NEPHROTIC SYNDROME IN PREGNANCY: CORTISONE AND PREDNISOLONE TREATMENT
Clinical case

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SUMMARY

A case of a woman affected by a nephrotic postnephritic syndrome and treated during pregnancy with cortisone and prednisolone, is reported. The patient delivered at the 40th week of gestation a neonate with no malformations or clinical signs of adrenal deficiency. No interference between corticosteroid therapy and estrogen metabolism was noticed, and the intrauterine fetal growth, evaluated measuring the biparietal diameter, appeared normal.

Data concerning cortisone induced foetal damages are extremely contradictory in literature. Many Authors ([1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17]) think that the chronic cortisone assumption since the first gestational weeks could be responsible for a percentual increase of abortions and malformations (palatoschisis, hypospadia, cataract, aortic coarctation). Others ([18, 19, 20, 21, 22, 23, 24, 25, 26, 27]) on the contrary, disagree at all and say that experimental acquisitions don't allow any sure correlation be confirmed between cortisone assumption in pregnancy and foetal damages. The only possible effect of the drug could be, in the opinion of the latter, a relative and transitory foetal adrenal inhibition, occurring in the last part of pregnancy if high doses are administered ([28, 29, 30, 31, 32, 33]).

The same controversy is found about the use of synthetic cortisone-like drugs, such as prednisone ([34, 35, 36, 37, 38, 39, 40, 41]) and prednisolone ([42, 43, 44, 45, 46, 47, 48]), which are widely used in the therapy of several chronic disease even in patients which could become pregnant ([49]).

To contribute to a better knowledge of the problem, we report, in this note, the case of a patient affected with a postnephritic nephrotic syndrome, who become pregnant while treated by cortisone and prednisolone, the only drugs which could correct her enormous renal protein loss and maintain in her an acceptable diuresis. In spite of the awareness that it might not be harmless, the therapy was continued throughout the pregnancy.

CLINICAL CASE

L.D., 23 year old, affected by a nephrotic postnephritic syndrome diagnosed in Feb. 1974 had been since then on corticosteroid therapy, with prednisone 25 mg daily till April 1975 and then with betametasone 1 mg daily till Feb. 1977. She started then a daily therapy with prednisolone 8 mg associated with cortisone 8 mg. While on this treatment she conceived: the treatment was continued as it was considered indispensable. She came in our Department in May 1978, at the 17th gestational week. The patient said that

Clin. Exp. Obst. Gyn. - ISSN: 0390-6663
VIII, n. 2, 1981

Table 1. — *Main considered parameters in renal function monitoring (weekly control with the lowest and highest values in the different periods of pregnancy).*

Gestational age	Diuresis cc/24 h	Albuminuria g/24 h	Plasma albumin g/100 ml	Plasma proteins g/100 ml	Creatinina mg/100ml	Na mEq/l	Ca mg/100 ml	K mEq/l
17-20	950/1600	1 -3	3.6-3.9	5.5-6.1	0.6-0.7	135-136	8.6-8.8	3.5-3.6
21-24	1000/1600	0.5-1	3.2-3.8	6.3-6.4	0.6-0.7	136-140	8.6-8.7	3.5-3.7
25-28	1200/1500	0.5-2	3.5-3.6	5.9-6.1	0.7-0.8	136-140	8.6-8.8	3.8-3.9
29-32	1150/1800	1 -2.5	3.4-3.8	5.9-6.2	0.6-0.7	136-140	8.7-8.9	3.6-3.8
33-36	1200/1500	0.5-2	3.2-3.6	5.8-6.1	0.6-0.7	136-138	8.8-8.9	3.6-3.7
37-40	1250/2000	0.5-1	3.4-3.6	6.1-6.3	0.5-0.7	137-138	8.6-8.7	3.5-3.6

Table 2. — *Main considered parameters in fetoplacental function monitoring (weekly control with the lowest and highest values in the different periods of pregnancy).*

