Proc EDTA–ERA (1985) Vol 22

IgA NEPHROPATHY AND PREGNANCY

P Jungers, D Forget, D Droz, L H Noel, *M Henry-Amar

*INSERM U25, Hôpital Necker, Paris, *Department of Statistics, Institut Gustave-Roussy, Villejuif, France*

Summary

The influence of pregnancy on primary IgA nephropathy was retrospectively analysed in 34 female patients followed at Necker Hospital from 1967 to 1982 who became pregnant at least once after clinical onset of IgA nephropathy (69 pregnancies, 70 fetuses). Pregnancy ended successfully in 80 per cent of cases. Fetal deaths were mainly observed in patients with impaired renal function and/or hypertension at conception or early in gestation. Onset of hypertension in pregnancy was highly predictive of subsequent permanent hypertension and of recurrence of hypertension in further pregnancies. An abnormally rapid decline in renal function was observed during pregnancy in three cases.

However, there was no significant difference in the actuarial curves of survival free of renal failure in this group of 36 patients and in a group of 24 patients followed during the same period who were never pregnant after the clinical onset of IgA nephropathy.

Introduction

Mesangial IgA nephropathy is the commonest form of chronic primary glomerulonephritis encountered in many countries [1]. As the disease mostly occurs in young adult patients and therefore in child-bearing women, the reciprocal influence of IgA nephropathy on pregnancy and of pregnancy on the course of renal disease is an important concern. Reports on pregnancy in patients having IgA nephropathy identified on the basis of renal biopsy with immunofluorescent staining and including at least 20 patients are few [2,3]. We report here our experience in 34 women having had a total of 69 pregnancies after the clinical onset of IgA nephropathy who were followed at Necker Hospital during the past two decades.

Patients and methods

We retrospectively reviewed the charts of all female patients with IgA nephropathy whose renal biopsy was performed at Necker Hospital from 1967 to 1982.

In all cases, diagnosis of IgA nephropathy was established on the basis of both immunofluoresence and light microscopy [4]. The studied population comprised 60 patients, of whom 34 were pregnant at least once, and 26 had no pregnancy after the apparent clinical onset of nephropathy. In the pregnant group, renal biopsy was performed before the index pregnancy in eight patients (3 years as a mean) and after the index pregnancy in the other 26 (6.2 years as a mean). No biopsy was taken during pregnancy or in the immediate post partum. The mean follow-up duration was 7.2±5.1 years (range 1–20) after last pregnancy and 15±7 years (range 1–27) after the apparent onset of nephropathy.

Results

Influence of nephropathy on fetal outcome

Of a total number of 69 pregnancies (70 fetuses), 50 (72%) ended in full-term delivery (including twins), nine (13%) in premature delivery, and 11 (15%) in spontaneous (7 cases) or therapeutic abortion (4 cases, all for severe hypertension). All full-term and six of nine premature infants were alive. Thus, the overall rate of live birth was 80 per cent (56 of 70). Perinatal death rate was five per cent (3 of 59) and the mean birthweight, known in 56 cases, was 3200± 500g (1900–4800g).

Renal failure complicated five pregnancies in four women. In three cases, it was present at conception. In one of them, the serum creatinine was moderately increased (133μmol/L) and did not rise during pregnancy, which ended successfully; in the other two, a higher initial serum creatinine (166 and 212μmol/L, respectively) rapidly increased together with severe hypertension, and gestation ended in early spontaneous abortion. In the other two cases, serum creatinine was initially normal but progressively rose (up to 210 and 260μmol/L, respectively) during pregnancy which ended in premature delivery of live infants.

Hypertension was present during 27 (39%) of 69 pregnancies. In this situation, fetal loss was higher than in normotensive pregnancies (7 of 27, or 26% versus 7 of 42, or 17%, NS). Moreover, of the 10 pregnancies where hypertension pre-existed (8 cases) or occurred early (2 cases), only five ended successfully and, in four of them, hypertension had been controlled by antihypertensive treatment. In the 17 pregnancies complicated by third-trimester hypertension, only two fetal deaths were observed.

