INTERNAL MEDICINE

□ CASE REPORT □

# Successful Treatment of a Patient with Primary Sjögren's Syndrome Complicated with Pericarditis during Pregnancy

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## Abstract

A 35-year-old woman with primary Sjögren's syndrome (pSS) developed fever and chest pain during pregnancy. When the dose of prednisolone was reduced, she experienced chest pain with elevated CRP and D-dimer, resulting in admission to our hospital with marked cardiomegaly and pleural effusion. Because there was no evidence of other autoimmune disorders or infection, oral prednisolone was increased to 30 mg daily with heparin, and hypercoagulopathy was carefully monitored. The patient's condition improved rapidly, and she delivered a healthy baby. This is the first case to support the beneficial effect of prednisolone in pericarditis with pSS, and illustrates its safety during pregnancy.

**Key words:** Sjögren's syndrome, pericarditis, pregnancy

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## Introduction

Primary Sjögren's syndrome (pSS) is a chronic autoimmune disorder characterized by dry eyes and dry mouth due to lymphocytic infiltration into the lacrimal and salivary glands. Extraglandular manifestation involving the skin, lungs, kidney and nervous system is common in patients with pSS (1, 2), while cardiac involvement including pericarditis has rarely been reported (1). The precise prevalence of cardiac involvement in pSS is not known, but past reports indicate that 10-33% of patients show echocardiographic evidence of present or previous pericarditis (3, 4), despite the few clinical chest signs and symptoms (3). On the other hand, the use of steroids is problematic in the treatment of autoimmune diseases, especially during pregnancy. Here, we report a rare case of pSS complicated with pericarditis during pregnancy which was successfully treated with oral prednisolone.

## Case Report

A 35-year-old woman in the 24th week of her first pregnancy was admitted to our hospital in June 2006, with the chief complaints of dyspnea during breathing, chest pain and pyrexia. She had been diagnosed with pSS at a local hospital in June 2004, on the basis of dry mouth, arthralgia, recurrent parotitis and pyrexia. Because she also had positive anti-SS-A antibody and positive results of magnetic resonance sialography, pSS was confirmed according to the criteria of the Japanese Ministry of Health and Welfare (5). Systemic lupus erythematosus (SLE) was excluded by her symptoms, without obvious arthritis or mucocutaneous manifestations, she did not fulfill the criteria of SLE. The patient was prescribed treatment with oral prednisolone at a daily dose of 10 mg. One month prior to her admission to our hospital, the dose of prednisolone was tapered from 10 mg to 5 mg daily. On admission, her temperature was 37.4 ℃, pulse was 106 bpm and regular, and blood pressure was 105/60 mmHg. Physical examination revealed coarse crackling sounds in the bilateral lungs. Her heart sounds revealed no murmur or pericardial friction rub. No peripheral edema was observed on the lower extremities. Neurological examination revealed no abnormalities. Laboratory tests (Table 1) revealed an elevated white blood cell count of 13,000/μl with 89% neutrophils, and the patient's red blood cell count, hemoglobin and hematocrit were decreased to $3.14\times10^6$/μl, 9.7 g/dl and 29.5%, respectively. Elevated levels of asparate

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**Table 1. Summary of Laboratory Findings**

| Variable | On admission (Jun. 14, 2006) | During therapy (Jun. 23, 2006) | After delivery (Oct. 18, 2006) | Normal range |
|---|---|---|---|---|
| WBC (/mm$^3$) | 13,000 | 11,400 | 8,900 | 3,500-9,000 |
| AST (IU/l) | 59 | 77 | 15 | 13-33 |
| ALT (IU/l) | 58 | 69 | 13 | 8-42 |
| ALP (IU/l) | 994 | 675 | 301 | 115-359 |
| γ-GTP (IU/l) | 103 | 112 | 28 | 10-47 |
| CRP (mg/dl) | 7.18 | 0.20 | 0.05 | <0.17 |
| Serum FDP (μg/ml) | 25.9 | 26.5 | 2.1 | <5 |
| Serum D-dimer (μg/ml) | 24.7 | 25.4 | 0.9 | <1 |

