serum levels of amylase (A) and lipase (L)*	Times in excess of the upper limit of normal	Manifestation of pancreatitis	Outcome of pancreatitis
38	11 y	Skin, joints, nephritis	18	yes	Hypertriglyceridemia (554mg/dL); disease activity?	US: suggestive of pancreatitis; CT: thickening of the pancreas	A=280 L=597	>2.5 >10	Clinical	Resolution
25	2 y	Skin, joints, thrombocytopenia, seizure, psychosis	14	no	Disease activity? Drugs? (vancomycin, fluconazole)	US: suggestive of pancreatitis	A=201 L=223	>2 >3	Clinical	Resolution
44	2 w	Skin, joints, vasculitis, thrombocytopenia, anticardiolipin positivity	16	yes	Disease activity	US: suggestive of pancreatitis	A= 196 L= 220	~2 >3	Clinical	Resolution
25	8 y	Skin, joints, nephritis, thrombocytopenia	0	no	Drugs? (Azathioprine + Chloroquine)	US and CT: normal	A=51 L=270	Normal >4.5	Subclinical	Resolution
40	3 y	Skin, joints, nephritis, thrombocytopenia	11	no	Mild chronic kidney failure (Cr=1.3mg/dL), mild hypertriglyceridemia (308mg/dL))	US: normal L=95	A=280 >1.5	>2	Subclinical	Resolution
44	8 y	Skin, joints, thrombocytopenia, nephritis	5	no	Mild hypertriglyceridemia (252mg/dL), mild chronic kidney failure (Cr=1.77mg/dL), azathioprine use	Us: normal L=158	A=163 >2.5	>1.5	Subclinical	Resolution
19	1 m	Skin, joints, vasculitis, nephritis, APS	25	yes	Disease activity	TC: normal	A=169 L=164	>1.5 >2	Subclinical	Resolution
19	6 m	Skin, serositis, nephritis	17	yes	Disease activity, moderate hypertriglyceridemia (499mg/dL)	US: normal	A=109 L=143	Normal 2	Subclinical	Resolution
30	6 y	Thrombocytopenia, nephritis, CNS involvement, APS	13	no	Terminal chronic kidney failure (Cr=4.5mg/dL)	US: normal	A= 205 L=111	>2 >1.5	Subclinical	Death from septic shock
22	4 y	Skin, joints, thrombocytopenia, nephritis, lupus ant.coag. positivity	0	no	Terminal chronic kidney failure (Cr=8.6mg/dL)	US: normal	A=225 L=147	>2 >2	Subclinical	Did not repeat tests

APS: Phospholipid antibody syndrome; US: ultrasound; CT: computed tomography; * serum amylase reference value: 28-100 U/L; serum lipase reference value: 13-60U/L; Cr: creatinine.

One of the 3 patients diagnosed with clinical pancreatitis presented clinical abdominal symptoms, enzyme levels and images compatible with pancreatitis (Table III), a SLEDAI score of 18, high levels of triglycerides (554mg/dL) and serum levels of amylase and lipase 2.5x and 10x in excess of the upper limit of normal, respectively. Pancreatitis resolved after treatment of SLE with corticosteroids concurrently with treatment for hypertriglyceridemia. Another patient with clinical pancreatitis presented no clinical abdominal complaints. Diagnosis was based on increased lipase levels (>3x in excess of the upper limit of normal) and compatible US findings. At the time of evaluation, the disease activity score was 14 and the patient was receiving high dosages of corticosteroids, antibiotics and antifungals. Amylase and lipase levels eventually normalised. One patient was hospitalised with a suspicion of SLE (skin and joint manifestations, vasculitis, thrombocytopenia and anticardiolipin positivity) and complaints of nausea, vomiting and abdominal pain and distension. The diagnosis of SLE and pancreatitis was confirmed, with the latter attributed to the former. The condition eventually resolved with the administration of corticosteroids and chloroquine.

For the 7 patients (all female) with subclinical pancreatitis, the duration of SLE following diagnosis ranged from 1 month to 8 years. The most frequently observed lupus-related manifestations were nephritis (n=7), skin and joint problems (n=6), thrombocytopenia (n=5), APS (n=2) and lupus anticoagulant positivity (n=1). Most of the patients (n=5) reported no abdominal clinical symptoms and none had com-

Table IV. Characteristics of subjects displaying levels of amylase and/or lipase >2x in excess of the upper limit of normal in a sample of 136 patients diagnosed with systemic lupus erythematosus.

