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SYSTEMIC LUPUS ERYTHEMATOSUS ASSOCIATED WITH PREGNANCY

Additional Report on its Clinical Course

by

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Considering the frequent occurrence of lupus erythematosus in women of reproductive age, the coincidence of this disease with pregnancy should not be rare, however, thus far only about 200 cases of such coincidence have appeared in the literature. In our previous paper in 1962, a case report was made on a patient aged 24, primigravida, who suffered from lupus erythemtosus at the 20th week but obtained complete remission successfully with prednisolone, ACTH, Chloroquine after termination of pregnancy. After discharge in a complete remission from the hospital 7 months following admission, prednisolone administration was continued for one year more and then completely stopped. It is worth to report that without any further medication she has maintained the complete remission and moreover, has had four subsequent normal pregnancies and deliveries: girl baby on Oct. 2, 1962, girl baby in Nov. 1964, boy baby in February 1967, girl baby in March 1968.

Lupus erythematosus was first described by dermatologists such as Casenave, Hebra and Kaposi early in the middle of the nineteenth century. However, it was not until the last decade that the disease aroused the interest of clinicians, owing to the advancement of the concept of the collagen disease by Klemperer 1941, the discovery of L. E. cell by Hargraves in 1948 and the introduction of the steroid hormone into the field of therapy by Hench in 1949. It is not merely one of the skin diseases as recognized in those early days but a systemic disease with various clinical manifestations associated with lesions of connective tissue in the vascular system, the dermis and serous and synovial membranes. Recently, its immunological peculiarities have been much discussed, however, the exact pathogenesis still remains to be determined.

The disease usually affects young females in the reproductive age, hence cases of SLE associated with pregnancy have been described frequently in the literature. But there is no unanimity of opinion about the interrelationship between them; some consider that pregnancy has little effect on the course of the disease while others regard that pregnancy and the disease are mutually antagonistic.

We described a young primigravida suffering from SLE in 1962[6]. The patient had been successfully treated with steroid hormone combined with Chloroquine phosphate and she had four normal term deliveries during the following 6 years without any acute exacerbation of SLE. An additional report on the clinical course after the last report is presented.

CASE HISTORY

Mrs. W. J. F., gravida 5, para 4, is a 34 year-old housewife. During her fiirst pregnancy when she was 24 years old, she suffered from acute systemic lupus erythematosus and was hospitalized on Oct. 30, 1959.

She married her husband in February 1959. Five months later, she became pregnant with L. M. P. dated on July 10, 1959. Since October, 1958, she had occasionally suffered from arthralgia, edema of the lower extremities and mild intermittent fever, but her general condition had been little affected.

Erythematous lesions appeared on both cheeks in February and persisted for about two months and faded without any specific treatment. However, her face gradually bec ime pale and marked edema of the face and l wer extremities occurred in August. Protei uria was proved by a practitioner who treated her as pregnancy complicated with chronic nephritis. She consulted our clinic on Oct. 30, with complaints of anasarca, pallor of the face, shortness of breathing, and asked us to terminate her pregnancy. Physically, she was a moderately developed woman with a pale and puffy face. Brownish pigmentations were noted on the left cheek, left chin and the back of the right hand and foot. B. P. was 110/70 mm Hg. Cardiac dullness was markedly enlarged to both sides and the heart sound was clear and not distant to auscultation. Hepatomegaly 1.5 f. b. and splenomegaly 2 f. b. were noted. Abdomen was distended and fluctuation demonstrable. Fundus uteri was 2 f. b. below the umbilicus. No lymphadenopathy. Roentgenological examination of the chest revealed an enlarged cardiac shadow and active minimal tuberculous lesions at the the apex of the right lung. Laboratory examinations revealed pancytopenia, low serum protein, inverted A/G ratio, increased bood sedimentation rate, three plus albuminuria, markedly impaired renal functions. L. E. cells were found in the peripheral blood. On the diagnosis of lupus erythematosus being established, steroid therapy was instituted with 45 mg of prednisolone daily. The therapy was tried for 6 days but not the slightest improvement of clinical symptoms was noted. Antituberculous therapy consisting of I. N. A. H. 400 mg daily and D. H. S. M. 1 gm every three days was also given. The patient was seriously embarassed by intensive dyspnea even while sitting. Therapeutic abortion was done on Dec. 1. Pathological examination of the placenta and fetus revealed no evidence of lupus erythematosus, nor of collagen disease.

