SYSTEMIC LUPUS ERYTHEMATOSUS IN PREGNANCY

(Case Reports and Review)

by

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Introduction

Systemic lupus erythematosus is a collagen disorder of unknown etiology involving multiple organ systems. It is predominantly a disease of women in the child bearing age graup. The obstetrician is often called upon to render advice to such patients regarding marriage and pregnancy. Most authors generally agree that pregnancy in patients with SLE is associated with increased foetal wastage (abortion and still births), post-partum exacerbations of disease activity and that the course of the disease and the pregnancy is more favourable when pregnancy occurs during a period of remission (Estes and Larson 1965 and Fraga *et al* 1974). This report reviews the maternal and foetal outcome in 3 patients of SLff with pregnancy who were treated and delivered in Nehru Hospital attached to the Postgraduate Institute of Medical Education and Research, Chandigarh.

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Accepted for publication on 7-12-82.

Case 1

A.K. 28 years old primigravida was a known case of SLE diagnosed 2 years back at this hospital. She was given high dose of prednisolone initially till she achieved remission and was then started on maintenance dose of 7.5 mg. of prednisolone daily. She conceived during this period and was being supervised by a general practitioner for her pregnancy. She had recurrent attacks of skin rash and arthritis during her course of pregnancy but the dose of prednisolone was not increased in spite of these exacerbations of SLE. She was found to have intrauterine death of foetus at 32 weeks of gestation. One week later she developed fever, dyspnoea and streaky haemoptysis when she came to PGI and was admitted on June 22, 1981. At that time, her period of gestation was 33 weeks, height of fundus was 24 weeks and foetal heart sounds were not audible. A diagnosis of intrauterine death with pneumonitis with multiple exacerbations of SLE was made. Her haemogram, platelet count, blood biochemistry, blood sugar and urine for microscopic examination and culture were normal. Her X-ray chest showed consolidation in right lower zone. Serum complement (C_3 and C_4) was decreased and antinuclear factor was strongly positive. She was started on antibiotics and dose of prednisolone was increased to 40 mg. daily. Spontaneous labour started on July 3, 1981 i.e. 11 days after her admission. She was given Inj. Hydrocortisone 500 mg. I.V. at the onset of labour and a still born female child was delivered vaginally the same day.

She had severe exacerbation of arthritis and skin rash on the fifth post-partum day and dose

of prednisolone was increased to 60 mg daily. She responded again and was discharged on 12th Post-partum day on 30 mg of prednisolone daily.

Case 2

B. K., 25 years old primigravida, was diagnosed as a case of SLE in PGI 5 years before the onset of this pregnancy. She was taking some indigenous medicines only and was in remission when she conceived. Thrice she had exacerbation of SLE during the first six months of her pregnancy but she continued taking the indigenous medicines during this period. At 30 weeks of gestation, she was admitted to the PGI with fever, severe arthritis and skin rash and was started on Tab. Prednisolone 40 mg daily and Tab. Aspirin, 350 mg thrice daily. She responded to treatment and was discharged on 8th day but discontinued the medicines after 2 weeks only because of gastritis. She did not seek any antenatal supervision. On August 27, 1981, She came again in labour when she had already completed 39 weeks of gestation. At that time, her B.P. was 124/70 mm of Hg. She had erythematous rash on her face. Height of the uterus was 30 weeks and foetal heart sounds were audible. She had premature rupture of membranes, and the liquor amnii was thick meconium stained. Cervix was 25% effaced and admitted one finger. Emergency caesarean section was done after giving 1 gm of Hydrocortisone intravenously. A live female child was delivered with Apgar score of 8 and 10 at 1 and 5 minutes respectively. The baby weighed 1.6 kg birth anl had no obvious congenital malformation.

The mother had exacerbation of SLE on the 5th post-partum day, evidenced by high fever, increased skin rash, flushing of the face and arthritis of multiple joints. Her serum complement was decreased and antinuclear factor was strongly positive. All other causes of fever were excluded after carrying out the specific investigations. She was again started on Tab. Prednisolone 40 mg daily. She responded to the treatment. Stitches were removed on the 8th post-partum day. There was superficial gaping and sepsis of the wound for which appropriate antibiotics were given and she was discharged well on October 3, 1981 i.e. 5 weeks post-partum.

