

## A Case of Lupus-Associated Pancreatitis in Jamaica

AK Soyibo<sup>1</sup>, R Alfred<sup>2</sup>

### ABSTRACT

*Pancreatitis complicating a diagnosis of systemic lupus erythematosus (SLE) is rarely reported in the literature and there are no known published cases thus far in the Caribbean. A 50-year old female diagnosed with SLE and discoid lupus erythematosus (DLE) since 1990, presented in February, 2009, to the University Hospital of the West Indies (UHWI), Kingston, Jamaica, with symptoms suggestive of lupus pancreatitis. Serum amylase level was 2341 IU/L and serum lipase was 203 IU/L. Pancreatitis has a 3–8% rate of occurrence in adult patients with SLE. Aetiology and management of this entity remains controversial in these cases, but one must bear the diagnosis in mind, when faced with a SLE patient presenting with abdominal pain, vomiting and diarrhoea.*

**Keywords:** Lupus pancreatitis, pancreatitis in Jamaica

## Un Caso de Pancreatitis Asociada con Lupus en Jamaica

AK Soyibo<sup>1</sup>, R Alfred<sup>2</sup>

### RESUMEN

*La pancreatitis que complica el diagnóstico del lupus eritematoso sistémico (LES), raramente se reporta en la literatura, y hasta hoy no se conoce de caso alguno publicado en el Caribe. Una mujer de 50 años de edad, a quien se le diagnosticara lupus eritematoso sistémico (LES), y lupus eritematoso discoide (LED) desde 1990, acudió en febrero de 2009 al Hospital Universitario de West Indies, Kingston, Jamaica, con síntomas que sugerían una pancreatitis por lupus. El nivel de amilasa sérica fue 2341 IU/L y el de lipasa sérica fue 203 IU/L. La pancreatitis tiene una tasa de ocurrencia de 3–8% en pacientes adultos con LES. La etiología y el tratamiento de esta entidad siguen siendo controversiales en estos casos, pero se debe tener presente el diagnóstico frente a pacientes de SLE que presenten dolor abdominal, vómito y diarrea.*

**Palabras claves:** pancreatitis por lupus, pancreatitis en Jamaica.

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### INTRODUCTION

Systemic lupus erythematosus is a multisystem disorder with protean manifestations. The association between SLE and pancreatitis was first described in 1939 by Reifstein *et al* (1). The presentation does not differ from that of patients

without SLE. Induce elevated levels of serum amylase have also been detected in SLE cases in the absence of pancreatitis (2). Some authors suggest that sub-clinical pancreatic damage may frequently lead to hyperamylasaemia. Thus, the diagnosis of acute pancreatitis in these patients must weigh heavily on clinical presentation and examination findings. Lupus-associated pancreatitis, though rare, is usually associated with other systemic lupus flares (3). The pathophysiology of pancreatitis in SLE is unknown, but formation of microthrombi (4, 5), vasculitis and intimal thickening have been shown to play a role. Drug toxicity (6, 7) and infection,

From: <sup>1</sup>Department of Medicine, The University of the West Indies, and the <sup>2</sup>University Hospital of the West Indies, Kingston 7, Jamaica West Indies.

Correspondence: Dr AK Soyibo, Department of Medicine, The University of the West Indies Kingston 7, Jamaica, West Indies, E-mail: demoskey@hotmail.com

such as cytomegalovirus (8), have been associated with Lupus pancreatitis. The role of antiphospholipid antibodies have been implicated but their role is unclear. Other mechanisms include complement activation, hypotension and autoimmune reaction secondary to anti-pancreatic antibodies (9). Autoimmune pancreatitis is recognized as a cause of pancreatitis in which immune response of the IgG4-positive plasma cell type is thought to play a role (10). There are published case reports of this clinical entity in the United States of America, Europe and Asian continents, but no published work in the Caribbean region.

### CASE REPORT

A 50-year old female, diagnosed with SLE and Discoid lupus erythematosus (DLE) since 1990, presented to the University Hospital of the West Indies (UHWI) with a five-day history of non-projectile vomiting and epigastric pain. There was no previous history of chronic ethanol use or biliary colicky abdominal pain. She had no diarrhoea or constipation or per rectal bleeding and no urinary symptoms. She had developed dyspnoea of gradual onset associated with a wheeze on presentation, however there was no report of cough, fever or pleurisy. She did not complain of painful joints, haematuria, new skin lesions and photosensitivity.

