Mod Rheumatol (2002) 12:174–177

CASE REPORT

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A case of systemic lupus erythematosus with severe acute pancreatitis

Received: January 30, 2001 / Accepted: October 4, 2001

Abstract A 39-year-old woman with systemic lupus erythematosus (SLE) developed severe acute pancreatitis during a well-controlled disease stage. Treatment with intraarterial injections of antipancreatic enzyme and a small amount of prednisone (20 mg/day) led to remission of the pancreatitis. Disease activity of the SLE did not flare up throughout the course of this treatment. The development of severe acute pancreatitis in SLE is rare. We discuss the cause of pancreatitis in SLE, and whether corticosteroids may induce or improve pancreatitis.

Key words Corticosteroids · Severe acute pancreatitis · Systemic lupus erythematosus (SLE)

Introduction

Severe acute pancreatitis is a rare and often fatal disease for which no treatment has been fully established.[1] Vasculitis caused by systemic lupus erythematosus (SLE) and the thrombosis related to lupus anticoagulant may be associated with pancreatitis in SLE.[2–4] Therapeutic agents for SLE, including corticosteroids and immunosuppressive drugs, are a possible cause of pancreatitis.[5,6] In other reports, however, corticosteroids have not appeared to be related to the pancreatitis, and if this is the case they could be used to treat pancreatitis with good result.[7–9]

Here we report a case of SLE with severe acute pancreatitis. Treatment with intraarterial injections of antipancreatic enzyme and a small amount of prednisone led to remission of the pancreatitis and prevented exacerbation of the SLE.

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Case report

A 39-year-old woman developed polyarthralgia in 1992. In 1994, she had erythema on her face and a fever of 38°C. She was diagnosed as having SLE on the basis of the following laboratory findings: leukopenia (3000/μl), thrombocytopenia (6.2×10^4/μl), proteinuria, hypocomplementemia (C3 41, C4 6 mg/dl, CH50 24 U/ml), immunological abnormalities (positive results for anti-RNP, anti-Sm, and anti-SS-A/Ro antibodies), and a high titer of anti-DNA antibodies (80.0 IU/ml). Raynaud's phenomenon suggestive of mixed connective tissue disease was not observed. Neither sicca symptoms nor keratoconjunctivitis consistent with Sjögren's syndrome were found. A biopsy specimen from the labial minor salivary gland was normal. Cryoglobulin and antigens and/or antibodies to hepatitis virus B or C were negative. She had never complained numbness or skin ulcers that could be associated with vasculitits. Prednisone, 40 mg/day, was given initially, and then tapered off gradually. She had been well controlled with 10 mg/day prednisone. She had had an operation to clip an aneurysm for subarachnoid hemorrhage at the age of 35, and developed diabetes insipidus after the operation. The family history was uneventful.

On February 13, 2000, she felt upper abdominal pain after drinking a glass of beer. She was admitted to our hospital the next day because of increasing abdominal pain and continuous vomiting. She was alert on arrival at the hospital. Her height, body weight, body temperature, blood pressure, pulse rate, and respiratory rate were 156 cm, 49 kg, 37.2°C, 126/70 mmHg, 74 b.p.m., and 23 r.p.m., respectively. There was upper abdominal tenderness with muscle defense. No symptoms or signs of cystitis were found.

Leukocytosis with a nuclear shift to the left (leukocyte count 9800/μl, neutrophilic cells 84.6%, basophilic cells

0.1%, eosinophilic cells 0.1%, monocytes 5.2%, lymphocytes 10.0%), mild hypoproteinemia (total protein 5.7, albumin 3.3 g/dl), and hypocalcemia (8.0 mg/dl) were found. Neither hyperlipoproteinemia nor an elevation of biliary enzyme was found. An elevation of pancreatic enzyme was detected: serum amylase (pancreatic type) was 4530 IU/l (normal is up to 115 IU/l), pancreatic phospholipase A2 was 1749 ng/dl (normal 130–400 ng/ml), and pancreatic secretory trypsin inhibitor (PSTI) was 240 ng/ml (normal 4.6–12.2 ng/ml).