Note. AST, asparate aminotransferase; ALT, alanine aminotransferase; ALP, alkaline phosphatase; γ-GTP, γ-glutamyl transpeptidase; CRP, C-reactive protein; FDP, fibrinogen degradation products

aminotransferase (59 IU/l), alanine aminotransferase (58 IU/l), alkaline phosphatase (994 IU/l), leucine aminopeptidase (209 IU/l), and γ-glutamyl transpeptidase (103 IU/l) were also demonstrated. Creatine kinase was normal, but the patient's C-reactive protein (CRP) level was elevated to 7.18 mg/dl. Serological tests showed positive results for antinuclear antibody (1: 80) with a speckled pattern, positive anti-SS-A/Ro antibody (143.7), and rheumatoid factor elevated to 70.9 IU/ml with an elevated serum IgG level (1720 mg/dl). Serum complement levels were also increased (C3, 167 mg/dl, and C4, 41.2 mg/dl). Antibodies against SS-B/La, double-stranded DNA, ribonucleoprotein (RNP), Sm, Scl-70, cardiolipin, CLβ2GPI, antineutrophil cytoplasmic antibodies (MPO-ANCA and PR3-ANCA), smooth muscle, liver-kidney microsomal antibodies (LKM) and mitochondrial M2 were all negative. The brain natriuretic polypeptide (BNP) level was markedly elevated to 126.0 pg/ml, suggesting the presence of congestive heart failure. Prothrombin time and partial thromboplasmin time test results were within the normal range, but the patient's D-dimer level was elevated to 24.7 μg/ml. Other serum testing showed an albumin level of 3.2 g/dl, blood urea nitrogen of 6 mg/dl and creatinine of 0.4 mg/dl. Thyroid functions were normal. Urinalysis revealed a specific gravity of 1.020, pH 6, slight proteinuria, and no erythrocytes. Beta-2 microglobulin in the urine was elevated to 1920 μg/l and N-acetyl-β-D-glucosaminidase (NAG) was 10.9 IU/l, suggesting tubular dysfunction. Arterial blood gas analysis showed pH 7.429, $PCO_2$ 30.2 torr, $PO_2$ 53 torr, $HCO_3^-$ 20.0 mEq/l and BE -4 (anion gap12) with the patient breathing air at room temperature. An electrocardiogram showed sinus tachycardia with a non-specific ST abnormality, and a chest X-ray (Fig. 1) showed cardiomegaly with bilateral pleural effusion. Transthoracic echocardiogram revealed mild to moderate pericardial effusion with an end systolic diameter of 8.2 mm at the anterior wall side and 13.6 mm at the posterior wall side, surrounding the heart with an estimated ejection fraction of 72%. Bright band echoes of thickened epicardium were also detected, suggesting pericarditis.

Pulmonary artery pressure could not be measured, suggesting no findings of cardiac tamponade or pulmonary embolism.

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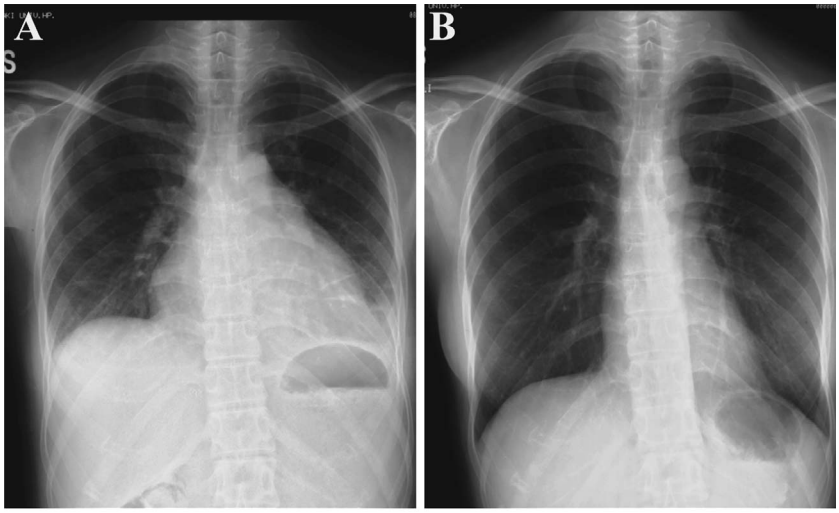


**Figure 1.** **A) When the patient was admitted to our hospital, obvious cardiomegaly and pleural effusion were observed. B) After the administration of prednisolone, both cardiomegaly and pleural effusion were reduced, accompanied by a reduction in serum CRP levels and markers for coagulation.**