She had been followed-up in the Dermatology and Rheumatology clinics at the UHWI for the past four years, and was compliant with her medication of daily prednisolone 30 mg per oral (po) daily azathioprine 50 mg po daily, gabapentin 300 mg po daily (for muscle cramps), amitriptyline 25 mg *po nocte*, along with topical steroids – betnovate and advantan creams were also added. Chloroquine was not used as the patient had developed chloroquine-induced retinopathy after a year of exposure. She has had prior admissions for lupus cerebritis and myositis within the past 7 months. She was recently diagnosed with hypertension and placed on an angiotensin converting enzyme inhibitor (ACE) and a calcium channel blocker. Of note, her serum creatinine was 157  $\mu\text{mol/L}$  (9–124  $\mu\text{mol/L}$ ) at the time of diagnosis. At the last clinic visit 3 months ago, she had 2<sup>++</sup> proteinuria on dipstick.

Previous laboratory findings in her follow-up had revealed positive antinuclear antibody, (ANA) Anti-SS-A/Ro, and anti-SS-B/La. She had a negative VDRL test, negative double stranded (ds) DNA, ribonucleoprotein (RNP), anti-Smith antibodies and rheumatoid factor with normal (CRP). Baseline C<sub>3</sub> was 81.3 mg/dl (normal 90–180 mg/dl) and ESR was 40 mm/hr. She had no past surgery and no family history of pancreatic cancer. She had four children.

Examination revealed a middle-age female in severe cardiopulmonary distress, mildly icteric, acyanotic, with mild pallor but fairly moist mucous membranes. Her blood pressure was 186/110 mmHg, tachycardia at 143/min, temperature 97.8°F and tachypnoeic at 38 breaths/minute with oxygen saturation of 87% on 5L of oxygen via face mask. Urinalysis showed concentrated urine with 2+ proteins and

3+ blood. She had scarring alopecia and generalized, non-erythematous, hypopigmented atrophied plaques with telangiectasiae, worst on sun-exposed areas, on her face, scalp, trunk and extremities. Cardiovascular examination revealed a normally placed apex beat, normal JVP and no gallop rhythm. She had bronchial breath sounds throughout all lung fields with generalized rhonchi and scattered crepitations. Her abdomen was soft, mildly distended with right upper quadrant and epigastric tenderness but no guarding. The liver measured 12 cm in span with no other organomegaly or masses and normal bowel sounds were heard. There was no blood found on digital rectal examination. She was restless with spontaneous eye opening, moving all limbs equally and no cranial nerve deficit. She was oriented in person and place but not time and had generalized brisk reflexes, with flexor plantar responses.

Laboratory investigation showed haemoglobin 11.2 g/dL, white blood cell (WBC) count of 15.8 X 10<sup>9</sup>/L and platelet count of 78 X 10<sup>9</sup>/L, Prothrombin Time (PT) was 12.0 (control 11.9), Partial thromboplastin time (PTT) 20.3 (control 29.6), serum sodium: 134 mmol/L, serum potassium: 3.9 mmol/L, serum chloride: 101 mmol/L, CO<sub>2</sub>: 13 mmol/L, serum urea 20 mmol/L, serum creatinine 299:  $\mu\text{mol/L}$ , glucose: 10.8 mmol/L, serum amylase: 2341 IU/L, serum lipase: 203 IU/L, corrected serum calcium: 2.05 mmol/L and serum albumin: 26 mg/dL. Other investigations showed C-Reactive protein (CRP) 15.1 mg/dL (normal < 0.5 mg/dL) C<sub>3</sub>: 73.3 mg/dL (normal 90–180 mg/dL), C<sub>4</sub>: < 9.0 mg/dL (normal 10–40 mg/dL), triglyceride: 5.14 mmol/L (normal 0.23–1.47). She was seronegative for HIV. Blood cultures showed no growth and sputum culture was positive for acinetobacter and stentrophomonas (post intubation). She was then assessed as pancreatitis secondary to lupus flare or azathioprine induced, with associated pneumonia and acute respiratory distress syndrome (APACHE score II–23). Other diagnoses included were lupus cerebritis and nephritis with uncontrolled hypertension. Ultrasound revealed renal parenchymal disease, a small right pleural effusion, a hypoechoic rounded area adjacent to the tail of the pancreas with no blood flow or calcification and a normal gallbladder.

An erect chest X-ray showed bilateral fluffy infiltrates. Within 10 hours, her serum amylase was 1084 IU/L then 621 IU/L by the following day. ECG showed sinus tachycardia. She was intubated and maintained on positive end expiratory pressures for ventilation, started on antibiotics for typical and atypical micro-organism coverage, and later pulsed steroid, bronchodilator nebulization continued and she was kept nil *per oral*.