The levels of IgG, C3, C4, CH50, and anti-DNA antibody were 734 mg/dl, 72 mg/dl, 6 mg/dl, 37 U/ml, and 11.0 U/ml (RIA), respectively. Negative results for lupus anticoagulant, which had been positive in 1994, were obtained twice, once at admission and again later. Anticardiolipin (β2-GPI dependent) antibody was negative.

A chest X-ray showed right pleural effusion. An abdominal X-ray showed gas in the ileum that suggested intestinal paralysis. Abdominal ultrasonography showed cholecytolithiasis of 3 mm diameter in the gallbladder. Neither a dilated bile duct nor a stone in the common bile duct were detected.

On February 15, the day after admission, the patient's temperature was 38.8°C, her respiratory rate was 33 r.p.m., and her pulse rate was 130 b.p.m., and she was in a state of shock. Tetanic spasm started and a blood examination revealed marked hypocalcemia (6.3 mg/dl), leukocytosis (12 000/μl), elevation of C-reactive protein (CRP) (27.5 mg/dl) and lactic dehydrogenase (LDH) (760 IU/l), and progression of the hypoproteinemia (total protein 5.0 g/dl). Computed tomography (CT) of her abdomen (Fig. 1) on the same day showed a swollen pancreas, fat necrosis, and the spread of inflammation into her pelvis. From the CT images, she was judged to have grade IV pancreatitis. She was diagnosed as having acute pancreatitis of severity score 11 by the criteria of the Ministry of Health and Welfare of Japan.[1]

Medication was started with intravenous antipancreatic enzyme (gabexate mesilate 2 g/day) and antibiotics. On February 16, because the severity of the pancreatitis was getting worse, she was given nafamostat mesilate (240 mg/day) directly into a branch of the celiac artery by which blood is supplied to the pancreas. Her symptoms and laboratory data relating to the pancreatitis then gradually improved (Fig. 2). Although no change in the SLE activity was seen throughout the course of this treatment, the prednisone dosage was increased from 10 to 20 mg/day during the acute phase of the pancreatitis to prevent a flare-up of the SLE. While she was on a low-fat diet and taking antipancreatic enzyme, her pancreatic secretory trypsin inhibitor (PSTI) level rose again, and epigastralgia was diagnosed on June 23. This was improved by increased prednisone (20 mg/day) and intravenous injections of gabexate mesilate (Fig. 2).

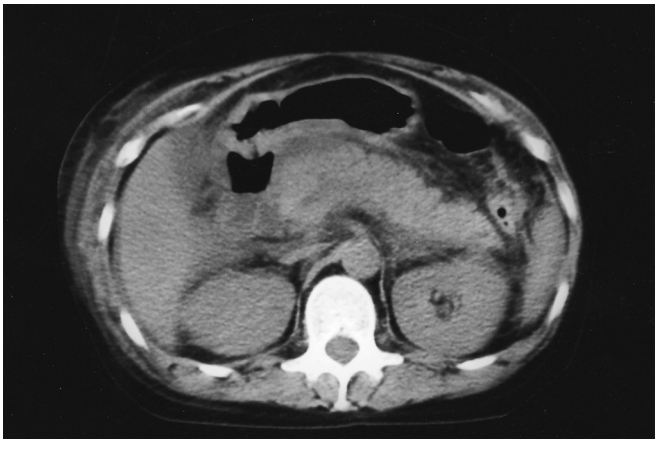

Fig. 1. Computed tomography of the abdomen on the day after admission showed the swollen pancreas, fat necrosis, and the spread of inflammation into the patient's pelvis

Discussion

It is reported that about 3% to 4% of SLE patients develop pancreatitis,[3] but severe acute pancreatitis is rare. Only one patient (the present case) has developed severe acute pancreatitis among the 400 SLE patients treated by us.

In many cases, the SLE itself does not seem to induce acute pancreatitis, although vasculitis caused by SLE and thrombosis related to antiphospholipid antibodies have been thought to be associated with pancreatitis.[2–4] The disease activity of SLE in this case remained inactive, and lupus anticoagulant and anticardiolipin antibodies were negative throughout the course of the treatment.

