Onset of Systemic Lupus Erythematosus During Pregnancy

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When systemic lupus erythematosus (SLE) is first suspected during pregnancy, though rare, the diagnostic criteria are not different from those for nonpregnant women. The pregnancy outcome is good if treatment with adequate immunosuppressive agents starts as soon as the diagnosis is made. There are 4 cases in this report who had SLE onset during pregnancy. Although 2 of them suffered from preeclampsia, all 4 pregnancies resulted in favorable outcomes after the lupus was controlled by medical treatment. [J Chin Med Assoc 2006;69(3):130–133]

Key Words: immunosuppressive agents, pregnancy, systemic lupus erythematosus

Introduction

Pregnancy complicated with systemic lupus erythematosus (SLE) is frequently encountered, as it is one of the commonest medical diseases of young women. Pregnancy outcome is influenced by the following factors: placental dysfunction, the presence of antiphospholipid antibodies, preconceptional lupus activity, the severity of renal involvement, and the onset of SLE during pregnancy.1 The diagnostic criteria for SLE are not different between pregnant and nonpregnant women, although the onset of SLE during pregnancy is very rare. Other than steroids, azathioprine and hydroxychloroquine (HCQ)2 can be used safely in pregnancy complicated with SLE. There are 4 cases in this report who had onset of SLE during their pregnancies. Management involves aggressive treatment with immunosuppressive agents, just as is given to nonpregnant women, instead of termination of pregnancy.

Case Report

Case 1

A 22-year-old primigravid female, 17 weeks pregnant, presented to the outpatient clinic with complaints of facial malar rash, cold fingers, and repeated attacks of high fever for several days. Both her medical and gynecologic histories were unremarkable. Antinuclear antibody (ANA) and the anti-double strand DNA (ds-DNA) antibody were 1:2,560 and 256 IU/mL, respectively. White blood cell (WBC) count was 3,570/mm3 and daily urinary protein loss was 3.81 g. Although prednisolone 10 mg and HCQ 200 mg per day were prescribed at the onset of lupus, superimposed severe preeclampsia developed in the early third trimester. A male baby weighing 1,420 g was born by cesarean section because of fetal distress at the 33rd week of gestation with Apgar scores of 3, 5, and 7 at 1, 5, and 10 minutes of life, respectively. The disease was well controlled postpartum by daily administration...
Onset of SLE in pregnancy

J Chin Med Assoc • March 2006 • Vol 69 • No 3

131

of HCQ 400 mg, methylprednisolone 8 mg, azathioprine 100 mg, and colchicine 0.5 mg (Table 1).

Case 2
A 24-year-old female, gravida 4, para 0, denied any health history except frequent urinary tract infections. SLE developed at the gestational age of 15 weeks when she complained of facial malar rash, respiratory distress, body weight loss and Raynaud’s phenomenon. Positive diagnosis of SLE was based on skin biopsy. Laboratory data were as follows: ANA 1:640, ds-DNA < 10 IU/mL, immunoglobulin (Ig)G 1,940 mg/dL, IgA 281 mg/dL, IgM 64 mg/dL, complement C3 (C3) 103 mg/dL, complement C4 (C4) 15.8 mg/dL, rheumatic factor (RF) 123 IU/mL, C-reactive protein (CRP) 0.4 mg/dL, and clearance of creatinine (CCr) 106 mL/min. The 24-hour urinary specimen contained 0.03 g of protein. The disease was controlled with prednisolone 10 mg daily as soon as the diagnosis of SLE was established. She gave birth to a male baby, weighing 2,690 g, spontaneously at the 37th week of gestation with Apgar scores of 8 and 9 at 1 and 5 minutes, respectively. The peripartum course was uneventful and the disease was controlled with HCQ 400 mg and prednisolone 10 mg per day (Table 1).

Case 3
A 31-year-old female, primigravida and positive for hepatitis B virus, came to the clinic at the 26th week of pregnancy with symptoms of skin rashes all over the extremities, lower leg edema, dizziness, palpitation, and leukopenia. The results of blood tests were as follows: RF 47.7 IU/mL, CRP 1.5 mg/dL, ds-DNA 47 IU/mL, IgE < 10 mg/dL, CCr 211.9 cc/min, and daily protein loss of 0.48 g. Immunosuppressive therapy with prednisolone 10 mg and azathioprine 50 mg was given thereafter. Unfortunately, preeclampsia developed at the 38th week of gestation. A male baby, weighing 3,542 g, with Apgar scores of 8 and 9 at 1 and 5 minutes of life, respectively, was delivered by cesarean section owing to arrest of descent. The postoperative course was complicated with pulmonary edema. The diagnostic criteria during pregnancy were insufficient

