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ABOUT COVER

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CASE REPORT

Immunotherapies application in active stage of systemic lupus erythematosus in pregnancy: A case report and review of literature

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Abstract

BACKGROUND

Pregnancy in the setting of systemic lupus erythematosus can worsen the condition from the stable to active stage, with quality of life and fertility desire being particular concerns. Pregnancy in the active stage of systemic lupus erythematosus (ASLE), although rare and complicated to manage, can be treated favorably with immunotherapies ifs used properly. Here we report such a success case.

CASE SUMMARY

A 31-year-old primigravida patient, diagnosed with SLE seven years ago, was induced ASLE after a cold at 21 + weeks. The patient's vital signs on presentation were normal. Her laboratory exam was remarkable for significant proteinuria, liver and renal dysfunction, and low C3 and C4 levels. Infectious work-up was negative. The patient was diagnosed with ASLE. She was given immuno-suppressive agents (methylprednisolone, gamma globulin and azathioprine *etc.*) and plasma adsorption therapy, monitoring blood pressure every 8 h, fetal heart rate twice a day, and liver and renal function at least twice a week. Successful maternal and fetal outcomes are presented here.

CONCLUSION

Child-bearing in ASLE has become more promising, even for this difficult case of ASLE with multiple organ damage. Thorough antepartum counseling, cautious maternal-fetal monitoring, and multi-organ function monitoring by multidisciplinary specialties are keys to favorable pregnancy outcomes.

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Core Tip: For systemic lupus erythematosus (SLE) patients who were stable prior to pregnancy, a considerable proportion of them will have varying degrees of disease activity after pregnancy. Therefore, immunotherapy during pregnancy is an essential tool to maintain stable condition. However, many treatments, especially immunotherapies, have some adverse reactions, so the use of this therapy during pregnancy should be done cautiously. This paper presents a case of pregnancy complicated with active stage (ASLE), expounds the importance of immunotherapy in the control of ASLE, and summarizes the traditional and emerging immunotherapies for ASLE in order to provide some guidance for the clinical use of immunotherapies in pregnancy.

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INTRODUCTION

Systemic lupus erythematosus (SLE) predominantly affects women during their reproductive years, occurring in about 1/1000 women aged between 15 and 45 years[1]. Disease flares are common in pregnant SLE patients, occurring in up to 65% of cases[2]. Preterm birth is the most common adverse pregnancy outcome in women with active stage of systemic lupus erythematosus (ASLE), with incidence close to 50% in women with high disease activity[3]. Preeclampsia (PE) and/or severe PE represent another major concern for ASLE pregnant women since they occur in nearly 35% of cases, which makes it 10 times more common than in the general population. In addition, pregnant women with ASLE have an increased risk of adverse maternal and fetal outcomes, as active disease and lupus nephritis (LN) can increase maternal mortality, which may be 20-fold higher in women with SLE. Two major causes of death are complications from lupus disease activity and opportunistic infection[4]. The abortion rate and stillbirth rate were 19%-26% and 1%-8%, respectively[5]. The fetal mortality rate of ASLE was 2.5 times higher than that of the normal population[6].

Pregnancy in ASLE takes high-risk pregnancy to a new horizon because of its complexity and the interplay among the maternal patient, the fetal patient, and multiple organ damage. With the cooperation between rheumatic immunologist and obstetrician, ASLE can be stabilized to restore not only longevity but also fertility. Here, we report a primigravida female, who suffered a life-threatening multisystem flare that required a prolonged stay at Rheumatism Immunology Department and interruption of pregnancy in the third trimester. Although many cases of life-threatening and even fatal maternal complications of SLE have been described in the literature[7], there are few successful reported cases in which such a large number of multiple organ systems are affected, as we describe here. A literature review regarding application of immunosuppressive agents in pregnancy with ASLE will be discussed.

CASE PRESENTATION

Chief complaints

A 31-year-old housewife, Han Chinese primigravida patient, had elevated blood pressure to 140/90 mmHg at 14 wk of pregnancy. She was given labetalol 100 mg twice daily, and ASLE was induced after a cold at 21+ wk. One week later, she presented to the Nephrology Department (ND) and the Obstetrics Department (OD) complaining of nasal congestion, sore throat, and stomachache at gestational age of

22+ wk for ASLE with multiple organ damage.