Gestational age	BPD	Plasma AFP ng/ml	Plasma HPL ng/ml	Total plasma E3 ng/ml	E3/C
17-20	3.2-3.8	40-110	—	—	—
21-24	4.5-5.6	70- 86	1.8-3.7	—	8.00-12.70
25-28	5.8-7.2	109-190	3.5-4.2	30.1- 65.4	8.60-15.30
29-32	7.3-8.2	100-240	5.1-6.1	28.4- 78.4	14.00-18.20
33-36	8.3-8.9	170-190	6.4-7.1	36.7-120.4	16.80-31.70
37-40	9.0-9.2	80-160	6.2-7.8	90.2-133.7	19.30-28.30

every withdrawal therapy, though short, started acute edema, periorbital at first and then generalized, with marked oliguria and hypoproteinemia, and with many subjective symptoms, such as general malaise, emotional instability, insomnia and worsening dyspnea. The patient's pregnancy was ascertained only one week before she entered our Department, because of her menstrual cycle irregularity dating from the beginning of corticosteroid therapy. The patient was fully conscious and afraid of the possible foetal damages due to her drug assumption in the first trimester of pregnancy, but she firmly wanted to have the baby and accepted the eventual risks. A common strategy was agreed with the nephrologist to correctly monitor the renal function and pregtill term. The values of the several considered parameters in this pregnancy–intensive monitoring parameters in this pregnancy intensive monitoring are reported in tables 1 and 2, related to groups of gestational weeks. On Oct. 21st 1978, the patient spontaneously delivered a male at term newborn, 3300 g/50 cm, with a head circumference of 34 cm; the Apgar score was 9/10 at 1', 10/10 at 5'. Neither symptom of adrenal insufficiency was present, nor clinically evident anomalies or malformations; up to date the baby, who is 3 year old, is in excellent conditions.

DISCUSSION AND CONCLUSIONS

The main aim of our note is to contribute, through the description of this personally observed case, to the controversy about drug administration in pregnancy and the hazards connected to it. In our case corticosteroid therapy since the beginning of pregnancy was quite necessary, as it was the only way to face nephrotic symptoms so letting pregnancy evolve physiologically. The patient's conscious acceptance of the possible risks for the foetus and herself certainly made our work easier and made us more and more convinced of the importance of the need every physician should feel of signaling even single cases of pregnancy treated with drugs known to be potentially embryofetotoxic or teratogenous; this could contribute to clear doubts and questions which still can be found in medical literature and are often a source of equivocations and alarms that hardly find serious

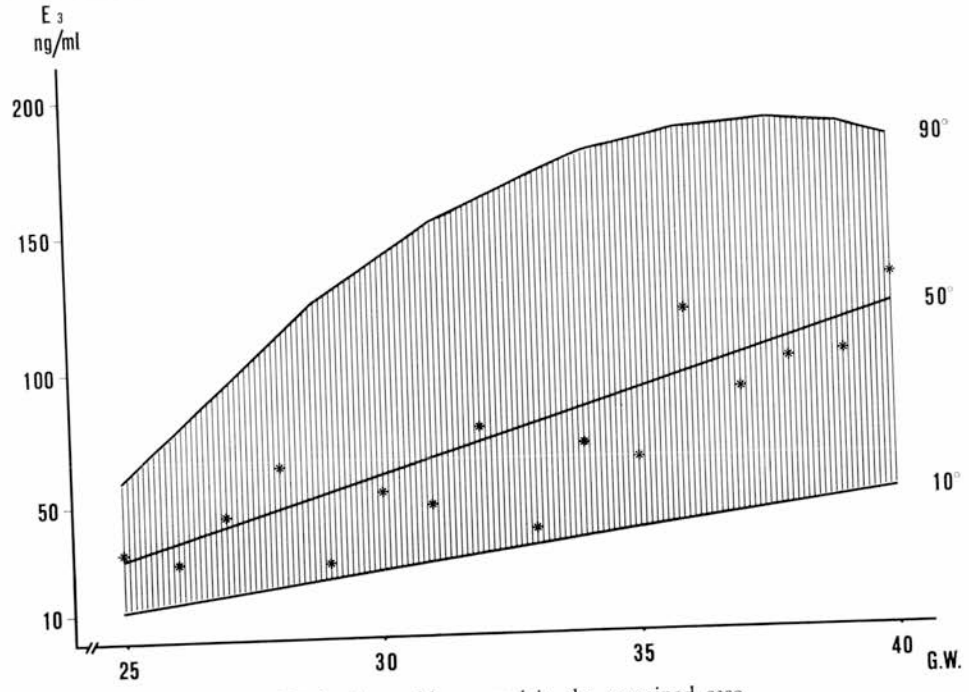

Fig. 1. — Total plasma E3 levels weekly assayed in the examined case.