Characteristics	SLE patients with clinical or subclinical pancreatitis (n=10)	SLE patients without pancreatitis (n=126)	*p*-value
Age (average ± SD)	30.3 ± 10.3	34.3 ± 11.3	NS
Time of diagnosis in months (average ± SD)	51.2 ± 45.9	83.9 ± 68.8	NS
SLEDAI score (average ± SD)	11.1 ± 8.03	6.3 ± 8.0	0.04
Clinical manifestations (%)			
Thrombocytopenia	50.0	11.1	0.001
Laboratory tests (average ± SD)*			
Haemoglobin (g/dL)	9.8 ± 2.8	11.8 ± 2.0	0.02
Platelets (cells/mm^3)	153,000 ± 45,900	250,000 ± 84,565	0.0002
Albumin (g/dL)	3.2 ± 0.7	3.7 ± 0.8	0.018
Glycemia (mg/dL)	90.11 ± 20.0	90.6 ± 31.0	NS
Serum calcium (mg/dL)	8.0 ± 1.5	8.6 ± 1.6	NS
Blood sedimentation (mm/h)	68.2 ± 46.4	43.7 ± 27.8	NS
Creatinine (mg/dL)	2.0 ± 2.6	1.1 ± 1.4	NS
Triglycerides (mg/dL)	297.8 ± 149.4	158.9 ± 102.9	0.001
Aspartate transaminase (UI/L)	53.7 ± 68.1	24.2 ± 13.6	0.008
Alanine transaminase (UI/L)	32.7 ± 37.0	24.2 ± 19.2	NS

* Normal values: Haemoglobin (11.5 –16.4g/dL); platelets (130,000–400,000/mm^3); albumin (4.3–5.1g/dL); glycemia (70–99mg/dL); serum calcium (8.6–10.4mg/dL); blood sedimentation rate (1-18mm); creatinine (0.4–1.0mg/dL); triglycerides (up to 199mg/dL); aspartate transaminase (5–32 U/L); alanine transaminase (6 –31 U/L). NS: non-significant *p*-value.

patible image findings. The causes most likely to be associated with increased enzyme levels were chronic kidney failure, drug use, disease activity and mild to moderate hypertriglyceridemia. Pancreatic enzyme levels eventually normalised in 5 patients, while one patient died of septic shock. One patient did not have her levels of amylase and lipase measured during follow-up in spite of the absence of clinical symptoms of active SLE or pancreatitis.

When comparing SLE patients with clinical and subclinical pancreatitis (n=10) to pancreatitis-free subjects, the former had more thrombocytopenia as clinical manifestation of the disease (50% *vs*. 11.1%; *p*=0.04), disease was more active (SLEDAI-2K score of 11.1 *vs*. 6.3; *p*=0.04), levels were lower for haemoglobin (9.8g/dL *vs*. 11.8g/dL; *p*=0.02), platelets (153,000/mm^3 *vs*. 250,000/mm^3; *p*=0.0002) and albumin (3.2g/dL *vs*. 3.7g/dL; *p*=0.018), and higher for triglycerides (297.8mg/dL *vs*. 158.9mg/dL; *p*=0.001) and AST (53.7U/L *vs*. 24.2U/L; *p*=0.008) (Table IV). Table V shows statistically significant variables for clinical and subclinical pancreatitis in a model of logistic regression.

Table V. Variables associated with clinical and subclinical pancreatitis in 136 patients with systemic lupus erythematosus.

Variable	*p*-value
Thrombocytopenia	0.003
High blood sedimentation rate	0.02
Hypertriglyceridemia	0.004

Discussion

Lupus-associated pancreatitis is a rare condition with only approximately 160 cases reported as of June 2010 and an annual incidence estimated at 0.4-1.1/1,000 lupus patients (19, 23). Subclinical pancreatitis, characterised by increased levels of lipase and amylase in the absence of clinical symptoms, is believed to be more common than symptomatic pancreatitis. However, to our knowledge this is the first systematical study on subclinical pancreatitis in SLE patients to be published.