History of present illness

The patient's symptoms started 1 wk prior to arrival to the ND and OD of Tongde Hospital of Zhejiang Province in China. She described symptoms of upper respiratory tract infection, nasal congestion, sore throat, and stomachache. She denied any rash (including malar erythema), aphthous ulcers, hematuria, pleuritic chest pain, shortness of breath, fever, or non-specific arthralgias (without swelling) of her wrists, fingers, and ankles. Her laboratory exam was remarkable for significant proteinuria, liver, and renal dysfunction and low C3 and C4 levels (Table 1). Infectious work-up was negative.

History of past illness

The patient had underlying SLE at age 24, complicated with LN (nephrotic syndrome) (Table 2). She was on multiple immunosuppressive agent maintenance [methylprednisolone 16 mg once daily, tacrolimus (TAC) 2 mg twice daily, and mycophenolate mofetil (MMF) 0.5 g once daily]. The condition of lupus and renal function were stable with a large amount of proteinuria, 24-h urinary protein fluctuated around 3 g, but the plasma albumin remained above 30 g/L. The patient was seen with her husband for advice regarding planning a pregnancy; drugs were adjusted to azathioprine (AZA, dose: 50 mg once daily), methylprednisolone (dose: 4 mg once daily) at 6 mo before pregnancy, but hydroxychloroquine was not used because of fundus lesions. The fetus was conceived naturally. When consulting during pre-pregnancy, related maternal and fetal risks, such as PE, abortion, preterm delivery, fetal growth restriction, and multiple organ dysfunction were explained to her. The patient's condition was still in a stable state until 21+ wk of pregnancy.

Personal and family history

No abnormalities.

Physical examination

On presentation, the patient's vital signs were normal: 36.7 °C, heart rate of 96 bpm, blood pressure of 145/96 mmHg, respiratory rate of 20, and oxygen saturation of 100% on room air. The height of uterus was 18 cm, the abdominal circumference was 104 cm, the estimated fetal weight was 550 g, the fetal heart rate was 140 times per mine, the uterine contraction was not obvious, and the fetal movement was felt.

Laboratory examinations

Initial laboratory testing included a complete blood count and a comprehensive metabolic panel measurement (Table 1).

FINAL DIAGNOSIS

G1P0 21+ wk of pregnancy, pregnancy with ASLE, multiple organ functional damage in lupus.

TREATMENT

The patient was admitted at gestation age of 22^{+5} wk for ASLE with methylprednisolone injection (dose: 500 mg once daily for 3 d) and gamma globulin injection (dose: 20 g once daily for 5 d). Drug dosage decreases gradually after remission, during 23^{+4} and 24^{+2} wk, she was on methylprednisolone injection (dose: 40 mg once daily) and (AZA injection (dose: 75 mg once daily) maintenance. However, at 24^{+3} wk of pregnancy, the condition deteriorated [alanine aminotransferase: 465 U/L, aspartate aminotransferase (AST): 525 U/L, gamma-glutamyl transferase 335 U/L, urea: 14.8 mmol/L, Cr: 163 μmol/L). She was given methylprednisolone injection (dose: 500 mg the 1st day, 300 mg Q12h the 2nd day), and then plasma adsorption therapy was added. Considering the treatment of the premature infant, the patient was transferred to the OD of The First Affiliated Hospital of Zhejiang University for better comprehensive care. Subsequently, she was admitted with methylprednisolone injection (dose: 40 mg once daily), AZA (dose: 75 mg once daily), hydroxychloroquine (dose: 200 mg once daily), and continuous fetal monitoring till 28 wk of pregnancy.