The main causes of pancreatitis are thought to be alcohol, gallbladder stones, and some types of drug, including thiazide, flosemide, estrogen, tetracycline, and therapeutic agents for SLE (corticosteroids and immunosuppressive drugs).[1,5,6] In this case, acute pancreatitis occurred after the patient drank a glass of beer, suggesting that alcohol might have been a triggering factor, but this was not the only cause of the pancreatitis since she does not drink alcohol every day. A gallstone detected in her gallbladder, but not in the common bile duct, is not likely to have induced pancreatitis. She had no history of medication which might induce pancreatitis except corticosteroids. The cause of her pancreatitis thus remains obscure.

There has been a major controversy about the role of corticosteroids in the pathogenesis of pancreatitis in SLE.[3,9–11] In animal models, corticosteroids cause pancreatic lesions and peripancreatic fat necrosis.[9,10] While autopsy studies in humans have confirmed an association between histological evidence of pancreatitis and corticosteroid use, clinical diagnoses of pancreatitis in these patients are exceedingly rare.[3,11]

Pancreatitis can occur in patients with active or inactive SLE before or during corticosteroid use, and it can improve in spite of continued corticosteroid treatment.[3–5,7–9,12,13] Saab et al.[7] reported eight pancreatitis patients with SLE. Only two of these patients manifested concurrent systemic disease related to the SLE. In the other six patients there was no evidence of SLE flare-up. They concluded that corticosteroids did not cause pancreatitis, but could be used, if

