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Clinical updates on systemic lupus erythematosus in pregnancy – the maternal-fetal medicine perspective

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ABSTRACT

Systemic lupus erythematosus (SLE) is common in women of reproductive age and can have serious consequences on pregnancy outcomes. Recent updates in the clinical management of this condition have brought improvements for mothers affected and their babies. The aim of this general review is to offer the perspective of the maternal-fetal medicine specialist on the recent updates in clinical management of SLE in pregnancy and to bring into the attention of the rheumatology specialists the tools that obstetricians have nowadays in monitoring high-risk pregnancies.

Keywords: systemic lupus erythematous, pregnancy, maternal-fetal medicine, diagnosis, management

INTRODUCTION

Systemic lupus erythematosus (SLE) is an autoimmune condition that can involve any organ and system. The condition is characterized by the presence of abnormal autoantibodies against various antigens in cells. It has a genetic component, but it can also be triggered by environmental factors such as viral infections and ultraviolet light (1). Systemic lupus erythematosus is one of the most common autoimmune conditions in women of reproductive age (2). In fact, many autoimmune conditions have a higher incidence in women, and they can affect women while in their reproductive years thus interfering with a pregnancy. The diagnosis of SLE needs specific clinical and paraclinical criteria however, many women will have a lupus-like syndrome without fulfilling these criteria (Figure 1). This aspect is relevant for pregnancy, since even in the absence of a formal SLE diagnosis, there may be consequences on the pregnancy outcomes (3).

The most common autoantibodies detected in women with SLE are the antinuclear antibodies (ANA) while the most specific are the anti-double stranded DNA (dsDNA) antibodies. Other antibodies that can be found in women with SLE or SLE-like illness and have been associated to adverse pregnancy outcomes, are the antiphospholipid antibod-

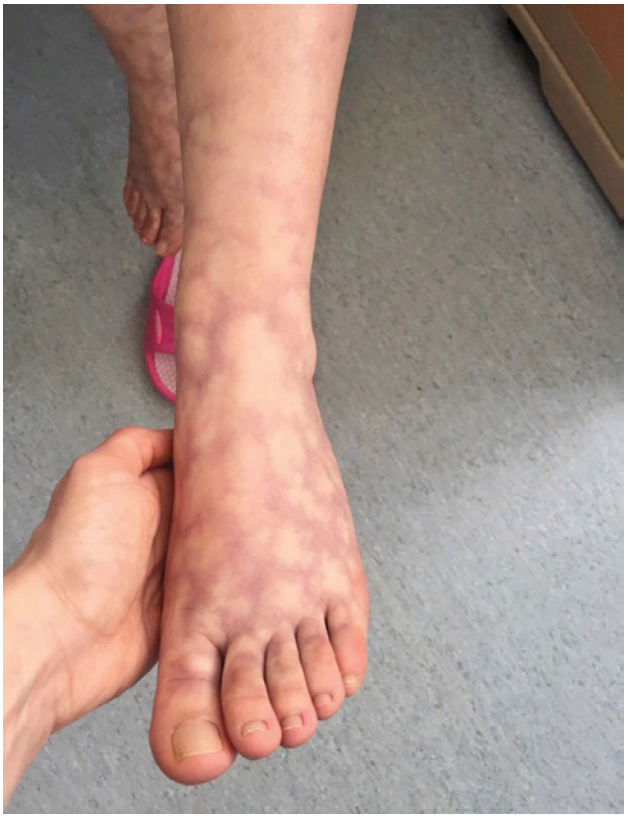

FIGURE 1. Livedo reticularis in a pregnant woman with antiphospholipid antibodies and fetal growth restriction (personal collection Anca Maria Panaitescu)

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ies, anti-Ro and La antibodies, anti-thyroid antibodies (Table 1).

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TABLE 1. Autoimmune antibodies present in SLE, or SLE-like syndrome associated with adverse pregnancy outcomes

Autoantibody type	Adverse pregnancy outcome
Anti-Ro/La	- neonatal lupus - congenital atrioventricular block - cardiac fibroelastosis
Antiphospholipid antibodies - lupus anticoagulant - anticardiolipin antibodies - anti-beta2 glycoprotein antibodies	- recurrent pregnancy loss - preeclampsia - intrauterine fetal demise - fetal growth restriction
TSH-receptor antibodies	- fetal goiter with hypothyroidism or hyperthyroidism
ATPO	- miscarriage

PLANNING A PREGNANCY BEING DIAGNOSED WITH SLE

Systemic lupus erythematosus does not seem to interfere with fertility. While is true that many women with autoimmune conditions are reluctant to undertake the reproductive path in fear of worsening their disease or of the consequences that it can have on the baby, with good clinical control, in many cases, pregnancy outcomes can be normal. A very important message for women with SLE and doctors caring for them is the importance of the preconceptional counselling. Women with SLE contemplating a pregnancy should be discussing with their doctors about the best terms that can be achieved in their case to have a good pregnancy outcome. These women should be under the care of a complex team, depending on the severity of their condition and, as a general rule, pregnancy should be thought out only when the condition is stable for at least 6 months and the medication required to control the disease has been changed to be compatible with pregnancy. The team that is usually involved in the preconceptional advice is made of the rheumatologist, family physician, obstetrician and in some case other medical specialists, depending on SLE involvement (nephrologist, hematologist, etc.) (3,4). The components that should be discussed during the preconceptional consultation are given in Table 2.