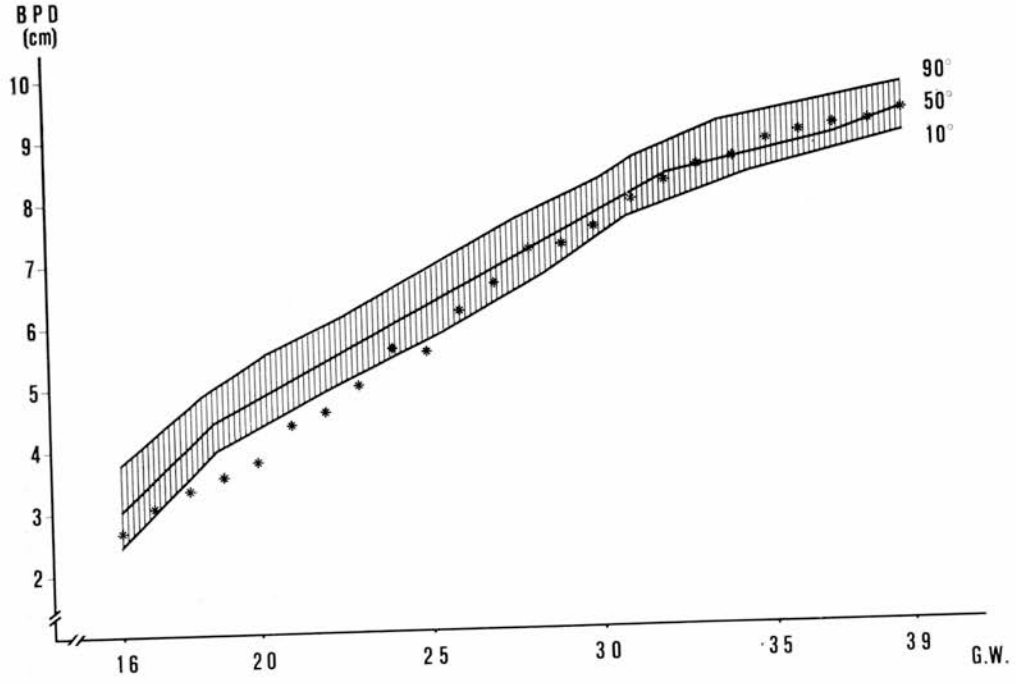

Fig. 2. — Fetal BPD increased curve in the examined case.

justifications, even if linked to sad past experiences.

After the observations made on our patient, studied in a prospective and not in a retrospective way, we can conclude that: 1) cortisone and prednisolone therapy since the beginning of pregnancy acceptably controlled the nephrotic syndrome maintaining an almost normal diuresis, a proteinuria within acceptable limits, and normal proteinemia, creatininemia and ionemia (tab. 1); 2) the analysis of the data from the biochemical and biophysical monitoring of the pregnancy (tab. 2) and the observations at birth show that cortisone and prednisolone, at the given doses, neither determine any malformation, nor any embryofetotoxic effect; 3) corticosteroid therapy induced no evident variation in total estriol plasma levels, compared to those found in control pregnancies, prospectively studied and physiologically concluded ([50]) (fig. 1). To support this opinion we can say that corticosteroids, at the administered doses, could not inhibit foetal ACTH ([51, 52]) and had no influence on foetal adrenal DHAS synthesis; this treatment, moreover, did not retard intrauterine foetal growth (cortisol action on DNA-polymerasis with a slowering of cell duplication rate in many actively growing tissues) monitored by the BPD increase curve and the birth weight (fig. 2).

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