Table 1 The changes of systemic lupus erythematosus in pregnancy of the patients

Time	Preconception	GA 23+ wk	GA 24+ wk	GA 24+ to 28 wk	Postpartum, 7-34 d
Related clinical manifestations and immune related indicators	24-h urine protein fluctuates around 3 g	ALT: 197 U/L; AST: 185 U/L	Hb: 87 g/L	Cr: 176 μmol/L	Hb: 77 g/L
			ALT: 465 U/L; AST: 525 U/L		ALT: 15 U/L; AST: 23 U/L
			Cr: 163 μmol/L		Cr: 79 μmol/L
			24-h urine protein 19.43 g		24-h urine protein 5.81 g
			C3: 0.60 g/L; C4: 0.11 g/L		C3: 0.45 g/L; C4: 0.16 g/L
SLE activity index (score)	4 (proteinuria)	9 (proteinuria, hematuria, fever)	15 (proteinuria, hematuria, cylindruria, fever)		9 (proteinuria, cylindruria, fever)
Immunosuppressant	AZA (dose: 50 mg/d)	AZA (dose: 75 mg/d)	MP injection (dose: 500 mg/d × 3 d, 300 mg/Q12 h × 2 d)	MP injection (dose: 40 mg/d, 80 mg/d × 3 d)	Rituximab 100 mg × 1/2 wk
	MP (dose: 4 mg /d)	MP injection (dose: 500 mg/d × 3 d)	Plasma adsorption therapy	AZA (dose: 75 mg/d)	CYC 200 mg × 2 wk
		IVIg (dose: 20 g /d × 5 d)		HCQ (dose: 200 mg/d)	MP injection (dose: 40 + 30 mg/d × 2 d, 40 + 20 mg/d × 8 d)
				TAC (0.5 mg × 1 d, 0.25 mg × 2 d)	
Clinical response		Hb: 93 g/L	Hb: 81 g/L		Hb: 85 g/L
		ALT: 56 U/L; AST: 39 U/L	ALT: 282 U/L; AST: 130 U/L		ALT: 23 U/L; AST: 10 U/L
		Cr: 102 μmol/L	Cr: 136 μmol/L		Cr: 82 μmol/L
		24-h urine protein fluctuates around 19.68 g			24-h urine protein 4.40 g
		C3: 0.52 g/L; C4: 0.10 g/L			C3: 0.68 g/L; C4: 0.18 g/L

ALT: Alanine aminotransferase; AST: Aspartate aminotransferase; AZA: Azathioprine; C3: Complement 3; C4: Complement 4; Cr: Creatinine; CYC: Cyclophosphamide; Hb: Hemoglobin; HCQ: Hydroxychloroquine; sIVIg: Intravenous immunoglobulin; ;MP: Methylprednisolone; SLE: Systemic lupus erythematosus; ; TAC: Tacrolimus .

During the period, because of progressive impairment of renal function (the highest level of serum creatinine was 176 μmol/L), methylprednisolone was adjusted to a dose of 80 mg once daily for 3 d, and TAC (0.5 mg the 1st day, 0.25 mg the other 2 d) was discontinued after 3 d of use. Cesarean section at gestational age of 28 wk was performed due to poor fetal heart beat variability. The Apgar score of the male newborn weighted 650 g at first min, fifth min, and tenth min were 5, 8, and 8, respectively. Methylprednisolone injection (dose: 80 mg once daily for 3 d) and gamma globulin (dose: 20 g once daily for 5 d) were given on the day of operation. The patient stopped breastfeeding after delivery, and returned to Tongde Hospital of Zhejiang Province 1 wk after the operation. The disease was still considered active, and the patient received methylprednisolone injection (dose: 40 + 30 mg once daily for 2 d, 40 + 20 mg for 8 d), rituximab (dose: 100 mg once 2 wk for 2 times), and cyclophosphamide (CYC) (dose: 200 mg twice a week for 7 times). The methylprednisolone gradually decreased on the 18th day after delivery, and it was changed to oral preparation on the 25th day. Methylprednisolone (dose: 40 mg once daily) was given at discharge. Meanwhile, AZA (dose: 50 mg once daily) and hydroxychloroquine (dose: 0.2 g once daily) maintained to leaving hospital.

Table 2 Related clinical manifestations and immune indicators of the patient

Serial	No.	Diagnostic indexes
Clinical manifestation	1	Fever (37.6-40 °C)
	2	Acute cutaneous lupus erythematosus ("butterfly rash", "discoid Rash")
	3	Serositis (lung CT images: Serous membrane fluid)
	4	Synovitis (mild joint pain of wrist joint of both hands)
	5	Blood system involvement (leukopenia 2.3 × 10^9/L, hemolytic anemia 95 g/L, thrombocytopenia 50 × 10^9/L; ESR 37 mmHg)
	6	Renal system involvement (24-h urine protein 5422.00 mg; RBC under microscope: ++/HP, protein: +2, RBC morphological information: Heterogeneous cell type)
	7	Aphthous ulcers
Immunological indicators	8	ANA level above laboratory reference range (1:1000)
	9	Anti-dsDNA antibodies (+)
	10	Anti-SSA (+)
	11	Anti-Sm antibodies (+)
	12	Antiphospholipid antibodies (IgA 4.21 mg/L, IgG 18.5 g/L)
	13	Low complement (C3: 0.21 g/L, C4: 0.04 g/L)
	14	CD3+CD4+CD28CD4 (37.0%)

ANA: Antinuclear antibodies; CT: Computed tomography; ESR: Erythrocyte sedimentation rate; RBC: Red blood cell.