After the interruption of the pregnancy, improvement occurred steadily though slowly. Chloroquine phosphate was started with an initial dose of 0.5 gm b. i. d. for 3 days, 0.25 gm for the next two weeks followed by a maintenance dose of 0.25 gm q. d. for one month. After these therapeutic measurements abnormalities in the blood picture such as pancytopenia, low hemoglobin, increased E. S. R., positive L. E. cells in the peripheral blood etc, were gradually corrected. Pericarditis also improved, chest film taken on March revealing a normal-sized cardiac shadow and essentially clear lung parenchyma. However, the renal damage was very refractory to the therapy. The daily fluctuation of protein in urine was schematically illustrated in Fig. 1. It took more than 7 months to obtain a satisfactory improvement.

B. B. T. was measured daily, and the curve was biphasic. Diagnostic curettage of endometrium in pre-menstrual stage was done and histological study revealed the endometrium was in secretory phase, indicative of the presence of ovulation.

On October 13, 1960, she had a sudden recurrence of typical eruptions with desquamation on her face. L. E. cells were found again on Oct. 16. Prednisolone was maintained at a daily dose of 20 mg, supplemented with 20 units of ACTH weekly. She was discharged in

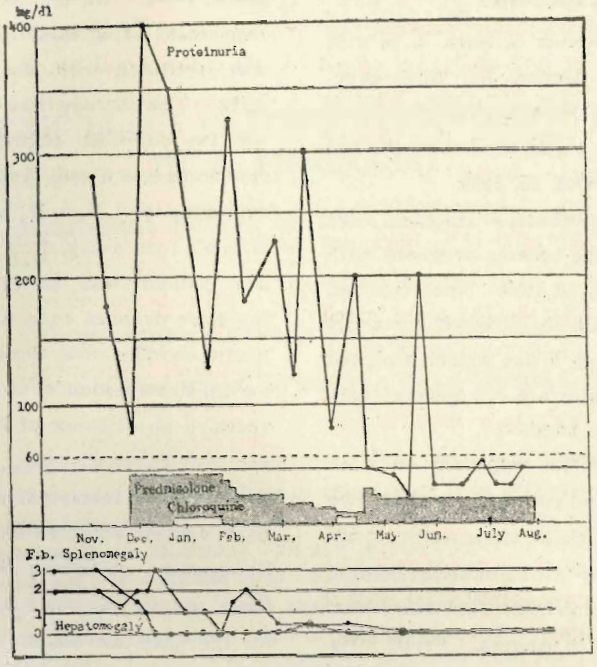

Figure 1. Fluctuation of albuminuria, hepato-and splenomegaly correlated with doses of prednisolone and chloroquine phosphate.

rather satisfatory condition on Dec. 30, 1960, the total hospitalization period being one year and two months.

On February, 1962, nearly two years after her first pregnancy, she was found to be pregnancy two months and had been apparently in perfect health, being free from any eruption and other signs of the disease, apart from a trace of albuminuria. The pregnancy was allowed to run its course at the strong request of the patient. According to the statement of the patient she continued with Prednisolone 10 mg daily for about one year after discharge and stopped therapy without consultating us. Considering the probable ill effect of steroid hormone on the fetus, and complete remission of the lesions, no specific therapy for S. L. E. was applied. The prenatal course had been uneventful except for mild albuminuria and she gave birth to a normal healthy female baby on Oct. 10, 1962.