Influence of gestation on the course of IgA nephropathy

At the end of follow-up, permanent hypertension was present in 17 of 34 (50%) and chronic renal failure in 9 of 34 (26%) of patients in the pregnant group. Of the eight women who were normotensive at conception and who became hypertensive in at least one pregnancy, seven subsequently developed permanent hypertension. The six women who were hypertensive at conception, remained hypertensive during pregnancy and five of them developed permanent hypertension. Thus, 12 (86%) of the 14 patients who were hypertensive in at least one

pregnancy developed permanent hypertension. By contrast only five (25%) of the 20 women who never were hypertensive during any of 43 pregnancies had permanent hypertension at the end of follow-up, a highly significant difference ($p<0.001$).

Protein excretion increased during 22 pregnancies in 16 patients, but was never associated with the nephrotic syndrome, whereas it was unchanged during 34 pregnancies in 18 patients (in the other 13, proteinuria was the revealing symptom of IgA nephropathy during the index pregnancy).

One hypertensive patient whose renal function was normal at conception exhibited progressive renal failure during pregnancy and progressed to end-stage renal failure within one year of premature delivery. Another patient whose renal function was slightly impaired at conception developed a slow, but irreversible increase in serum creatinine during pregnancy which rapidly worsened during a further pregnancy started one year later, leading to chronic dialysis within 16 months. In two other patients, renal impairment was present at conception: in one case, increase in serum creatinine was moderate (133μmol/L) and did not progress during pregnancy; in the other case, serum creatinine rose rapidly from 210 to 280μmol/L early in gestation and further progressed to end-stage renal failure within eight months. Thus, in three patients, pregnancy was associated with an unexpectedly rapid decline in renal function, leading from moderate renal impairment to end-stage renal failure within 12 months of the end of pregnancy. By contrast, of the 30 patients who did not exhibit renal impairment during any of 64 pregnancies, only five (17%) progressed to advanced renal failure within, as a mean, six years of the end of the last pregnancy.

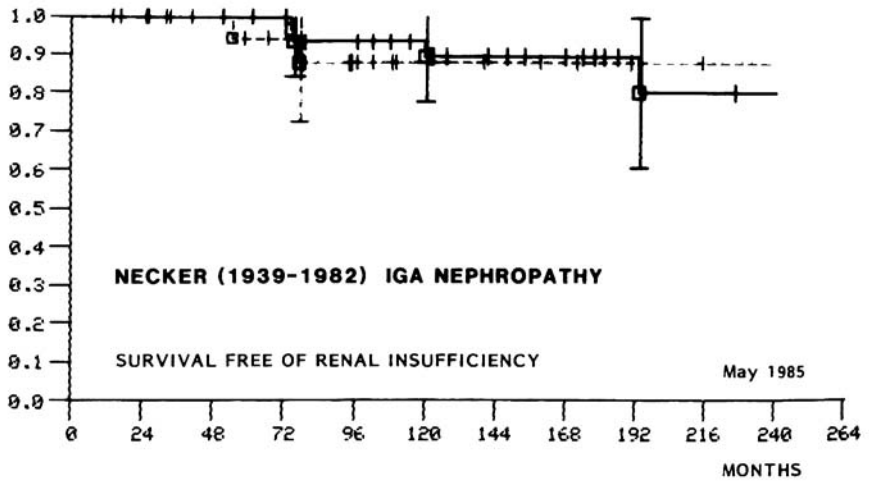

Figure 1. Actuarial curve of chronic renal failure in 34 patients who had at least one pregnancy and in 26 patients who never were pregnant after clinical onset of IgA nephropathy. — with pregnancies (n=34); - - - - without pregnancy (n=27)

When comparing the time curve of renal function in the whole group of 34 women having had at least one pregnancy after the apparent clinical onset of IgA nephropathy, and in the group of 26 women who had no pregnancy after clinical onset of nephropathy, there was no significant difference in the actuarial curves of occurrence of chronic renal failure defined by serum creatinine definitely above 135μmol/L, in the two groups, even when adjusted on age, using the Log-rank test and the Kaplan-Maier test (Figure 1).