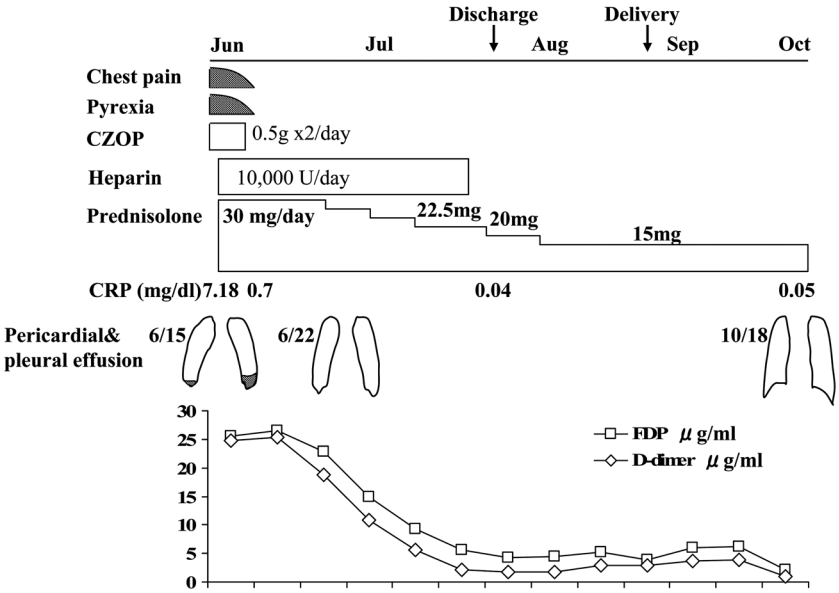


**Figure 2.** **Clinical course. Administration of 30 mg of oral prednisolone and 10,000 units of heparin a day effectively reduced pericardial effusion and C-reactive protein. Although serum level of D-dimer and fibrinogen degradation products (FDP) elevated at the beginning of treatment, they were controllable by the above administration and they were remarkably improved after delivery.**

At first, the patient was treated with cefozopran (CZOP) 1.0 g daily given intravenously, because we could not rule out biliary tract infection. However, spiking fever persisted and the patient showed no improvement in her symptoms. Since her CRP level also remained unresolved, we stopped the antimicrobial therapy and increased the dose of oral prednisolone to 30 mg daily, tapering gradually to 20 mg daily (Fig. 2). In addition, anti-coagulant therapy using heparin (10,000 U/day) was simultaneously administrated intravenously because the patient's D-dimer level was elevated. A few weeks after beginning these treatments, her symptoms improved and her CRP level became negative. A chest X-ray taken one week after admission showed a decrease in the cardiothoracic ratio as well as in pleural effusion, and a transthoracic echocardiogram revealed the disappearance of the patient's pericardial effusion. As a result, she was diagnosed with pericarditis complicated with pSS. The patient was then discharged, but remained under treatment with oral prednisolone as an outpatient of our hospital, without complications. At 38 weeks of gestation, she under-

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**Table 2. Reported Cases of Primary Sjögren's Syndrome Complicated with Pericarditis**

| Authors | | Age, Sex | Treatment | Therapeutic effect | Pregnancy |
|---|---|---|---|---|---|
| Nakashima et al. | (1988) | 66, F | PSL 35mg | (+) | (−) |
| Niho et al. | (1990) | 77, F | PSL dose NA | (+) | (−) |
| Ishikawa et al. | (1994) | 65, M | NA | (−) | (−) |
| Suzuki et al. | (1996) | 53, F | mPSL 1,000mg IV PE, AZA, CY | (+) | (−) |
| Hasunuma et al. | (1999) | 18, M | PSL 30mg | (+) | (−) |
| Sotodate et al. | (2000) | 19, M | PSL 30mg | (+) | (−) |
| Sato et al. | (2006) | 75, F | PSL 20mg | (+) | (−) |
| Our case | (2007) | 35, F | PSL 30mg, Heparin 10,000 U | (+) | (+) |

**Abbreviations:**PSL; prednisolone, mPSL;methylprednisolone, IV; intravenously PE;plasma exchange, AZA;azathioprine, CY;cyclophosphamide, NA;not available

went a cesarean section and delivered a 2,350-g healthy female baby who had no cardiac complications. The patient's hypercoagulopathy with elevated serum fibrinogen degradation products (FDPs) and D-dimer levels improved gradually and decreased dramatically after delivery (Fig. 2). Although she had recurrent parotitis or arthralgia before the above treatment, she did not have any of these manifestations after discharge.