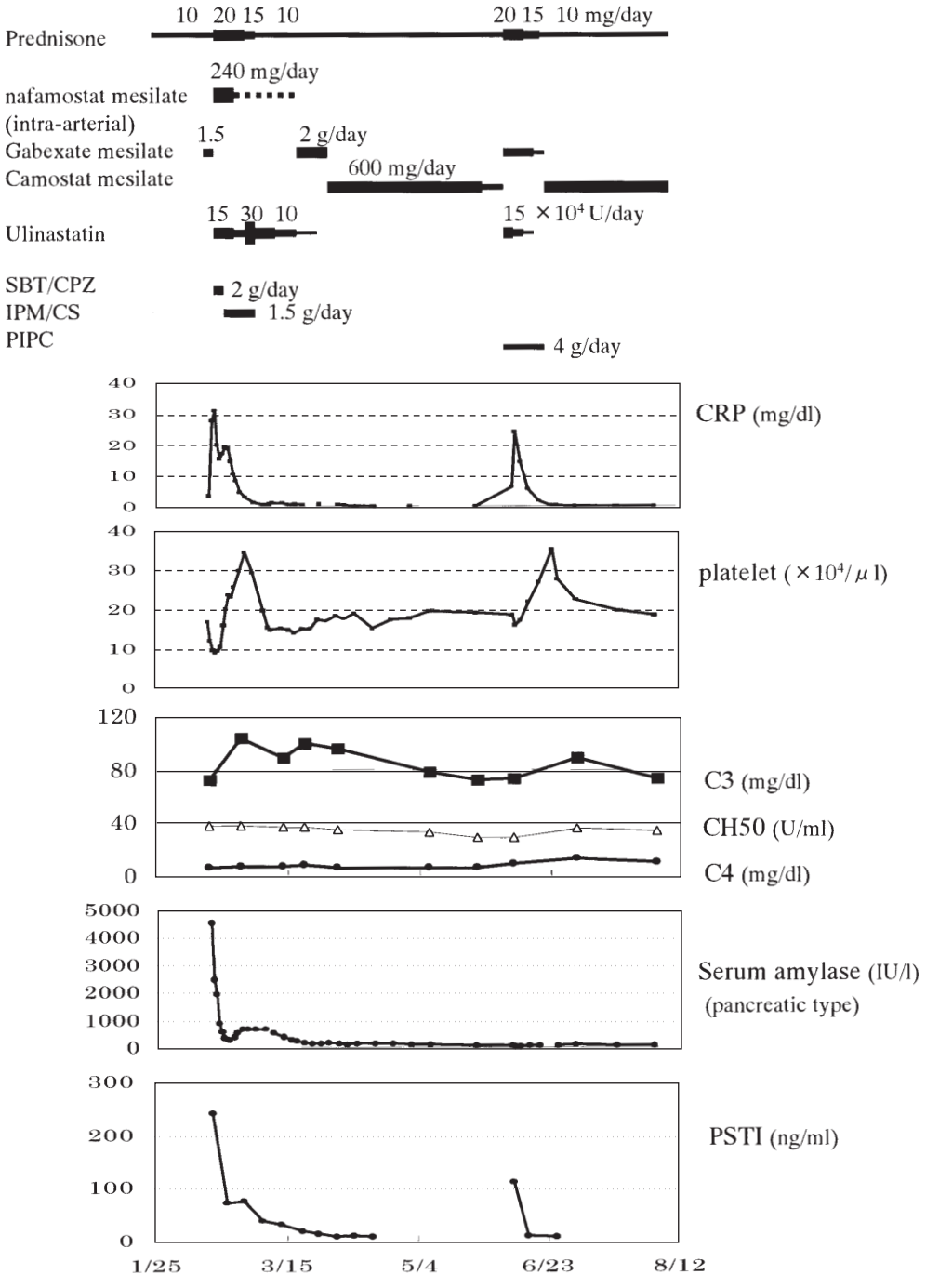

Fig. 2. The clinical course of the patient with the combination treatment with antipancreatic enzyme, antibiotics, and prednisone. The maintenance dose of prednisone (10 mg/day) was increased to 20 mg/day in the acute phase of the pancreatitis

necessary, for the treatment of pancreatitis with good results. All those findings are consistent with other reports.[8,9,12,13] The present case also developed acute pancreatitis during an inactive stage of SLE with a maintenance dose of prednisone. No exacerbation of the pancreatitis was found after a slight increase in the prednisone to prevent an SLE flare-up. Thus, prednisone might not be either a cause or an aggravating factor for her pancreatitis.

Tahara et al.[12] recently reported a case of SLE with severe acute pancreatitis. Table 1 gives a comparison of their patient and ours. The disease activity of their patient was high (low serum complement, high IgG, and anti-dsDNA antibody levels). A high dose of prednisone with pulse therapy and cyclophosphamide, as well as intraarterial injections of nafamostat mesilate, were effective in suppressing both SLE activity and the pancreatitis. Although the SLE activity in our patient was low, a slight increase in prednisone and intraarterial injections of nafamostat mesilate were also thought to be effective in suppressing an exacerbation of both SLE and pancreatitis. Both patients

Table 1. Comparison of a previous Japanese case of systemic lupus erythematosus with severe acute pancreatitis and the present case

	Tahara et al.[12]	This case
Age, sex	22 years, female	39 years, female
Anti-dsDNA antibody	23 U/ml (ELISA)	11 IU/ml (RIA)
Anti-RNP antibody	+	+
Anti-Sm antibody	+	−
Anti-SS-A/Ro antibody	+	+
Anti-SS-B/La antibody	+	−
C3	<10	72
C4	<3	6
CH50	7.5	37
IgG	4230	734
IgA	196	185
IgM	90	39
Lupus anticoagulant	−	−
Severity score of acute pancreatitis	11	11
CT grade of pancreatitis	IV	IV
Steroid pulse therapy	+	−
Maximum dose of prednisone	100 mg/day	20 mg/day
Cyclophosphamide	50 mg/day	−
Intraarterial injection of nafamostat mesilate	100 mg/day	240 mg/day

are still alive, and thus prednisone might not be a cause of pancreatitis, but rather a curative agent. All these findings are consistent with those reported by Saab et al.,[7] who concluded that the pathogenesis and clinical characteristics of acute pancreatitis in SLE remains poorly understood, and most likely results from multiple mechanisms. In conclusion, there are few available data about severe acute pancreatitis associated with SLE. An accumulation of similar case reports might clarify the pathogenesis of pancreatitis and resolve the argument about whether corticosteroids should be used or not.

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