Patient Report

Acute pancreatitis associated with systemic lupus erythematosus: Successful treatment with plasmapheresis followed by aggressive immunosuppressive therapy

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Introduction

Systemic lupus erythematosus (SLE) is a multisystemic disease, and can involve the digestive system. Although the occurrence of pancreatitis in SLE has long been recognized[1], it is a rare but often fatal complication especially in childhood[2].

Plasmapheresis has been recommended in extremely ill patients with autoimmune disorders who have not responded to conventional therapies[3]. It is expected to diminish circulating immune complexes, antibodies and active complement components as well as proinflammatory cytokines.

Here we present a girl with SLE who developed acute pancreatitis shortly after presentation. Plasmapheresis, followed by intravenous pulse therapy with methyl prednisolone and cyclophosphamide, has brought complete recovery from this fatal complication.

Case report

A 12-year-old girl was referred to us because annual medical examinations at school pointed out proteinuria and hematuria. She also complained of malaise and had Raynaud's phenomenon, but otherwise she had stable vital signs and normal physical findings. Laboratory studies on admission showed elevated antinuclear antibody (ANA) titers of 1: 640 with a speckled pattern using Hep2 cells, and elevated anti-single-stranded DNA and anti-double-stranded DNA antibodies (Table I). Antibodies to Sm-antigen, RNP-antigen and La/SSB-antigen were also detectable. Further laboratory analyses showed elevated IgG level (1950 mg/dl) and decreased C4 level (Table II). C-reactive protein was repeatedly negative and serum amylase level was slightly elevated. Urinalysis showed proteinurea (2.5 g/day) and hematuria. 24-h endogenous creatinine clearance revealed normal result (101ml/min). After admission, her white blood cell count decreased to below 4000/μl. Renal biopsy were compatible with membranous lupus nephritis (Class V-B by WHO classification). On the 10th hospital day, she started treatment with prednisolone (1 mg/kg daily), azathioprine (1 mg/kg daily), dipyridamole, and warfarin. Within a week after treatment, malaise, proteinuria and hematuria were disappeared but there were no significant changes of laboratory parameters indicative for SLE activity, and hyperamylasemia yet existed. After 2 weeks of clinically stable period upon treatment, she developed high-grade fever and butterfly rash associated with serological disease activity. Because CRP value was

markedly increased and she was highly immunosuppressed, she was suspected to acquire invasive bacterial infections, and received intravenous immunoglobulin therapy. But the patient's condition deteriorated rapidly and profoundly with cardiovascular collapse and severe upper abdominal pain. Hyperamylasemia became exacerbated and other blood chemistry parameters also elevated (Table II). Abdominal computed tomography (CT) revealed diffusely dilated pancreas, mild ascites, and intact gallbladder and bile duct (Fig. 1 A, B). Diagnosed as pancreatogenic shock associated with acute exacerbation of SLE, she was transferred to intensive care unit and received 3 courses of plasmapheresis. On the next day of the last plasmapheresis, she started strong immunosuppressive therapy such as 3-day~~s~~ consecutive intravenous pulse therapy with methyl prednisolone followed by intravenous pulse therapy with cyclophosphamide. She well tolerated those therapies and had a rapid clinical response. After the second course~~s~~ of plasmapheresis, had minimal abdominal tenderness and no fever. Subsequently after methyl prednisolone pulse therapy, serum amylase value started decreasing and complement increased to normal range. Therefore, the prednisolone dose was reduced to 0.5 mg/kg daily without recurrence of symptoms or an increase in inflammatory serum parameters. Almost a month after the first cyclophosphamide pulse therapy, repeated abdominal CT showed reduction of pancreas size (Fig.1 C, D). She was once discharged after the third course of cyclophosphamide pulse therapy. Cyclophosphamide pulse therapy was performed for a total of 8 courses, the first 6 courses monthly and the last 2 courses bimonthly. After a year from the initial diagnosis, all laboratory findings were improved and ANA titer decreased to 1: 80. Now she remains in remission on mild immunosuppressive therapy including prednisolone at 0.3 mg/kg daily.

Discussion

SLE is a multisystemic disease with the potential to involve almost every organ in the body and exhibits protean manifestations[4]. Acute pancreatitis is a rare complication of SLE, and only 9 cases have been reported to present with pancreatitis as an initial manifestation of SLE[2, 5].

A number of mechanisms have been proposed including vasculitis with ischemia, auto-immunity and drug toxicity[6]. While steroids and immunosuppressive drugs have long been suspected to cause pancreatitis in those patients, Saab *et al*. reviewed 10 SLE

patients with pancreatitis and found no etiological association of steroids with pancreatitis[7].