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<tr>
<th>Table 1. Summary of cases</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Case no.</strong></td>
</tr>
<tr>
<td><strong>Age, yr</strong></td>
</tr>
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<td><strong>G and P</strong></td>
</tr>
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<td><strong>Onset GA, wk</strong></td>
</tr>
<tr>
<td><strong>Diagnostic criteria</strong></td>
</tr>
<tr>
<td><strong>Medicine during pregnancy</strong></td>
</tr>
<tr>
<td><strong>Obstetrical complications</strong></td>
</tr>
<tr>
<td><strong>Birth GA, wk</strong></td>
</tr>
<tr>
<td><strong>Delivery method</strong></td>
</tr>
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<td><strong>NB weight, g</strong></td>
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<td><strong>Treatment after delivery</strong></td>
</tr>
</tbody>
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Azath = azathioprine; C/S = cesarean section; G = gravidity; GA = gestational age; HCQ = hydroxychloroquine; MTPred = methylprednisolone; NB = newborn; NSD = normal spontaneous delivery; P = parity; Pred = prednisolone.
to rule in SLE, but after delivery, lupus was established based on the following findings: C3 28.0 mg/dL, C4 6.4 mg/dL, ds-DNA > 500 IU/mL, WBC 3, 100/mm³, ANA 1:1,280, and daily urinary protein loss of 3.6 g. Treatment was HCQ 200 mg, methylprednisolone 8 mg, and azathioprine 100 mg daily (Table 1).

Case 4
A 27-year-old female, gravida 3, para 0, abortion 2, presented with repeated attacks of malar rash, polyarthritis, and dyspnea on exertion at 10 weeks of conception. Blood tests showed ANA 1:160, ds-DNA 220 IU/mL, C3/C4 60.8/13.7 mg/dL, and WBC 3,600/mm³. With the impression of SLE, prednisolone 10 mg and HCQ 200 mg daily were given. A male newborn, weighing 3,220 g, with Apgar scores of 8 and 9 at 1 and 5 minutes, respectively, was born at the 39th week of pregnancy by cesarean section because of protracted cervical dilatation. Lupus was controlled with prednisolone 5 mg and HCQ 200 mg per day thereafter (Table 1).

Discussion
The revised diagnostic criteria for SLE, established in 1997, revealed no overlap in its symptoms and signs with the normal physiologic changes of pregnancy. The complements C3 and C4 change frequently in pregnant women compared with nonpregnant women, which means the change is more significant when serum levels are low during pregnancy. Therefore, there is no difference in the diagnosis of SLE whether the patient is pregnant or not.

All 4 cases discussed in this report had positive ANA, which is the screening test for SLE. The ds-DNA antibody, found in 80–90% of patients, was not only the most specific marker for the presence of SLE, but also served as an indicator of the disease activity. In Case 3, the diagnostic criteria for lupus during pregnancy based on the positive findings of ANA in serum and the skin lesion were insufficient. However, the presence of serologic findings of high titer of ds-DNA and low levels of C3 and C4, as well as high daily protein loss after delivery due to exacerbation were compatible with the diagnosis for lupus.

Because methotrexate and cyclophosphamide are harmful to the fetus, they are not used during pregnancy, especially during the first trimester, unless it is absolutely needed in specific cases. HCs is safe to use during pregnancy, especially in cases with malar rash, and discontinuation may result in lupus flare. The use of azathioprine is also safe for lupus pregnancy, although fetal growth and neonatal immunity impairments have been reported. In this study, although all 4 cases suffered from skin lesions, only 2 cases involved the use of HCQ. In our experience, the combination of prednisolone with either HCQ or azathioprine, depending on the disease activity, not only reduces the dosage of steroids, but also is safe during pregnancy. This may be the reason for the favorable outcomes in all 4 cases.

Two cases suffered from preeclampsia in this report. To make a differential diagnosis between lupus nephritis or SLE flare and preeclampsia based on laboratory findings is still undecided currently. However, prompt delivery in a relatively short time is the optimal management for mothers with SLE to avoid serious complications of preeclampsia including fetal hypoxemia.

Onset of SLE during pregnancy may pose a serious threat to the conceptus with an overall loss rate of 29%. Although the question of whether SLE is provoked by pregnancy still remains, the worsening of SLE in pregnancy is uncommon. In the 4 cases mentioned in this report, the mean gestational age of the onset of SLE was around 18 weeks, with the range between 10 and 25 weeks. Except for 1 patient who gave birth to her baby at the 33rd week of gestation due to an early attack of preeclampsia, the other 3 newborns were delivered near or at term. All pregnancy outcomes were favorable after medical treatments were administered. The case number in this report, however, is too small to draw a conclusion, but, overall, aggressive control of SLE during pregnancy is critical to achieve a favorable pregnancy outcome.

In conclusion, (1) based on the criteria needed for SLE, it is easy to make the diagnosis of SLE that develops during pregnancy; (2) good medical care is mandatory when the onset of SLE occurs during pregnancy; and (3) unless there is specific indication, such as acute pulmonary edema due to heart failure, or renal failure, it is unnecessary to terminate the pregnancy because the outcome can be favorable with the use of adequate immunosuppressive agents.

References