Discussion

There is general agreement that underlying renal disease has an unfavourable influence on the outcome of pregnancy when high blood pressure and/or renal impairment is present at conception [5], but the influence of pregnancy on the course of underlying renal disease is still a matter of discussion [6]. This is especially true in IgA nephropathy, mainly because published reports are based on very small numbers of patients, with only the exception of two recent studies [2,3]. Our series is on a sufficiently large number of patients and pregnancies to allow statistical analysis.

Similar to Whitworth et al [2] and Surian et al [3], we observed a favourable fetal outcome, except in the cases where hypertension and/or renal failure existed at conception or early in gestation. Hypertension was a frequent problem during pregnancy in women with IgA nephropathy, with an incidence of nearly 40 per cent, both in the experience of others [2,3] and in ours. We observed a highly significant correlation between occurrence of hypertension in pregnancy and further development of permanent hypertension (and with recurrence of hypertension in subsequent pregnancies as well). Moreover, we observed a marked improvement in fetal prognosis when pre-existent or early hypertension was controlled by antihypertensive treatment, as in other varieties of chronic primary glomerulonephritis [7].

More crucial is whether there is, or is not, an adverse effect of pregnancy on the course of the maternal renal disease. Whereas Surian et al reported no case of rapid decline in renal function among 21 patients, Whitworth et al reported a rapid worsening of pre-existent renal failure in one of 20 patients [2]. We also observed a rapid worsening in incipient or moderate renal failure in three patients, leading to end-stage renal failure within one year of the last gestation. This may be considered a more rapid decline in renal function than would be expected in the natural course of the disease [8]. However, we did not obtain renal biopsy during or immediately following pregnancy in these three patients and therefore cannot assess the mechanism of this deterioration. Nevertheless, such an unusually rapid course suggests a possible adverse effect of pregnancy. Similarly, Hou et al recently reported an unexpectedly rapid decline in renal function during pregnancy in six of 12 patients with primary glomerulonephritis who had a moderate degree of renal failure at conception and, of these six patients, three had IgA nephropathy [9]. Thus, an adverse influence of pregnancy on the course of IgA nephropathy cannot be excluded at least in individual cases. However, we were unable to demonstrate an overall influence of pregnancy

on the course of IgA nephropathy, because the actuarial time curve for renal function did not significantly differ between the group of patients having been pregnant at least once and the group of patients never having been pregnant after clinical onset of IgA nephropathy (Figure 1).

We conclude that successful pregnancy may be expected in most patients with IgA nephropathy without deterioration of maternal condition, but pregnancy should be considered cautiously in women having impaired renal function and/or hypertension, especially when previous pregnancies were complicated by hypertension.

References

1 D'Amico G, Imbasciati E, Barbiano di Belgiojoso G. *Medicine 1985; 64:* 49
2 Whitworth J, Kincaid-Smith P, Fairley KF. In Sammour MB et al, eds. *Pregnancy Hypertension.* Cairo: Ain Shams University Press. 1981: 403
3 Surian M, Imbasciati E, Cosci P. *Nephron 1984; 36:* 101
4 Berger J, Hinglais N. *J Urol Nephrol 1968; 74:* 694
5 Kincaid-Smith P. In Seldin DW, Giebisch G, eds. *The Kidney: Physiology and Pathophysiology.* New York: Raven Press. 1985: 2043
6 Katz AI, Davison JM, Hayslett JP et al. *Kidney Int 1980; 18:* 192
7 Jungers P, Forget D, Henry-Amar M et al. *Actualités Néphrologiques de l'Hôpital Necker.* Paris: Flammarion. 1985: 95
8 Droz D, Kramar A, Nawar T, Noel LH. *Contr Nephrol 1984; 40:* 202
9 Hou S, Grossman SD, Madias NE. *Am J Med 1985; 78:* 185