Against our advice, thereafter, she had successive conceptions; being delivered of a female healthy baby on Nov. 13, 1964, a male healthy baby on Feb. 11, 1967 and another female baby on March 7, 1968. The course of these three pregnancies had been uneventful, without any trace of symptoms or signs of S. L. E. except for mild albuminuria which quickly disappeared after delivery. I. U. D. has been applied soon after the last delivery.

COMMENT

Before the introduction of steroid hormone in therapy, patients with SLE usually died within 2 years; howeveer, the dramatic effect of steroid hormone changes the gloomy prognosis[9]. Acute fulminating cases are rather rare and patients may be in reasonably good health for 15 or even 20 years despite occasional episodes of active disease[8]. Soffer[12] reported 26 cases out of 90 treated during 1949-1959 died within 7 years, with 22 deaths within 3 years because of renal insufficiency. The most common causes of death are uremia and pneumonia or other types of infections[11].

As pointed out in our previous paper[6], the enigma of interrelationship between pregnancy and SLE can not easily be solved merely by a review of the literature. Whether or not an artificial interruption of pregnancy is indicated is debatable. Acute exacerbation after artificial abortion has been described by authors, such as Friedman *et al*[2], Hayamizu *et al*[4], Ishikawa *et al*[5], while Murray[10] emphasized that pregnancy should be terminated in case of increasing albuminuria which would be indicative of progressive renal lesion. Persistent renal damage is a most serious feature. Murray found that nine out of eleven mothers suffering from SLE with persistent renal involvment died shortly after the end of pregnancy and even in those patients who survived, the albuminuria persisted for several months. After analysing the cause of death from SLE by necropsy in Japan, Shiokawa *et al*[11] found that the most common cause of death is uremia and they have warned against abuse of administration of steroid hormone which may impair renal function. The renal lesion was very refractory to therapy in our case. The artificial abortion did not bring about immediate relief, and it took more than seven months to obtain a satisfactory improvement with comblined therapy of prednisolone and chloroquine.

DeCosta & Abelman[1] stated that the administration of cortisone may not interfere with ovulation and conception. Margulis & Hodgkinson[8] studied 28 pregnant patients receiving corticotropin and cortisone to evaluate the safety of these steroids in pregnancy. They concluded that steroid hormone did not prevent ovulation or future conception, nor significantly altered the electrolyte balance. It would appear that the longstanding administration of prednisolone in this case did not do harm to the ovarian function; menses appeared regularly every month, B.B.T. curve revealed biphasic and the endometrial tissue in premenstrual stage was that of secretary phase. Against our strong advice of contraception, she became pregnant about 2 years after discharge. During her three successive pregnancies, the course had been quite smooth except for a trace of albuminuria. All of her babies, one boy and three girls are normal and healthy.

SUMMARY

A young primigravida with systemic lupus erythematosus, treated with prednisolone, ACTH and chloroquine is presented. Acute exacerbation occurred during pregnancy and therapeutic abortion was done on 20 weeks' gestation, resulting in a fresh stillborn fetus which showed no abnormalities on autopsy. Therapeutic abortion brought a notable subjective relief, but the basic disease process was arrested mainly by steroid and antimalarial drugs. The complete remission of the disease in spite of four successive pregnancies and deliveries in this case merits an additional report.

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妊娠與全身性紅斑性狼瘡之合併例

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紅斑性狼瘡常發生於成熟婦女，因此妊婦患本病之可能性頗大，但迄今文獻上只將近有200例之報告，我們在一九六二年曾提出報告一個24歲的初妊婦，在妊娠20週時罹患本病，本病人經人工流產後，使用 Prednisolone, A. C. T H., Chloroquine 等藥劑治療七個月始有顯著的改善，出院（住院將近一年）後繼續服用 Prendisolone 一年左右，於九一六二年二月再妊娠，並於同年十月二日生產一健康女嬰，又於一九六四年十一月生一女嬰，一九六七年二月生男嬰，一九六八年三月生女嬰，在這些妊娠期間，病人情形良好，並無紅斑性狼瘡之再發，亦無使用 steroid hormone 這種幸運的病例似乎很少見，茲再提出追加報告。