The etiology of pancreatitis in our case remains unclear; however, we consider pancreatitis might be due to exacerbation of SLE because of the following reasons. First, hyperamylasemia existed on the first examination before using any drugs. Second, emergence of abdominal pain and rapid increase in serum amylase level correlated very well with deterioration of SLE and lupus nephritis. And finally, aggressive immunosuppressive therapies including steroid were effective against pancreatitis.

Watts *et al* emphasized the importance of low pancreatic blood flow in the etiology of acute pancreatitis[1]. Vascular lesions as well as hypotension caused by systemically ill state in SLE patients could have an important influence on pancreatic blood flow. It is of note that during the exacerbated period her bilateral fundi showed engorged and tortuous retinal veins that had not seen before. These findings might reflect ischemic events caused by blood flow obstructions on her retina. It is not unlikely that similar vascular lesions and/or cardiovascular collapse might reduce pancreatic blood flow, resulting in pancreatitis in our patient.

During the exacerbated period, SLE patients have circulating immune complexes, autoantibodies and active complement components. Furthermore, we demonstrated in our patient extremely high levels of serum ferritin and β2-microglobulin, indicative of “cytokine storm”. It appears that plasmapheresis could diminish such inflammatory factors effectively and rapidly, although temporarily.

Acute pancreatitis in association with SLE exhibits various degrees of clinical impact. Some are fatal and others are subclinical[8]. But the mortality rate for acute pancreatitis complicated with active SLE is extremely high[1]. In the literatures, aggressive treatments such as plasmapheresis and intravenous pulse therapy with methyl prednisolone and/or cyclophosphamide have brought favorable outcomes in these acute exacerbations of SLE[3, 9,10].

This case report may remind pediatricians of such rare but serious complication as acute pancreatitis in patients with SLE and re-emphasize that plasmapheresis followed by strong immunosuppressive therapy should be considered early in active SLE patients who fail to respond to conventional therapy.

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Table I

Autoantibody profile

	At first admission	After a year from first admission
ANA titre (negative)	1 : 640	1 : 80
Anti-ssDNA Ab † (< 25)	38.5 AU /ml	9.1 AU /ml
Anti-dsDNA Ab (< 12)	34.9 IU /ml	0.5 IU /ml
Anticardiolipin Ab (< 10)	4.6 U/ml	0.7 U/ml
Anti-Sm Ab (< 7)	107.1 index	1.9 index
Anti-RNP Ab (< 15)	236.6 index	116.2 index
Anti-Ro/SS-A Ab (< 10)	1.2 index	0.4 index
Anti-La/SS-B Ab (< 15)	30.6 index	5.0 index
Anti-Scl-70 Ab (< 16)	4.9 index	N.E.*

Ab†; antibody. N.E.*; not examined.

Table II

Laboratory findings

	At initial diagnosis	At acute exacerbation phase	After a year from initial diagnosis
Hemoglobin (12.0-18.0)	13.3 g/dl	11.2 g/dl	12.3 g/dl
WBC (3500-9000)	4100 / μ l	4700 / μ l	3500 / μ l
Platelets (140-330)	208 tsd / μ l	57 tsd / μ l	231 tsd / μ l
ESR (< 20)	89.8 mm/h	79.4 mm/h	11.7 mm/h
FDP (< 5)	N.E.*	587.7 μ g/ml	2.6 μ g/ml
CRP (< 0.17)	0.06 mg/dl	11.17 mg/dl	0.08 mg/dl
AST (13-33)	21 IU/l	160 IU/l	20 IU/l
ALT (8-42)	15 IU/l	49 IU/l	19 IU/l
LDH (119-229)	220 IU/l	1795 IU/l	191 IU/l
Amylase (40-130)	252 IU/l	4002 IU/l	185 IU/l
CH50 (20-50)	32.5 E/ml	14.0 E/ml	38.4 E/ml
C3 (65-135)	99.1 mg/dl	48.5 mg/dl	113.0 mg/dl
C4 (13-35)	7.3 mg/dl	14.5 mg/dl	20.0 mg/dl
ferritin (5-100)	N.E.	18620 ng/ml	11 ng/ml
β2-microglobulin urine (20-360)	210 μ g/l	70800 μ g/l	60 μ g/l
24-h CCr † (70-130)	101 ml/min	89.2 ml/min	N.E.

N.E.*; not examined. CCr†; creatinine clearance.

Figure legends

Fig. 1: Abdominal computed tomography of our patient. (A and B) At the time of acute exacerbation phase of pancreatitis, white arrows show diffusely dilated pancreas. (C and D) A month after the first course of intravenous cyclophosphamide pulse therapy, white arrows show pancreas of reduced size.

Figure 1.