Case Report

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New-onset Systemic Lupus Erythematosus in a Woman with Previous Lymphoma during Late Pregnancy: A Case Report and Literature Review

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ABSTRACT

Background: Systemic lupus erythematosus (SLE) is most likely to occur during the first and second trimesters of pregnancy. There were few studies focused on the new-onset SLE during the late pregnancy or puerperium. SLE has been considered an important cause of thrombocytopenia. However, lymphoma may also be a cause of thrombocytopenia. Here, we reported a challenging case of new-onset SLE occurred at the gestational age of 33 weeks, and the pregnant woman suffered lymphoma before.

Case Presentation: A 25-year-old primigravid Chinese woman with a medical history of non-Hodgkin lymphoma (NHL) suffered thrombocytopenia at 30+5 weeks of gestation. Her skin rashes occurred one week later. Her platelet count was decreased progressively. She had been misdiagnosed with the recrudescence of NHL. The final diagnosis of new-onset SLE was confirmed and a cesarean section was performed at the 34th week of pregnancy. Both the pregnant woman and the newborn were cured with good prognosis.

Conclusion: SLE should be considered in a pregnant woman with a medical history of malignancy to rule out other diseases, especially the rheumatic immune diseases.

Keywords: Late pregnancy, Lymphoma, Systemic lupus erythematosus, Thrombocytopenia

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INTRODUCTION

Systemic lupus erythematosus (SLE) is a kind of common chronic autoimmune disease among women of reproductive age (1). Despite the fact that there have been numerous research on the influence of SLE on pregnancy, (2), few of them have focused on the new-onset SLE during late pregnancy or puerperium. It has been reported that pregnant women with the onset of SLE are more likely to experience kidney and platelet involvement, which could lead to poor outcomes on both maternal and fetal aspects (3). The mechanism of SLE in pregnant women remains unclear (4). SLE in pregnant woman has been reported to occur often during the first and second trimesters, ranging from 10 to 25 weeks (5). The levels of estrogen and progesterone significantly change during pregnancy. It is not clear

whether the onset of SLE is provoked by pregnancy, given that some cases of SLE are onset at the stage of puerperium. A growing number of studies have confirmed that patients with SLE are at an overall increased risk of malignancies, particularly hematological malignancy and lung/liver/thyroid cancers (6-8). However, patients with SLE secondary to the above cancers have not been reported and the relative mechanisms is also unclear. Thus, this case report describes a difficult case of new-onset SLE that arose at 33 weeks of pregnancy and the pregnant mother had previously suffered from lymphoma.

CASE PRESENTATION

A 25-year-old primigravid Chinese woman with a medical history of non-Hodgkin lymphoma (NHL) was admitted to our hospital. Two years earlier, she had been diagnosed with small B-cell lymphoma and discharged successfully after four R-COP chemotherapy cycles (rituximab, cyclophosphamide, vindesine, and prednisone). She recovered well and was classified as complete remission. After pregnancy, she underwent prenatal examination regularly and there was no remarkable abnormality during the first and second trimester, except anemia (hemoglobin level of 9.0-9.7 g/dL). However, she suffered thrombocytopenia (platelet count of 88×10^9/L) at after 30^{+5} weeks of gestation without any other discomforts.

One week later, her complaint of skin rashes brought her to the Dermatology Outpatient Clinic. Erythema appeared in both palms with well-defined boundary. There was no malar rash, discoid rash, oral ulcers, or photosensitivity. The blood tests showed negative results of allergen, immunoglobulin E (IgE), anti-coxsackie virus IgM (COX) and anti-herpes simplex virus IgM. Calamine was then prescribed to relieve her uncomfortable symptoms. However, her platelet count were decreased to 51×10^9/L at 33 weeks of gestation, while it further dropped to 42×10^9/L in the following four days. Therefore, she was admitted to the Department of Hematology under the suspicion of recurrence of hematological disease. The pregnant woman rejected bone marrow aspiration and received gamma globulin treatment (25 g/d) when the platelet count was 31×10^9/L. However, the effect of medication was poor and her platelet count were decreasing progressively (Figure 1). Then, she was transferred to the Obstetrics Department on the request of termination of pregnancy at 34 weeks of gestation.

A multidisciplinary consultation was held and a complete evaluation for possible inducing factors was measured, especially the immune indicators associated with rheumatic diseases. Laboratory examinations showed rheumatic factor of 258 IU/mL (RF, normal: <20), complement C3 of 0.3 g/L (normal: 0.79-1.52), complement C4 of 0.05 g/L (normal:0.16-0.38), anti-dsDNA of 1:100

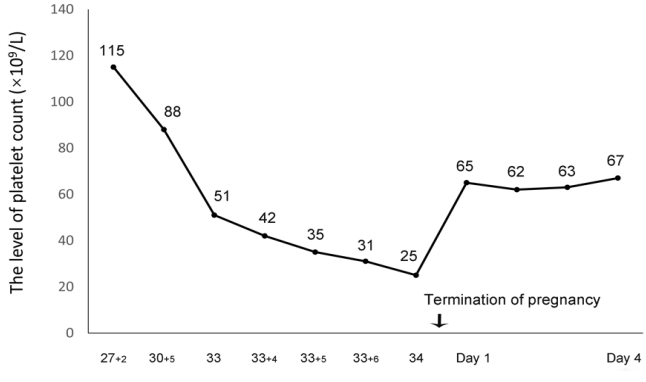

Figure 1. The changing trend of platelet count. The patient suffered thrombocytopenia (platelet count of 88×10^9/L) at 30^{+5} weeks of gestation. It then gradually diminished in size. Platelet levels increased after the pregnancy was terminated at 34 weeks.