OUTCOME AND FOLLOW-UP

As of the date of article submission, the patient has been relatively stable and her child thrived.

DISCUSSION

This case described a successful case of a stable maternal-fetal outcome for a pregnant woman with ASLE. The patient in this case was given immunosuppressive agents (methylprednisolone, gamma globulin and AZA, *etc.*) emaintenance and plasma adsorption therapy, blood pressure, fetal heart rate, and liver and renal function were monitored regularly. Combining thorough antepartum counseling with cautious maternal-fetal health outcome monitoring and multi-organ function monitoring by multidisciplinary specialties, favorable pregnancy outcomes were achieved. This case suggested that it is necessary to standardize the management of SLE in pregnancy in order to improve effectively the pregnancy outcome of patients.

SLE is a highly heterogeneous and complex autoimmune disease with various clinical manifestations and various organ involvement, including kidney, joints, skin, central and peripheral nervous system, cardiovascular system, and more. The mechanism of SLE pathogenesis still remains largely unknown. The current treatment cornerstones include antimalarial and immunosuppressive medications and glucocorticosteroids. Belimumab has been the only SLE treatment drug approved by the United States Food and Drug Administration in more than 50 years. Recently, great effort has been made in identifying new SLE-targeted drugs with better control of the disease and less adverse events (AEs). LN is one of the most serious complications of ASLE[8-10]. In an international observational study of newly diagnosed SLE patients, LN occurred in 38.3% of subjects[11]. When the kidneys are affected in SLE patients, stronger immune suppressing treatment is usually needed. The traditional drugs used in treatment of LN often cause serious side effects, therefore, research into new treatments is necessary. Pregnancy can aggravate SLE, induce ASLE, increase the incidence of complications and adverse outcomes, and pose a great threat to maternal and fetal health[7,12,13]. Based on disease activity and serological profile, preconception counselling, risk stratification, individualized treatments, and close monitoring for maternal and fetal complications are important for successful pregnancies with

ASLE[14]. Considering various immunological defects of SLE pathogenesis, here we review and summarize traditional and emerging immunotherapies for SLE and prospect some novel immunotherapies, which may be helpful for better treatments for pregnancies with ASLE and LN in the future.

Traditional immunotherapies

In this case, multiple traditional synthetic drugs were given to the patient, including AZA, methylprednisolone, TAC, CYC, rituximab, and MMF, although clear previous demonstrations of their clinical efficacy were limited[15]. Implementation of immunosuppressive drugs is largely based on clinical experience. Traditional immunotherapies, mainly targeting T cells, normally had serious side effects[16]. CYC has several potential side effects, including chromosomal damage, leukopenia, infection, and increased risk of malignancy[17,18], depending on the dosage and duration of therapy. Thus, CYC should not be prescribed during the first trimester of pregnancy. Its use in the second or third trimester should be limited to cases of flares refractory to methylprednisolone pulses or other drugs. MMF side-effects include gastrointestinal symptoms, bone marrow suppression, infection, and risk of neoplasia[19,20].

The European Teratology Information Services reported that the probability of spontaneous abortion in women who received MMF was about 45%. Prematurity (62%) and low birth weight (31%) were frequent. CYC is a non-specific steroid hormone drug for certain SLE and is effective for immediately reducing inflammation; however, long-term use of CYC can cause serious side effects. Three drugs play roles by inhibiting autoimmune T lymphocyte proliferation: MTX is a folate analogue, MMF can inhibit inosine monophosphate dehydrogenase, while CSA and TAC function as calcineurin inhibitors. CYC, an alkylating agent, is often used as an induction treatment for severe lupus and is replaced by agents such as mycophenolic acid or MMF or AZA for long-term maintenance therapy[15]. Low-dose combinations of TAC and MMF seem to be more effective than pulse CYC as induction therapy in Chinese patients[18,21]. The 10-year long-term follow-up data of the MAINTAIN Trial suggested that MMF was not superior to AZA as maintenance therapy in a Caucasian population with proliferative LN[22]. CSA or TAC usually has fewer side-effects and better long-term maintenance outcomes for LN[18]. Patients with LN treated with MMF should be changed to AZA during pregnancy, glucocorticoid and AZA are recommended for the recurrence of LN in pregnancy (if necessary for relapse)[14,23]. Methotrexate, MMF, and CYC require discontinuation before conception due to proven teratogenicity[24]. Prasterone and vitamin D represent two other immunomodulatory agents, which may be used as supplements to control SLE activity and reduce use of CYC[25-27]. Compatibility with pregnancy and lactation was suggested for antimalarials, sulfasalazine, AZA, ciclosporin, TAC, colchicine, intravenous immunoglobulin, and glucocorticoids. Among them, intravenous immunoglobulin has non-specific anti-infective effect, which can protect the immune contusion caused by high-dose glucocorticoids and CYC. It is especially suitable for patients with high activity of lupus with severe infection and poor response to hormone immunosuppressive agents. Insufficient documentation was found for leflunomide, tofacitinib as well as abatacept, rituximab, belimumab, tocilizumab, ustekinumab, and anakinra in regard to pregnancy safety[28].

