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Case Report

Sexuality and Pregnancy in Juvenile Systemic Lupus Erythematosus

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ABSTRACT

Patients with systemic lupus erythematosus (SLE) have an increased frequency of SLE flares during pregnancy, compared to after delivery and to nonpregnant SLE patients. Active renal disease and maternal hypertension are important predictors of fetal loss. A case of active juvenile SLE and pregnancy was described. A 16-year-old white adolescent girl has had SLE for 9 years. She had delay in menarche, early sexual activity and didn't use any contraceptive methods. She had a very severe pregnancy with hypertension and renal failure. The SLEDAI was 20 and SLICC/ACR Damage Index was 4. Despite treatment with plasmapheresis, intravenous methylprednisolone pulse therapy, prednisone and azathioprine, she had a spontaneous abortion as well as renal failure requiring dialysis. Seven months later, she is waiting renal transplantation.

Keywords: Systemic Lupus Erythematosus, Adolescent, Pregnancy.

INTRODUCTION

With the improved survival of children and adolescents with SLE, pediatric rheumatologists have to care for an ever increasing population of adolescents with systemic lupus erythematosus (SLE). Rheumatologists and other physicians must take into consideration the many aspects of adolescence, particularly early beginning of sexual activity and possible consequences, such as pregnancy.

A study performed in the Brazil demonstrated that 42.5% of young females begin their sexual activity before the 18th year. In 1996, almost one third of births in the Brazil occurred in adolescents [1]. The characteristics of adolescence with incomplete growth and physical development along with changes in the socialization process and organization of the personality confer great complexity to adolescent gestations and subsequent physical and psychosocial difficulties for both mothers and children after the birth [2].

Patients with SLE have an increased frequency of SLE flares in pregnancy, compared to after delivery and to nonpregnant SLE patients [3]. Active renal disease and maternal hypertension are important predictors of fetal loss [4].

CASE REPORT

A 16-year-old white adolescent girl has had juvenile SLE for 9 years. She was initially diagnosed as having juvenile SLE based on the presence of malaise, alopecia, malar rash, photosensitivity, pericarditis, leucopenia, hypertension, proteinuria, hypocomplementemia, positive antinuclear and anti-DNA antibodies. The initial renal biopsy showed membranous glomerulonephritis (World Health Organization Class V) with activity index of 4 and chronicity index of 4. Her major clinical problems included hypertension, persistent nephrotic syndrome, vasculitis and arthritis. SLE activity for this period of follow-up was classified into relapsing-remitting according Barr et al [5]. She was treated in this period with prednisone (cumulative dose of 65.5g), intravenous cyclophosphamide (cumulative dose of 5.18g), azathioprine (cumulative dose of 82.66g), methotrexate (cumulative dose of 0.55g), cyclosporine (cumulative dose of 3.9g) and chloroquine (cumulative dose of 174.9g).

Her menarche was at 15 years. After one year, her menses were normal. The menstrual cycles were associated with dysmenorrhea. The first sexual activity was on 15.8 years old with frequency of intercourse four per month. Despite extensive counseling on sex, pregnancy and contraception, she did not use barrier contraceptive methods (male or female condom), emergency contraception (levonorgestrel), an injectable contraceptive (depo-medroxyprogesterone acetate), or other forms of contraception.

At the age of 16, she stopped her SLE treatment and follow-up and her disease appeared to be in remission. At the age of 16 and 8 months, she was admitted in our hospital in the first trimester of pregnancy with fatigue, edema, hypertension, arthritis and renal insufficiency. The pregnancy was unplanned, unwanted and she received no help from the baby's father.

Laboratory testing revealed a hemoglobin of 9.8 g/dl, platelet count of 328.000/mm³ and white blood cell count of 10.600/mm³ (76% neutrophils, 11% lymphocytes and 13% monocytes). Antinuclear antibodies (HEp-2) and anti-dsDNA antibody (*Chritidia luciliae*) were positive. The C3 and C4 were reduced. Antiphospholipid antibodies: anticardiolipin antibodies (ELISA) and lupus anticoagulant (kaolin clotting) were negative. The urinalysis showed microscopic urine blood, casts and pyuria. The proteinuria was 0.45 g/day, urea nitrogen 143 mg/dl and plasma creatinine 5.2 mg/dl. The ultrasound showed a 5 week pregnancy. The systemic lupus erythematosus disease activity index (SLEDAI) was 20.

She was treated with both plasmapheresis and intravenous pulse therapy with methylprednisolone for 3 days plus prednisone 60 mg/day. However, despite this treatment, one week later the hypertension, edema and renal insufficiency worsened and azathioprine and hemodialysis were added to the treatment. Two weeks later, it was decided that a therapeutic abortion was indicated but the pregnancy ended in spontaneous abortion.

At the age of 19, a second renal biopsy demonstrated a proliferative glomerulonephritis (World Health Organization Class IV) with activity index of 3 and chronicity index of 9. The Systemic Lupus International Collaborating Clinics/ACR (SLICC/ACR) Damage Index was 4. By the age of 20, she was on dialysis, waiting for

kidney transplant and was then transitioned to the adult rheumatology service of our University Hospital.

DISCUSSION

Patients with juvenile SLE often become sexually active during adolescence like their peers and despite their disease and medications, may become pregnant. Our patient became pregnant despite a delay in menarche, major disease activity and previous high doses of immunosuppressive agents.