TABLE 2. Components of the preconception counselling; these should be ideally performed by a multidisciplinary team with the involvement of the rheumatologist and the obstetrician

Folic acid supplementation 5 mg/day
Vaccination against COVID-19
Vaccination against flu
Checking for other autoimmune conditions and autoantibodies that can be associated adverse pregnancy outcomes: - thyroid function and antithyroid antibodies (TSH-receptor antibodies and ATPO) - antiphospholipid antibodies - anti-Ro/La
Confirming disease remission – clinical and laboratory: - full blood count; platelet - creatinine; proteinuria; hematuria; casts - complement levels - clinical remission
Confirming medication is suitable for pregnancy: - hydroxychloroquine should be continued if introduced and effective - corticosteroids may be used - azathioprine and non-steroid antiinflamatory drugs (NSAID) can be used

PREGNANCY MANAGEMENT IN WOMEN WITH SLE

Having SLE increases the chance of adverse pregnancy outcomes: preeclampsia, preterm birth, fetal growth restriction, stillbirth, requiring a cesarean section (4-6). These risks are lower in pregnant women with adequate control of their disease activity, in women without antiphospholipid antibodies, with no lupus nephritis or hypertension. Flares of SLE can occur in pregnancy and particularly in the postpartum period. Inadvertently stopping medication, including hydroxychloroquine can trigger flares during pregnancy and this should be avoided (7,8). For the team monitoring women with SLE in pregnancy is important to establish baseline values of the blood tests during the first trimester in order to have a reference. More frequent clinical visits are required as compared to healthy pregnant women (9). During these visits disease activity and control need to be checked and blood and urine tests are recommended. Fetal ultrasound scans are important in confirming that the pregnancy is developing well. The first detailed ultrasound scan that can be done during pregnancy is the first trimester fetal scan which is performed at 11 to 13 weeks of pregnancy. During this visit the obstetrician (usually a maternal-fetal medicine specialist) undertakes a complete maternal and fetal check-up. The components of this visit are given in Table 3.

TABLE 3. First trimester maternal-fetal assessment by the obstetrician (maternal-fetal medicine specialist)

Fetal assessment	**Maternal assessment**
Viability: - checking heart rate	Maternal characteristics: - weight, height, BMI - blood pressure
Dating the pregnancy: - based on the measurement of the crown-to-rump length	Mode of conception: - natural vs. assisted reproductive techniques
Location: - intrauterine vs. extrauterine pregnancy	Smoking, alcohol, addictive drugs consumption
Chorionicity (in case of twins and triplets) - dichorionic vs. monochorionic with increased advers pregnancy outcomes	Medication, screen for potential adverse reactions
First trimester combined test for chromosomal anomalies: - nuchal translucency measurement - additional markers: nasal bone; ultrasound pattern flow in ductus venosus and in the tricuspid fetal valve - beta HCG and PAPP-A maternal serum levels - optional: cell free DNA test	Immunization and infection screening status, including HIV, hepatitis and syphilis screening, TORCH screening
Fetal anatomy check-up Placenta location and umbilical cord insertion	Blood and urine tests for baseline; blood group and Rhesus status - full blood count - kidney - liver - thyroid
Screening for preeclampsia: - uterine artery Doppler measurement - placental growth factor (PLGF maternal serum levels - blood pressure measurement	Associated disease
Screening for fetal growth restriction and preterm birth: - cervical length assessment	

The aims of this assessment in the general population are to establish viability of the pregnancy, localization, chorionicity in case of multiple pregnancy, to perform the first trimester combined screening for common chromosomal anomalies, perform the structural check-up of the fetal anatomy, perform screening for preeclampsia and preterm birth (10-12). For pregnant women with SLE this visit is very important. Ultrasound scan of fetal anatomy as early as the end of the first trimester will reassure the women and her partner that the fetus is developing normally and there are no structural abnormalities. This is important since many patients are concerned about the risks that medication or the disease may have on their babies (13). Major fetal defects can be detected during this scan, thus giving the couple reproductive options early in pregnancy. Assessment of the uterine arteries, the arteries that are perfusing the uterus and the placenta in pregnancy, is also important in pregnant women, particularly with SLE. A combined screening test for establishing the risk of development of preeclampsia and fetal growth restriction is used for all pregnant women and is of particular interest in SLE (14). Women found to be at high risk for preeclampsia and fetal growth restriction are prescribed aspirin. After the first trimester, maternal-fetal assessments including clinical and fetal ultrasound scans are offered at least at 20-22 weeks and 30-34 weeks of pregnancy but this may be more often depending on the clinical scenario. The second trimester detailed fetal scan that is performed around the 22 weeks has as major objectives the assessment of the fetal anatomy, cervical length measurement, uterine artery Doppler evaluation, placental evaluation, amniotic fluid measurement. Ultrasound scans offered after this time will evaluate fetal growth and well-being. In women with anti-Ro antibodies, serial fetal echocardiograms are needed to detect cardiac rhythm abnormalities (Figure2) and exclude cardiac fibroelastosis (15).