Emerging and novel immunotherapies

Emerging and novel therapies for SLE focus on targeting B cells, T cells, cytokines/chemokines, and immune regulating signaling pathways, human papilloma virus (HPV) vaccines, and stem cell therapy. B cell-based therapies consisted of targeting B cell surface proteins CD19, CD20, and CD22[29-31] or targeting costimulatory receptor/ligands including CD40/CD40-ligand, CD30/CD30 ligand, or inducible costimulator ICOS (CD278)/ICOS ligand interactions[32-34], or targeting B cell antigen receptor signaling pathway related protein spleen tyrosine kinase, *etc*[35]. Other therapies include targeting cytokines that inhibit B cell survival and differentiation, including interleukin (IL)-6, IL-21, IL-17, IL-10 IL-37, CD257 (B lymphocyte stimulator, B cell activating factor), CD256 (a proliferation-inducing ligand), and type I interferons[36-39] or targeting homing receptors necessary for B cell migration to germinal centers or effector niches, such as chemokine receptors/chemokines including CXCR4/CXCL12, CXCR5/CXCL13, and CXCR3/CXCL9[40-42]. In addition, therapies block toll-like receptor (TLR) stimulation, including TLR7 and TLR9[43,44], and block T and B cell costimulation by preventing CD28 binding to CD80/CD86[45,46]. Rituximab is the best characterized of the anti-CD20 monoclonal antibodies (mAbs).

Belimumab, a fully humanized monoclonal mAb against B lymphocyte stimulator,

can decrease the activation of B-cells and consequently decreases antibody production. In 2017, the United States Food and Drug Administration approved subcutaneous (SC) belimumab as a novel add-on therapy for the treatment of active autoantibody positive SLE patients receiving standard therapy[47]. Belimumab is generally safe and well tolerated and is used in combination with standard immunosuppressants. SC belimumab (200 mg/wk) has demonstrated similar efficacy, safety, and tolerability with monthly intravenous (IV) belimumab. In a retrospective study of the OBSErve registry in Germany on 102 patients treated with IV belimumab as an add-on therapy in active SLE, during the first 6 mo of treatment, a reduction of SLE Disease Activity Index scores and glucocorticoid usage was recorded, and an improvement in overall disease activity for 78% of patients has been shown[48]. Overall, SC belimumab appears to be preferred over IV belimumab for easier use, more convenience, and higher patient satisfaction. The drug administration route is time-saving and less costly. In a randomized 52-wk phase III study (BLISS-SC) on 839 patients with moderate-to-severe SLE, SC belimumab added to standard of care showed significantly higher efficacy with improved SLE response index (SRI-4), decreased time to severe flare, and corticosteroid dose reduction compared to standard of care plus placebo. Safety results in the belimumab group were comparable to the placebo group[49].

Rituximab is a B cell-depleting anti-CD20 antibody[50-52], and belimumab and rituximab combination may be a highly effective treatment of SLE through complementary B cell depletion mechanisms[53]. A randomized, phase III, 104-wk study of BLISS-BELIEVE comparing the efficacy, safety of SC belimumab in combination with rituximab in SLE patients with belimumab alone[54], and clinical trials investigating belimumab and rituximab combination therapy in LN are underway. Pregnancy data for belimumab are limited now.