Britto et al [6] studied 178 adolescents with pediatric rheumatic diseases (mean age of 18.1 years; 67% female; 69% with juvenile rheumatoid arthritis and 8% with juvenile SLE). Of the 52 females undergoing screening at follow-up, 31 (60%) were sexually active. Eleven (41%) of 27 sexually active females were not using contraception other than condoms (4 were not asked about contraception). Studies show that women with SLE have a high abstention rate, a low frequency of masturbation and genital petting, diminished vaginal lubrication, poor general sexual adjustment, and a poor ability to adjust to psychosocial stresses and increased depression [7,8]. Normal sex drive, motivation, subjective arousal, orgasmic attainment and satisfaction were not found to be different than controls [7]. Our patient reported normal sex motivation, masturbation, and orgasm with four intercoursures per month.

Our service has also previously shown that the delay of menarche in patients with juvenile SLE [9]. The mean age of menarche (13.5 ± 1.4 years) was greater than that found among 2578 healthy Brazilian adolescents (12.5 ± 1.3 years) ($p=0.0002$). The delay in menarche correlated with an increase in the duration of the disease ($p=0.0085$) and the cumulative dose of prednisone ($p=0.0013$) used until the appearance of the menarche. The fertility of patients with juvenile SLE can be altered by the activity of disease or medications in male [10] and female [9] adolescents. The glucocorticoid therapy, especially in high doses [11] and immunosuppressive agents [12], such as cyclophosphamide and chlorambucil, can lead to a pubertal delay and gonadal dysfunction in both sexes. The alkylating agents most frequently associated to infertility are chlorambucil and cyclophosphamide [12]. Our group has also analyzed the gonadal function of 23 adolescents and young female with juvenile SLE [9]. Sixteen

female (70%) patients showed normal gonadal function and seven (30%) abnormal. Gonadal function was not correlated with disease activity of juvenile SLE or therapy with prednisone, cyclophosphamide, azathioprine and methotrexate. In Brazil, 18% of the entire female population from 15 to 19 years of age has currently already been pregnant at least once. On our Pediatric Rheumatology Service, pregnancy occurred in 6 (14%) adolescents and young women with SLE. The patients were selected from a total of 51 patients (43 female) with SLE, followed during 1999 and 2000 [8].

Studies published in the 1960s underlined the increased fetal and maternal risk and recommended against pregnancy in lupus patients. The prognosis for non-pregnant SLE active patients was also poor, making it difficult to know whether pregnancy altered the prognosis of the disease. Recent prospective studies indicate that the majority of lupus mothers can sustain pregnancy without detrimental effects, providing that pregnancy is planned during the inactive phase of the disease [13]. Pre-existing lupus renal involvement increases the risk for hypertension, but it does not contraindicate pregnancy if it is adequately planned and monitored [14].

Rahman et al [15] prospectively studied 141 SLE pregnancies to identify clinical predictors of fetal outcome. Active renal disease was statistically significant predictor for fetal loss, with 13.4% patients with live births having active renal disease compared to 33% with fetal losses. Hypertension was a statistically significant predictor for pre-term delivery and intrauterine growth restriction. Cervera et al [14] also studied 103 pregnancies in 76 SLE patients. They showed that the frequency of lupus flare was approximately 23%. The type of flare was cutaneous in 54%, thrombocytopenia in 33%, pericarditis in 21%, arthritis in 21% and nephritis in 17%. Any flare was found in 23% of patients. Petri et al [16] found an increased of SLE flare in pregnancy compared to after delivery and to nonpregnant patients. Flare of the disease occurred in all trimesters: 18% in first trimester, 47% in second trimester, 15% in third trimester and 20% in postpartum. Pregnant lupus patients are susceptible to pre-eclampsia, especially if they suffer from lupus nephritis, steroid-induced hypertension, and hyperglycemia [17]. SLE pregnancy had also significantly increased urinary tract infection, diabetes and premature rupture of membranes [16]. Fetuses are susceptible to placental insufficiency

if antiphospholipid antibody or other procoagulant states are present, and to neonatal lupus if anti-Ro/La antibodies are present [17].

Because of the limitations on medications that can be used safely during pregnancy, management of lupus flare can be problematic, as in our patient. Intravenous methylprednisolone pulse, 1000 mg/day for 3 days can be used. Azathioprine can be added if the patient has had a major renal, hematologic or neurologic system flare [16]. Plasmapheresis can be safely performed during pregnancy and has been used for years in Rh-incompatible pregnancies. Four patients with lupus have been treated during pregnancy [18]. Methotrexate, cyclophosphamide, mycophenolate, and several other drugs should be avoided as they are teratogenic.

From our perspective, despite knowledge and concern about the interaction of immunosuppressive therapy and risk behaviors, few rheumatologists adequately screen the sexual behavior of their adolescent and young adult patients with SLE. Time constraints, organizational issues and physician beliefs remain barriers to widespread screening [6]. Women who take cytotoxic drugs also should be informed of the risks of impaired fertility and congenital malformations, and must use effective methods of contraception [19].

If a pregnancy is desired, the best time to plan a pregnancy is during an inactive period of SLE, although there is no guarantee that the disease will remain inactive. It should be emphasized that the chance of a flare with conception after 5 to 6 months of remission is 10% or less [18].

In summary, pediatric and adult rheumatologists have a crucial role in addressing these issues as they are often the only health workers providing sexual counseling for these patients [20]. Consequently, the pediatric rheumatologist and his/her staff need to create space within the appointment times to approach and discuss aspects of sexuality, offer guidance regarding contraceptive methods and warn about the risks of sexually transmitted diseases (STD) and their prevention. Though the risk of pregnancy to the mother and fetus in this situation has greatly decreased in the last several decades, there still significant associated risk for the mother and fetus and much care must be taken.

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