## Discussion

Among the systemic manifestations of pSS, articular, lung, kidney, vascular, gastrointestinal, skin and nervous system involvement are well known (1, 2). In contrast, cardiac manifestations involving serosa such as pericardium have rarely been reported in pSS patients (Table 2). Pericarditis is known to be caused by other autoimmune disorders, especially SLE and rheumatoid arthritis (RA). However, there was no evidence of autoimmune disorders other than pSS in the present case. With respect to cardiac manifestations in pSS, Gyongyosi et al (6) previously reported the echocardiographic examination results of 64 pSS cases, demonstrating that 33% of their patients had previous symptom-free pericarditis with a high pulmonary pressure although none of their patients showed decreased left ventricular systolic function. With respect to the treatment of serositis such as pericarditis observed in lupus patients, it is known that non-steroidal anti-inflammatory drugs (NSAIDs) or moderate doses of oral prednisolone are effective to control pericardial effusion in lupus patients (7). In the present case, the patient's cardiac symptoms were reduced by the administration of oral prednisolone, suggesting that pericarditis in pSS tends to respond well to prednisolone without cardiac systolic dysfunction. The immunopathology of pericarditis found in autoimmune diseases remains unclear. Bidani et al (8) reported that immune complex deposition in lupus patients was detected in the walls of the blood vessels of the myocardium (8 of 10 of their patients) or pericardium (2/3) accompanied by serological disease activity. Ansari et al (9) also reviewed cardiovascular manifestations including pericarditis, myocarditis and endocarditis due to immune complex deposition and the subsequent inflammatory reaction.

With regard to the administration of steroids to pregnant SS patients, there have been only a few reports. Aslan et al (10) describe a case of typical pSS who was treated with methylprednisolone and intravenous cyclophosphamide. In their case, the patient underwent hemodialysis for renal dys-

function. The dose of prednisolone was 100 mg daily accompanied by 500 mg of intravenous cyclophosphamide per month. Another reported case was a pregnant pSS patient complicated with proliferative glomerulonephritis (11). In both of these cases, the dose of prednisolone was no more than 100 mg daily. In the case of pregnant SLE patients, there is a detailed description with regard to various conditions of SLE (12). These patients with proliferative glomerulonephritis during pregnancy needed 20-75 mg of oral prednisolone instead of cyclophosphamide. These reports demonstrated that the required amount of oral prednisolone in pSS or SLE patients was no more than 100 mg a day. Although there have been no detailed descriptions of the appropriate steroid dosage in pSS cases, we agree that the dose should be low because the administration of excessive steroids during pregnancy might induce hypercoagulopathy or obstruction of the small vessels of the placenta, which would lead to incomplete fetal development or abortion.

It is generally thought that the disease activity of serositis such as pericarditis in autoimmune disorders can be improved only with large doses of steroids (3). However, in pregnant women, we must consider the disease activity of both pericarditis and hypercoagulation, the latter of which might occur if steroids are administered during pregnancy. There is a review that pregnancy itself does not appear to the influence clinical course of pSS (13) although there is a risk of congenital heart block of the baby. To predict the possibility of hypercoagulation in the placenta, we examined both serum FDP and D-dimer levels. Enhancement of coagulation is a crucial issue in late pregnancy. Morikawa et al (14) recently demonstrated that coagulation is more enhanced in twin gestation than in singleton gestation and they also suggested that plasma levels of FDP and D-dimer were elevated during pregnancy with twins. Although the usefulness of serum FDP and D-dimer as predictive markers is controversial because there are some reports to show that these markers had no association with thrombosis during pregnancy (15), both pregnancy and administration of oral prednisolone might act to accelerate coagulation synergistically. In the present case, these markers increased with the increased administration of oral prednisolone and decreased with its reduction, finally nearly normalizing after delivery. Thus, these markers could be useful in such cases.

In summary, we present here the first case report demonstrating successful treatment for a pregnant pSS patient with pericarditis. To achieve balance between the treatment of pericarditis and the hypercoagulation which might occur in the placenta, it is essential to carefully monitor the steroid dosage through serum FDP and D-dimer levels in order to protect the safety of both the patient and the fetus.

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