In pregnant women with SLE that advance with their pregnancy at term, vaginal delivery is the best option, however in many cases of preeclampsia or fetal growth restriction, delivery by cesarean section may be required.

In the postpartum, flares of the diseases can be expected. A multidisciplinary visit at 6 weeks after delivery can be arranged to evaluate for clinical and biological changes and adjust treatment.

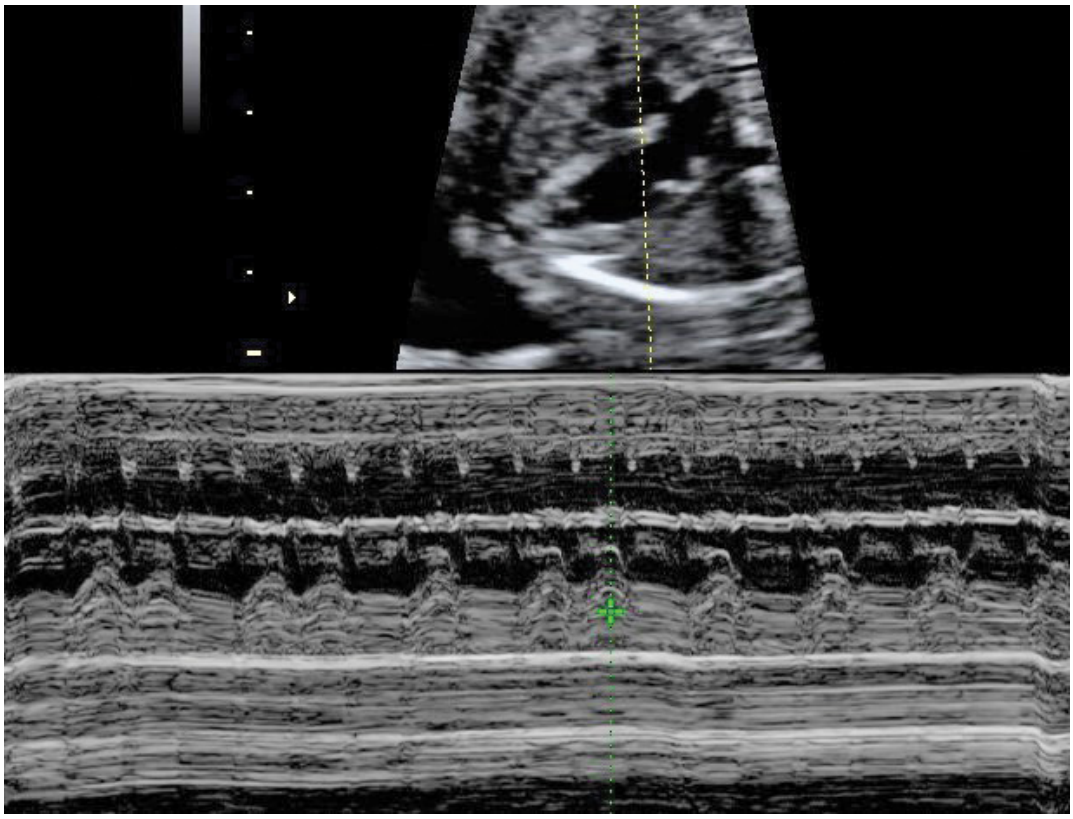

FIGURE 2. Fetal echocardiogram in a 24 weeks pregnancy. M-mode shows abnormal atrioventricular conduction with type 2 atrioventricular fetal block (personal collection Anca Maria Panaitescu)

CONCLUSIONS

Systemic lupus erythematous is one of the most frequent autoimmune conditions in women of reproductive age and can interfere with pregnancy. Recent advances in the field of obstetrics have made it possible that women with SLE could be monitored in order to achieve a normal pregnancy outcome. A good communication between the rheumatology specialist and the obstetrician with rigorous planning of pregnancy in a suitable clinical frame of the disease, careful monitoring throughout pregnancy and postpartum are paramount in achieving optimal results for women with SLE.

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