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Pregnancy in systemic lupus erythematosus and antiphospholipid syndrome

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A B S T R A C T

Systemic lupus erythematosus (SLE) is a chronic inflammatory autoimmune disease with a high prevalence in females of childbearing age. Pregnancy in SLE nowadays has favorable outcomes for the majority of women. However, flares of disease activity, preeclampsia, fetal loss, and preterm birth are well-known risks in such pregnancies. Anti-SS-A(Ro)/SS-B(La) antibodies put fetuses at risk for congenital heart block and neonatal lupus. Several risk factors for adverse pregnancy outcomes have been identified. Women with antiphospholipid antibodies or antiphospholipid syndrome and lupus nephritis represent a group with high risk for obstetric complications. Factors such as appropriate preconception counseling and medication adjustment, strict disease control prior to pregnancy, and intensive surveillance during and after pregnancy are essential to improve pregnancy outcome. The aim of this review article is to update on the medical care of pregnancy in these women to ensure the best maternal and fetal prognosis.

Introduction

Systemic lupus erythematosus (SLE) and the antiphospholipid syndrome (APS) mostly affect women of childbearing age. Earlier recognition of the disease and advances in medical treatment

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improved the long-term prognosis. As a result, an increasing number of women affected by these diseases can realize their desire of having children. The number of pregnancies in women with SLE in the USA is estimated at 4500 per year [1,2]. There are no reliable figures for Europe, but in 2016, the Germany-wide pregnancy register Rhekiss recorded over 100 SLE-pregnancies within 1 year (www.rhekiss.de). Complications during pregnancy may be divided into maternal (lupus flares, worsening of renal function, preeclampsia, and thrombotic events) and/or fetal-neonatal (miscarriage, preterm birth, intrauterine growth retardation (IUGR), and neonatal lupus (NL) syndrome). Best pregnancy outcomes are obtained with a cohesive multidisciplinary approach. This includes effective pre-pregnancy risk assessment and stratification followed by individually tailored management and monitoring during pregnancy.

Fertility, reproductive health procedures, and contraception

Fertility in women with SLE or APS

The rate of infertility in women with SLE equals the rate in healthy women (11%–16%) [3,4]. However, women with SLE have on average fewer children than women in the general population [4]. Subfertility could result from the disease itself or from patients' concerns [5]. Antiphospholipid antibodies (aPL) are not associated with infertility, and fertility of women with APS is not impaired. However, a higher rate of miscarriages and fewer live births contribute to smaller family size [6–8]. Active disease, especially lupus nephritis (LN) and severe renal insufficiency, may lead to anovulatory menstrual cycles [9,10]. Thus, women should be counseled that effective treatment of SLE can have a significant favorable effect on fertility. However, alkylating agents such as cyclophosphamide may cause premature ovarian failure, which is age and dosage dependent [11]. Alternative treatments such as azathioprine, mycophenolate mofetil (MMF), or mycophenolic acid and treatment protocols with a low cumulative cyclophosphamide dose are preferred in women of childbearing age [12,13]. Some studies have described reduced ovarian reserve and decreased anti-Müllerian hormone (AMH) levels in women with SLE compared with age-matched controls, while others failed to show this [14–16]. A matched cohort study confirmed that AMH levels are low in SLE patients and decrease significantly with age and cyclophosphamide exposure [17]. Nonetheless, the risk of failure to conceive was low and predicted by cyclophosphamide exposure and age but not by AMH levels.

Reproductive health procedures

Similar to women in the general population, a situation may arise for lupus patients in which assisted reproduction techniques are indicated. In this context, women should be counseled about the increased risk of lupus flares and thrombotic events (especially women with ovarian hyperstimulation and/or prothrombotic risk factors such as aPL). The literature on this topic is currently limited. A 2015 review identified three studies with a total of 61 SLE patients with 186 treatment cycles [18]. SLE flares were described in 8%–31% of cases; thrombosis and ovarian hyperstimulation syndrome were rare. Interestingly, in these studies, half the complications were explained by poor adherence to the recommended treatment. Ovarian stimulation with clomiphene, single embryo transfer, ongoing therapy (appropriate for pregnancy) to avoid flares, avoidance of ovarian hyperstimulation syndrome, and use of natural estradiol and/or progestin through a non-oral route may constitute approaches with fewer complications [19].

Contraception

Educating patients about appropriate contraception is crucial to avoid unplanned pregnancies. Contraceptive methods should be addressed by both the rheumatologist and gynecologist to determine a safe, effective, and convenient form for each patient. SLE patients are often discouraged from using estrogen-containing contraceptives. However, the results of a randomized study (SELENA) in 183 women with inactive or stable SLE (exclusion criterion were positive aPL or a previous thrombosis)

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