This was a systematic investigation of pancreatitis-related signs and symptoms observed in 136 SLE patients attending a rheumatology service at a Brazilian university hospital. Based on American College of Gastroenterology diagnostic criteria, approximately 2.2% had clinical pancreatitis and 5.1% had subclinical pancreatitis.

The incidence of clinical pancreatitis observed at rheumatology services in the U.S., Europe, China and Mexico varies from 0.7 to 4% (1-2, 4, 24-25). In spite of differences in the ethnic composition of the respective study populations, the incidence found in the present study lies within the expected range.

Determining the etiology of pancreatic damage in lupus patients can be very challenging but is important when planning individual therapy. In the general population, pancreatitis is related to biliary lithiasis and alcohol consumption with a frequency of 60–80% (26). In lupus patients, apart from the most well-known pathogenic factors, pancreatitis may be associated with the activity of the disease itself or with toxicity from drug therapy, or it may result from a combination of multiple factors. In one of the 3 patients diagnosed with clinical pancreatitis, the disorder was found to be an early manifestation of SLE activity. This form of manifestation has been described in the literature for 17 cases so far (27), making the current case number 18. The patient was treated with corticosteroids and chloroquine followed by complete resolution of clinical symptoms of SLE and pancreatitis.

In a cohort of 1,811 SLE patients from Johns Hopkins University (4), 71 experienced one or more episodes of clinical pancreatitis. The etiology of pancreatitis was found to be related to SLE in 63 patients (3.5% of the cohort), while it was attributed to other causes in 7 patients (alcoholism n=2; post-traumatic shock n=1; sepsis n=1, cholelithiasis n=1; Depakote-induced toxicity n=1; pancreatic anatomic abnormality n=1). In contrast, in a cohort of 895 SLE patients from Mexico (2) with a prevalence of clinical pancreatitis of 3.5%, sixty percent of the episodes were attributed to mechanical causes (especially cholelithiasis) or toxic/metabolic causes (especially terminal chronic kidney failure, hypertriglyceridemia and alcohol). Thus, to distinguish between lupus-induced pancreatitis and idiopathic pancreatitis, mechanical and toxic/metabolic causes

must first be ruled out. Even then, the pathogenic mechanisms responsible for pancreatic injury remain unexplained, although vascular mechanisms have been pointed out as the most likely, including vasculitis and arterial occlusion associated with APS (5- 9, 11).

SLE activity has been associated with the appearance of clinical pancreatitis in a number of reports (2, 19). In a review of 77 subjects with SLE and clinical pancreatitis, disease activity was associated with a frequency of 84% (19). SLE activity was significantly greater among lupus patients with idiopathic pancreatitis than in lupus patients with pancreatitis associated with mechanical and toxic/metabolic causes (2). In our study, all 3 patients with clinical pancreatitis displayed high SLEDAI-2K scores. However, clinical pancreatitis in SLE patients may present in various forms: it may be associated with a flare of the disease, it may occur during remission or at the beginning of SLE, and it may unexpectedly affect patients with long-standing disease (26).

Some drugs used in the treatment of SLE (corticosteroids, azathioprine) have been implicated in the etiology of clinical pancreatitis, but causality has never been clearly established (14-17). In a study by Saab *et al*. involving a series of 8 patients with inactive lupus, clinical and laboratory parameters of acute pancreatitis improved with increased administration of corticoids (16). Other studies have confirmed the therapeutic effect of corticosteroids on lupus-related pancreatitis (2, 3, 19, 26, 27). Several authors suggest treating pancreatitis with corticosteroids only after ruling out toxic/metabolic and mechanical factors, and recommend discontinuing any drug suspected of inducing pancreatitis.

Lipase levels were higher than amylase levels in all 3 cases of clinical pancreatitis. Thus, in these patients the laboratory criterion for clinical pancreatitis (amylase and/or lipase levels >3x in excess of the upper limit of normal) was met for lipase only. The proportion of clinical pancreatitis patients with hyperlipasemia alone is reported to be up to 32% (28-32). Nevertheless, some authors believe hyperlipasemia in the presence of normal amylase levels is more likely related to non-pancreatic sources of lipase (kidney failure, malignant neoplasia, acute cholecystitis, esophagitis and hypertriglyceridemia) (33).