Case 3

S., 25 years old second gravida, P1 + 0 + 0 + 1, a known case of SLE was on treatment with corticosteroids but had stopped the treatment herself for last one year. Her last child birth was 5 years back. Her pregnancy this time was unsupervised, and in spite of repeated exacerbations of SLE, she did not take any treatment. She reported in PGI at 35 weeks period of gestation with history of 8 attacks of convulsions at home, loss of consciousness and oliguria. She was in grade IV coma and had blood pressure of 200/160 mm of Hg at the time of admission. Investigations revealed her hemoglobin to be 14.0 gm%, total leucocyte count of 10,800/cumm, platelet count of 86,000/cumm, blood urea 190 mg%, serum creatinine 4.7 mg%, serum uric acid 11 mg%, s. bilirubin 1.0 mg% and random blood sugar 130 mg%. Serum Electrolytes, ECG, and X-ray chest were within normal limits. Urine analysis was positive for albumin but negative for sugar. Prothrombin Index was 67%. Initially, she was thought to be a case of eclampsia and was started on Menon's Lytic cocktail regimen. Later she was put on Aldomet and Dilantin through Ryle's tube and continuous diazepam drip with the impression that it was an epilepsy. It was later known that she was a proved case of SLE and was immediately started on Inj. Hydrocortisone 100 mg I.V. 6 hourly. However, the patient showed no signs of improvement and died within 48 hours of admission.

Discussion

All 3 cases of SLE were practically unsupervised throughout their course of pregnancy. Disease exacerbations during pregnancy were not properly managed by monitoring the dose of corticosteroids and therefore, they had repeated attacks of exacerbations of SLE during pregnancy and in the post-partum period also. The first 2 cases did not have any obvious systemic involvement but the third case had definite evidence of central nervous system and renal involvement. The maternal and foetal death occurred in this case because of negligent attitude of the

patient and relatives. She did not take any treatment for SLE even after exacerbations of diseases during pregnancy as a result of which the disease worsened with fatal outcome. The first case had foetal wastage again because of the improper management of the SLE during her course of pregnancy. In the second case there was foetal morbidity in the form of severe intrauterine growth retardation, but fortunately the baby survived. Both the first and second cases had severe exacerbations of SLE in the post-partum period.

The effect of pregnancy on the course of SLE is variable. Many such surveys indicate that a proportion of patients improve or are unchanged during pregnancy (Donaldson and DeAlvarez, 1962; Zurier, 1975) while on the other hand, there are reports of increased risk of SLE exacerbation in the first half of pregnancy and in the third trimester (Garstentein *et al* 1962; Mund *et al* 1963). Incidence of post-partum exacerbation is seen in 24-38% of cases (Zurier, 1975). Severe exacerbations can occur within several weeks post-partum (Friedman and Rutherford 1956; Donaldson and DeAlvarez, 1962; Garstentein *et al* 1962 and Mund *et al* 1963). However, the cause of such exacerbations remains speculative. It is known that certain adjustments to the immune system occur during pregnancy. Maternal serum levels of 17-hydroxycorticosteroids are elevated during pregnancy and fall precipitously with delivery (Cohen *et al* 1958). Furthemore, HCG is known to interfere with the lymphocyte function and cellular immunity (Adcock *et al* 1973). The mechanism of the apparent increase in the activity of lupus nephritis and symptoms due to central nervous system involvement during pregnancy is also not known. Pregnancy results in further insult to renal and central nervous system integrity and may even lead to lethal activation of SLE.