(normal: negative), and antinuclear antibody (ANA) of 1:1000 (normal: negative). The 24-h urinary specimen contained 4.607 g of protein. According to the 1997 revised American College of Rheumatology criteria for SLE, she fulfilled 5 out of 11 diagnostic criteria for new-onset SLE, including skin rashes, albuminuria, thrombocytopenia, positive ANA and positive anti-dsDNA and low C3/C4. Therefore, the diagnosis of SLE was then considered.

The patient rejected medical treatments such as prednisone and insisted on terminating the pregnancy. The cesarean section was performed on the second day and a 1860 g male infant was born with Apgar scores of 10 at 1 and 5 min after birth, respectively. The lupus was managed with gamma globulin therapy. (25 g/day, q.d) and methylprednisolone (40 mg/day, bid) for 5 days after cesarean section. The patient was referred to get followed-up by Rheumatology Immunology Department. The maintenance treatments included hydroxychloroquine (0.2 g/day, q.d) and methylprednisolone (4 mg/day, q.d). Both the patient and the newborn were cured with good prognosis. Informed written consent was obtained from the patient for publication. This study was approved by the ethics committee of Zhejiang Provincial People's Hospital.

DISCUSSION

Increased lupus activity increases the risks of complications during pregnancy, such as miscarriage and stillbirth. In some patients, SLE activity even can be life-threatening during pregnancy. It has been widely debated whether SLE activity increases during pregnancy or not. In this case report, the pregnant woman was first diagnosed with SLE during the third trimester of pregnancy. Her history of lymphoma made it more difficult to diagnose SLE (9). It is considered that the malignancy rates in SLE patients are increased, while the mechanisms underlying the cancer development in SLE have been reported to be associated with the activity of multiple inflammatory cytokines and possible viral factors (9). The data regarding lymphoma survival and outcome in SLE patients are sparse (10). In the present case report, it seems that pregnancy plays a more important role in the survival and outcome. The procedure is effective once the pregnancy has been terminated. During the past two years' follow-up, this patient had recovered well without the recurrence of lymphoma.

According to the new SLE diagnostic criteria, whether a patient is pregnant or not makes no difference in the diagnosis of SLE (11). Most patients with SLE in pregnancy are diagnosed before pregnancy. It is reported that the flare-ups in patients with SLE often occur during the first and second trimesters of pregnancy, and few onsets at the third trimesters of pregnancy or puerperium. Yang et al. have reported that the mean gestational age of the onset of SLE is 18 weeks, with the range between 10-25 weeks (5). It could be explained that the levels of hormones and serum cytokines change greatly during the first and second trimesters of pregnancy while these changes decrease during the third trimester (12, 13). It is difficult to diagnose SLE according to the clinical symptoms, because there are no significant differences occurring in clinical symptoms between new-onset patients and pre-existing or active SLE. The clinical symptoms may also be similar to those of normal pregnancy. Throughout this case report, we suggest that if skin or joint problems emerge in the third trimester of pregnancy, supervision must be intensified.

Patients with new onset of SLE during pregnancy tend to experience more severe symptoms with a higher prevalence of thrombocytopenia and renal involvement (14). Other symptoms included facial and palmar erythema, dyspnea, arthralgia and fever. The blood volume of pregnant women increases by 50% in normal pregnancies, therefore, up to 50% healthy pregnant women are diagnosed with anemia (15). Mild thrombocytopenia can

occur in up to 8% of normal pregnancies. However, if severe low platelet count combines with hypertension, HELLP syndrome should be considered, which is a severe derivative of preeclampsia with hemolysis, elevated liver tests, and low platelets. It is reported that some patients develop preeclampsia after the diagnosis of SLE (16). The rate of preeclampsia secondary in SLE is 13%-35% (17). In this case report, both the patient's blood pressure and liver enzymes were normal, so the decreased platelet count caused by preeclampsia was ruled out. She was admitted to the hematological ward and was advised to have bone marrow puncture for a confirmed diagnosis. Her skin involvement was so inappreciable that the diagnosis and management of SLE were delayed, although the platelet count decreased progressively.

The therapy of SLE in pregnancy involves aggressive treatment with immunosuppressive agents, which is the same as the non-pregnant women. It has been reported that azathioprine and hydroxychloroquine are safe in pregnant patients combined with SLE (18). However, termination of pregnancy is also a good choice of management. This patient accepted the cesarean section when the platelet count decreased to 25×10^9/L at the 34th week of pregnancy. After the termination of pregnancy, the platelet count was stable, with the concentration fluctuating between 62×10^9/L and 67×10^9/L. There was no need for blood or plates transfusion after the operation except for 24 units of platelets infused before the operation.

CONCLUSION

In conclusion, we introduced a rare new case of SLE in the third trimester of pregnancy, accompanied by a medical history of lymphoma that was misdiagnosed as a blood disease. Its incipient atypical symptoms posed a challenge to the obstetricians. SLE should be considered as one of the potential differential diagnoses when we encounter pregnant patients with unexplained thrombocytopenia. More screening examinations should be performed to rule out other diseases. However, after timely termination of pregnancy, both the patient and the fetus achieved good recovery and prognosis. This data demonstrates that SLE can arise throughout any trimester of pregnancy. Coupled with this, the combination of SLE and lymphoma in this pregnant woman warrant additional investigation.

Conflict of Interest: None declared.

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