Although serum levels of amylase are conventionally considered the gold standard for diagnosing pancreatitis due to their high sensitivity, as a marker lipase displays both high sensitivity and high specificity as it is mainly released by the acinar cells of the pancreas. In contrast, amylase may come not only from the pancreas, but from the salivary glands and, to a smaller extent, the Fallopian tubes, lungs and liver. Several non-pancreas-related conditions are also associated with hyperamylasemia, including kidney failure, macroamylasemia, parotitis, perforated esophagus, pregnancy and endoscopic retrograde cholangiopancreatography, but amylase levels 3x in excess of the upper limit of normal are highly specific for pancreatitis.

Although about 57% of lupus patients affected with clinical pancreatitis are reported to develop severe complications with 45% mortality (19), no complications or deaths were observed in our patients. It is possible that the systematic investigation carried out for this study helped diagnose and treat patients earlier, thereby affecting the outcome positively. Likewise, the mortality rate of the Hopkins Lupus Cohort (3%) was considerably lower than average due to close monitoring and early diagnosis and treatment (4).

Based on ACG criteria, the incidence of subclinical pancreatitis (5.1%) in our sample was considerably lower than the incidence reported by most authors. Eberhard *et al*. measured serum immunoreactive cationic trypsinogen levels sequentially in 20 children with SLE (high levels reflect pancreatic injury) and found a 35% increase at the time of diagnosis, which normalised during treatment for lupus (34). In a study from 1988 evaluating amylase levels in 25 SLE patients and 15 controls, 5 patients (20%) had hyperamylasemia without symptoms (controls displayed normal levels) (35). Several authors refer to a ~30% incidence of hyperamylasemia in asymptomatic SLE-related pancreatitis; to our knowledge no other studies systematically evaluating amylase and lipase levels in asymptomatic SLE patients have been published. The observed incidence of 5.1% might at first sight appear underestimated, but the figure is based on blood samples collected from all consented SLE in- and outpatients, regardless of demographic and clinical aspects. The low or moderate SLEDAI scores (average: 6.7) and low rates of alcohol consumption, cholecystopathy and dyslipidemia among our patients may have contributed to reduce the incidence.

None of our patients with subclinical pancreatitis displayed pancreatic changes on US or CT and most had no clinical abdominal complaints. Two were diagnosed with APS and one was lupus anticoagulant-positive, but none had thrombotic manifestations at the time of diagnosis of pancreatitis. Of the 7 patients with subclinical pancreatitis, only one (with active SLE) presented no other factors potentially associated with increased pancreatic enzyme levels. Interestingly, 4 of the 7 patients experienced chronic kidney failure, including 2 patients receiving haemodialysis. Amylase and lipase levels may be moderately increased in patients with chronic kidney failure due to reduced renal excretion of enzymes.

Clinical and subclinical pancreatitis were associated with the same conditions: disease activity, mild to moderate hypertriglyceridemia, terminal chronic kidney failure, use of azathioprine and use of mycophenolate mofetil. Overall, more than one factor was associated with the observed increase enzyme levels. The latter returned to normal in almost all cases.

Interestingly, thrombocytopenia was an unusually common manifestation of SLE in patients with both clinical and subclinical pancreatitis. In fact, thrombocytopenia, high blood sedimentation rate and hypertriglyceridemia were the only variables to remain independently associated with clinical and/or subclinical pancreatitis in the logistic regression model. A high blood sedimentation rate may reflect either pancreatitis-related SLE activity or inflammatory

injury from pancreatitis. Hypertriglyceridemia is known to be associated with pancreatic injury, especially at high levels. SLE patients may present several conditions associated with increased levels of triglycerides, including obesity, diabetes mellitus, hypothyroidism, alcoholism and corticotherapy. Levels of triglycerides above 1000mg/dL may cause pancreatitis, while levels above 2000mg/dL practically indicate a causal relation (36). Since none of our patients with hypertriglyceridemia displayed levels above 600mg/dL, the etiology of pancreatitis must in this case be attributed to a combination of factors. The finding of thrombocytopenia and pancreatitis in SLE patients gives rise to a range of speculations. It may reflect severe disease and a greater potential for complications caused by the disease itself or by the toxicity of the drugs employed in the treatment, or it may be secondary to APS-related or non-APS-related vascular thrombotic manifestations. The association of thrombocytopenia and pancreatitis in SLE patients requires further studies.

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