Proc EDTA–ERA (1985) Vol 22

THE EFFECT OF PREGNANCY ON AMYLOID NEPHROPATHY IN FAMILIAL MEDITERRANEAN FEVER

S Cabili, *O Rabinovitch, *D Zemer, A Aviram, *M Pras

*Rokach Hospital, Tel Aviv, *Sheba Medical Centre, Tel-Hashomer, Israel*

Summary

The effect of pregnancy on renal amyloidosis was examined retrospectively in 15 women (26 full-term pregnancies) with familial mediterranean fever and established proteinuria. Two of three patients who began pregnancy with mild renal insufficiency progressed rapidly to renal failure following delivery and the third reached terminal renal failure only after seven years. In 12 women with normal renal function no deterioration was observed in 21 pregnancies; after their last deliveries, however, five progressed to renal failure, four reaching end-stage renal failure within 10–20 months and one recovered slowly over a period of three years. The outcome of the renal disease was independent of normal kidney function, degree of proteinuria or blood pressure before conception. This suggests that amyloidosis is unique among other chronic renal diseases as pregnancy imposes a tangible risk of deterioration of renal function unrelated to accepted favourable prognostic features, such as normal blood pressure, normal renal function and the amount of protein excretion.

Introduction

There is no consensus of opinion in the literature on the influence of pregnancy on the course of pre-existing kidney disease. Although older [1] as well as recent comprehensive studies [2] conclude that "in normotensive women with underlying renal disease with normal or only mildly decreased kidney function, pregnancy will not adversely affect the course of the disease" this statement 'has to be tempered somewhat' in certain nephropathies such as lupus of possibly IgA nephropathy [2]. Reports on the effect of pregnancy on renal amyloidosis are extremely rare. We therefore undertook an essentially retrospective study of the effects of pregnancy on the course of renal amyloidosis in all our affected patients with familial mediterranean fever.

Patients and methods

The effect of pregnancy on the course of amyloid nephropathy in familial mediterranean fever was studied in 15 women (26 full-term pregnancies). All were followed up between the years 1970–1985, and had established proteinuria before the beginning of pregnancy. This series includes all pregnancies among our patients with renal amyloidosis. Parameters studied were clinical findings such as blood pressure, as well as creatinine determinations and quantitative assessment of proteinuria, before, during and after gestation. None of the patients received colchicine during pregnancy, since we thought that the medication might have a deleterious affect on the fetus. This study focuses on the last pregnancy; previous uneventful pregnancies are also presented if the patient conceived while afflicted with documented amyloidosis.

Results

Pertinent data of all patients are presented in Table I. There were 15 women with 26 full-term pregnancies. Amyloidosis as shown by established proteinuria was documented in all patients. The time elapsed from the discovery of amyloidosis until pregnancy ranged from less than one year to 17 years. The age of the patients during their last pregnancy ranged from 23 to 37 years (mean 29.3±3 years). All patients were proteinuric, excretion ranging from 1–8g/day; all were normotensive. Three women had mild renal insufficiency (serum creatinine >1.6mg/dl) at the time of conception. All had proteinuria in the nephrotic range. In the first patient an elevated creatinine was first documented eight months after an apparently uneventful earlier pregnancy. Two of the three progressed to severe renal failure during pregnancy, developed hypertension, and reached end-stage renal disease within a short period. The third showed progressive deterioration to renal failure after seven years, probably reflecting the natural course of her disease.

The remaining 12 women with amyloidosis and normal renal function experienced neither aggravation of proteinuria, nor deterioration of renal function during a total of 21 pregnancies. After their last deliveries, however, five of them progressed to renal failure within 4–8 months. Four reached end-stage failure within 10–30 months, and the fifth recovered slowly over three years. All five failed to show the expected increase in glomerular filtration rate (GFR) with progression of pregnancy suggesting that deterioration did in fact occur during pregnancy; by contrast in five of the seven women whose renal function did not deteriorate post partum, such an increase was documented by a fall in serum creatinine during pregnancy.

Discussion

The major aim of this study was to evaluate the immediate and delayed effects of pregnancy on the course of maternal renal amyloidosis. Our results show that pregnancy imposes a tangible risk of deterioration of renal function – the risk cannot be individually assessed, since deterioration can occur despite normal

TABLE I

Patient	Diagnosis of amyloidosis	Earlier pregnancy	Last pregnancy				Post partum		Last follow-up	
	Age	Age	Age	Proteinuria g/24hr	Serum creatinine* start	delivery	months**	creatinine	years**	Status
1	28	28	32	4.5	3.0	4.5	1	6.2	0.5	ESRD
2	12	–	23	7.0	2.0	3.0	4	4.1	2	ESRD
3	24	–	28	9.0	1.9	–	36	3.5	7	ESRD
4	19	–	30	2.0	1.1	1.1	8	1.8	2.5	ESRD
5	19	24	28	7.0–8.0	1.0	1.0	4	7.0	1	Death
6	16	25,28	32	1.6–2.0	1.1	1.1	2	5.0	1.5	ESRD
7	21	–	30	1.8–2.5	0.8	1.2	5	2.2	1.0	ESRD
8	25	–	26	6.7	1.5	4.4	2	3.3	3	Cr 1.3
9	23	23,25	28	4.5–6.0	0.8	0.6	–	–	6	Cr 1.2
10	16	21,22	35	0.5–1.0	0.9	0.7	–	–	6	Cr 1.0
11	13	21	30	3.0	1.0	0.6	–	–	1	Cr 1.0
12	20	–	37	0.5–1.0	1.0	0.8	–	–	1.3	Cr 1.3
13	29	–	30	1.0	0.8	0.6	–	–	4	Cr 1.0
14	21	24	28	3	1.2	0.6	3	0.7	1	Cr 0.7
15	14	21	23	3.5	1.0	0.8	3	0.8	1	Cr 0.8

* mg/dl

** time elapsed from last delivery

ESRD=end-stage renal disease

renal function, lack of hypertension and irrespective of the quantity of protein excretion. Renal insufficiency, even mild, probably increases the risk of deterioration. On the other hand, proteinuria even in the nephrotic range does not necessarily imply a bad prognosis. Since all women were normotensive at the beginning of pregnancy we cannot comment on the risk of initial elevated blood pressure – on the contrary we can say that a normal blood pressure is irrelevant in predicting the outcome of gestation in this disease. An additional point of interest, shown by some of our patients, was that renal function, although normal at delivery, can abruptly deteriorate a few months following gestation. The only clue to deterioration was the absence of the expected increase in GFR that normally occurs during pregnancy; obviously this observation is of no value in contemplating the outcome for a patient before pregnancy.

Thus, renal amyloidosis does not fit into some of the accepted favourable prognostic features of other renal diseases and pregnancies such as normal blood pressure, minimal proteinuria and normal renal function. Fortunately the prevention of amyloidosis in familial mediterranean fever with colchicine will diminish the number of affected patients and thus the severity of the problem.

References

1 Katz AI, Davison JM, Hayslett JP et al. *Kidney Int 1980; 18:* 192
2 Katz AI, Lindheimer MD. *Seminars in Nephrol 1984; 4:* 252