Novel immune-modulating drugs consisting of anifrolumab[55], sifalimumab[56,57], rontalizumab[58], epratuzumab[59,60], and SM03[61], all anti-interferon-α/receptor monoclonal antibodies, are currently in phase I and II clinical trials to treat patients resistant to conventional therapies[8]. Obinutuzumab[62], an anti-CD20 mAb for B cell depletion, is in phase II trials for proliferative LN. These early phase clinical studies suggested promising efficacy and safety results for patients with ASLE.

Proposals for vaccination in SLE patients has increased recently. A phase I study by Dhar *et al*[63] on quadrivalent HPV in 34 African-American women patients with active SLE disease (SLE Disease Activity Index > 2) confirmed that the vaccine is safe, well tolerated, and highly immunogenic; no patient experienced a lupus flare or a serious AE related to vaccine. The quadrivalent HPV vaccine GARDASIL was shown to be well tolerated and reasonably efficacious in female Chinese patients with stable SLE[64]. The follow-up study at 5 years demonstrated that the immunogenicity of GARDASIL was persistent in the majority. Patients with more SLE renal flares and had received more immunosuppression (prednisolone, MMF, and TAC) were more likely to have lower total immunoglobulin G anti-HPV titers. Other immunosuppressive agents (CYC, AZA, hydroxychloroquine, and CSA) did not show any significant relationship with the anti-HPV titers[65]. The factors decreasing immunogenicity of HPV vaccines in SLE include an active SLE disease, treatment with an immunosuppressant, *etc*. In clinical trials, solicited AEs and serious AEs following GARDASIL vaccination were similar in the vaccine and placebo groups of subjects. It should be kept in mind that the data are obtained on a small number of patients, future large scale patient clinical trials are needed.

Encouraging results using immunosuppressive extracellular vesicles derived from human mesenchymal stem cells (MSC) to treat refractory SLE have indicated the efficacy and well-tolerated safety in clinical trials[66]. MSCs possess immunosuppressive capacity through inhibiting lymphocyte activation/proliferation and proinflammatory cytokine secretion. More trials, however, still need to be performed to determine the clinical efficacy of MSCs to treat SLE. Moreover, the study is subject to strict regulatory constraints of stem cell-based pharmacological development.

There is no radical cure for perinatal SLE. Early diagnosis and treatment are emphasized to avoid or delay irreversible pathological damage of tissues and organs, clinicians should master the indications and contraindications of drugs and measure the risks and benefits of pregnancy treatment according to the severity of the disease. However, there are still some controversies about the dosage and course of immunosuppressive therapy during pregnancy. Bao *et al*[67] first put forward the concept of multi-target therapy. The combination of immunosuppressive agents with different targets can reduce the dose of each immunosuppressant, which not only ensures the effectiveness of drugs but also reduces the risk of adverse reactions.

In this case, patient was applied immunosuppressive agents (methylprednisolone, gamma globulin, AZA, *etc*.). In addition, there are immunosorbent therapies that

achieve the goal of treatment by removing pathogenic lipoproteins or autoantibodies. It is worth mentioning that immunosorbent therapy can be used as a new technology for patients with severe pregnancy complications whose traditional treatment methods are ineffective[68]. In addition, SLE is the connective tissue disease with the highest mortality, and patients with chronic inflammatory immune-mediated diseases are at high risk of acquiring infections as they are often treated with immunosuppressive or biological drugs. They are at higher risk for influenza and *Streptococcus pneumoniae* infections. The current EULAR guideline about vaccination for patients with rheumatic diseases strongly recommends vaccination against seasonal influenza[69]. Therefore, if the patient can be vaccinated against influenza before pregnancy, lupus activity may be avoided during pregnancy.

Puerperium is still a high-risk period for SLE patients, with the risk of exacerbation and thromboembolism. The renal function, urinary protein, coagulation function, blood pressure and the amount of incoming and outgoing blood still need to be monitored closely at 3 wk postpartum. Especially in the anti-phospholipid antibody positive patients, low molecular weight heparin should be used to prevent thrombosis until 4-6 wk postpartum. Long-term use of heparin requires calcium and vitamin D supplements until the end of lactation. Postpartum application of bromocriptine may reduce the aggravation of SLE.

CONCLUSION

Child-bearing in ASLE has become more promising nowadays, even for a difficult case of ASLE with multiple organ damage. Thorough antepartum counseling, cautious maternal-fetal monitoring, and multi-organ function monitoring by multidisciplinary specialties are keys to favorable pregnancy outcomes.

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