The pancreatitis resolved quickly. On later review by the rheumatologist, it was thought that her pancreatitis was caused by a lupus vasculitis. The ARDS and pneumonia responded quite well to treatment and follow-up chest X-rays showed significant improvement (Fig. 2). She was subsequently discharged from ICU to the Medical floor within a week with 100% saturation on room air. Her acute nephritis

and renal failure was managed with pulse intravenous methylprednisolone on Day 10 of admission when all cultures were negative. She also received haemodialysis. Her cerebritis however has been quite slow in resolving. She received initially ceftriaxone and azithromycin and subsequently ciprofloxacin and trimethoprim-sulphamethoxazole. Renal biopsy later confirmed membranous nephritis (stage V).



Fig. 1: Showing discoid features.

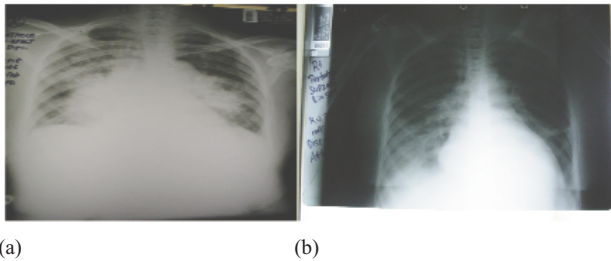


Fig. 2: Displaying chest radiographs (a) before and (b) after 3 days of ventilation.

## DISCUSSION

Systemic Lupus Erythematosus is defined by its clinical features and presence of autoantibody. Most common clinical presentations are polyarthritides and dermatitis, although any clinical manifestation can occur. Pancreatitis in SLE is a well recognized but rare complication. It has a 3–8% incidence in adult SLE patients (11). The diagnosis should be suspected in patients with SLE who present with abdominal pain and vomiting. A diagnosis of lupus-associated pancreatitis should be made after exclusion of the common causes of acute pancreatitis (12), which would be, for example, a history of alcohol abuse and gallstones, neither of which the patient had. She had no symptoms suggestive of hypercalcaemia, mumps infection, scorpion sting or a history of trauma or of thiazide diuretic use. She had no prior history of hypertriglyceridaemia and serum level was not significant to relate it to her pancreatitis. Severe hypertriglyceridaemia is defined as  $> 22.6$  mmol/L (2000 mg/dl) according to the National Cholesterol Education Programme (NCEP) Adult Treatment Panel III (ATP III) and this can result in pancreatitis. We believe that her pancreatitis was related to vasculitis from a generalized lupus flare, causing multi-organ involvement, pancreatitis, pneumonitis and nephritis. We also believe that she had an underlying infection as well, which may have worsened the lupus flare. The history of abdominal pain with vomiting and the epigastric

tenderness elicited on physical examination, along with elevated serum amylase ( $> 10$  times the upper limit of normal) and lipase levels, supported the diagnosis of acute pancreatitis. Useful markers of lupus activity/flare are an increased ESR and CRP, as well as hypocomplementaemia (C3 and C4) as seen in the index case. Many of the cases reviewed in the literature did not have exceedingly elevated ESR levels, but did have an accompanying thrombocytopenia and anaemia, also seen in the index case. Further imaging studies with Computed tomography (CT) or Magnetic resonance imaging (MRI) has been recommended for further evaluation. The index case had an ultrasound which did not show dilated pancreatic or cystic ducts, and no evidence of stone. Further evaluation with a contrast CT was delayed since there was strong clinical evidence of pancreatitis and significant renal impairment.

Another aetiological factor of this patient's acute pancreatitis that should be considered was that of drug induced pancreatitis. Was it related to azathioprine or steroid use (though rare) or SLE? Her remarkable response to steroids supports the latter. In a review of 77 patients (median age 27 years), 44% developed pancreatitis within a year of being diagnosed with lupus and 84% of these patients had active lupus at the time of pancreatitis (13). Azathioprine and glucocorticoids have been implicated as causes of pancreatitis in patients who do not have SLE. Treatment with these medications improves prognosis in lupus-associated pancreatitis. One drug, mycophenolate mofetil has been associated with recurrence of pancreatitis when used in the treatment of severe lupus nephritis; drug toxicity is certainly not discounted (14). Arguments against steroid-induced pancreatitis in lupus patients include the rarity of occurrence of pancreatitis in non-SLE patients receiving steroids, increasing documentation of pancreatitis as an initial manifestation of SLE, findings of vasculitic lesions in the pancreas of SLE patients during autopsy and the resolution of lupus associated pancreatitis with steroids (15).

The rate of severe and fatal episodes of pancreatitis is higher in SLE patients than in patients without SLE. Management of these patients is controversial, but recent studies suggest corticosteroids and bowel rest as the mainstay of treatment and even newer studies have suggested the use of plasmapheresis in severe cases (16).

Clinicians must, therefore have a high index of suspicion of pancreatitis in a patient with SLE presenting with abdominal pain and vomiting.

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