SLE has important effects on the outcome of pregnancy. The spontaneous abortion rate is 30% that is 3 times the incidence of normal population (Madsen Anderson 1961; Cox, 1965, Grigger, 1977 and Warren *et al* 1978). There is also an increased risk of foetal death; Estes and Larson, 1965). The prematurity rate is reported to be 28-37 per cent in all cases of SLE (Madsen, 1961; Cox, 1965) and newborn infants are often small for dates. Uterine arteriolar lesions may be responsible in part for the increased foetal morbidity and mortality (Benirshke and Driscoll, 1967). There is a substantial increase of foetal wastage in pregnancies even prior to the diagnosis of SLE (Cox, 1965; Estes and Larson, 1965; Fraga *et al* 1974 and Griggor *et al* 1977). Antinuclear antibodies and a positive LE cell phenomenon have been described in cord blood in several pregnancies associated with SLE, although these were absent in the baby of case No. 2. A few neonatal cases of discoid lupus and of haemolytic anaemia, neutropenia and thrombocytopenia have been reported. Several instances of congenital complete heart block have been diagnosed before and after delivery in offspring of women with SLE. A few infants died of cardiomyopathy. The autopsies revealed subendocardial fibroelastosis which presumably interrupts atrioventricular conduction (Hogg, 157; Hull *et al* 1966; Chameides *et al* 1977). However, the lone surviving baby in our cases showed none of these complications.

Serologic data is useful in the diagnosis and more recently in the treatment evaluation of SLE (Warren *et al* 1978). Clinically active lupus is associated with low or declining complement (C_3 or C_4) levels and rising antinuclear factors and quies-

cent disease by reverse laboratory trends. These alterations reflect fluctuating complement consumption and formation of antigen antibody complexes which accompany the tissue response to SLE. Changes in serologic values generally precede apparent clinical changes. In all 3 of our patients, antinuclear factors were strongly positive and complement levels were decreased although we were not able to carry out serial estimations as the patients were unsupervised and turned up late, though it is of tremendous value for predicting the behaviour of the disease in anticipation and taking the precautionary measures.

Underlying lupus nephritis is likely to increase the risk of toxaemia (Donaldson and DeAlverez 1962; Fraga *et al* 1974 and Bear, 1977). Our case 3 probably had lupus nephritis with superimposed toxaemia, in addition to central nervous system involvement and the result was fatal. When conception occurs during remission more benign courses have been reported (Estes and Larson 1965). Out of our 3 cases, the first 2 cases conceived during remission while the third patient conceived during active phase of SLE. The course in first 2 cases was therefore, definitely more benign than in the third case.

Current medical management has placed increased emphasis on antepartum usage of steroids (McGee and Makowski, 1970), although it is somewhat controversial. Cortisteroids are indicated for serositis, decrease in blood elements or nephritis. Garstentein (1962) observed fewer antepartum or post-partum exacerbations in patients treated with corticosteroids throughout pregnancy. McGee and Makowski (1970) reported the use of high dose of intravenous hydrocortisone (100 mg 8 hourly) during labour and immediately post-partum in order to prevent puerperal exacerbation in 11 pregnancies complicated by SLE. Continuation of corticosteroid treatment during the first 2 months post-partum is advised to limit the incidence of exacerbation of SLE activity, following delivery (Warren *et al* 1978). The clinical experience with other agents such as azothioprine (Sharon *et al* 1974) is limited.

Vigorous corticosteroid treatment rather than induced abortion is indicated for suppression of disease activity during pregnancy. The decision to induce therapeutic abortion in SLE patients must be counter-balanced by the significant risks of post-abortal exacerbations which are equally severe as the post-partum exacerbation. Induced abortion exerts little, if any, positive influence on subsequent course of SLE. A noteworthy exception should be made for patients with severe cardiac or renal complications when they would be jeopardised by advancing gestation (Lawrence and Roger, 1979). In any circumstance if therapeutic abortion is performed, steroid regimens similar to those in term parturition should be employed.

Improving maternal management has had little apparent effect on foetal outcome over the past three decades (Friedman and Rutherford, 1956; Lawrence and Roger, 1979). Broadly speaking, patients with SLE should avoid pregnancy. Since oral contraception may itself lead to lupus like syndrome (drug-induced lupus syndrome), such patients should employ alternate modes of contraception.

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