Renal Thrombotic Microangiopathy in a Pregnant Patient with Membranoproliferative Glomerulonephritis

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Dear Sir,

Because glomerular diseases have an unforeseeable course during pregnancy, appropriate counseling is always compromised. Opposed evidence has been reported without firm conclusions, and some risk factors are only considered as reference, e.g. serum creatinine (sCr) higher than 2 mg/dl, especially in the presence of severe hypertension.

We report of a young female known to have membranoproliferative glomerulonephritis (MPGN) with stable renal function, controlled arterial pressure and moderate proteinuria, who developed a renal thrombotic microangiopathy in the later part of her second pregnancy.

Case Report

A 24-year-old female, who had never taken oral contraceptives, presented at the age of 13 years with microscopic hematuria but no nephrotic proteinuria. She had normal renal function (sCr 0.6 mg/dl) and blood pressure was 110/70 mm Hg. A percutaneous renal biopsy was performed 3 months later due to persistent urinalysis disorders. It contained 23 glomeruli, all of which were impaired, with lobulation of the tufts and marked mesangial hypercellularity. The capillary walls were thickened to a variable degree, and double-contoured basement membranes were present. With Masson trichrome, deposits on the subendothelial side of the basement membrane were observed. There were no sclerosis, crescents, nor interstitial or vascular damage. An immunofluorescence technique was not performed. In short, it was a membranoproliferative glomerulonephritis type I, with subendothelial deposits.

After treatment with steroids, her condition remained stable with 24-hour proteinuria 1.4 g. Seric C3 and C4 levels were normal and ANA and anti-ds-DNA antibodies negative. In 1982, she had her first pregnancy and the course as well as the delivery in February 1983 were normal without detrimental effects on nephropathy. Despite an intrauterine device that was fitted in August 1983, she became pregnant in September. 2½ months later, she developed high blood pressure (160/100 mm Hg) and proteinuria increased to 3 g/day without edema, but renal function was normal. Oral methyl-

dopa 1 g/day was initiated. At 30 weeks of pregnancy, hematocrit was 36%, sCr 1.0 mg/dl and arterial pressure 160/105 mm Hg; hydralazine and propranolol were associated. 2 weeks later she was admitted to hospital for worsening of renal function (sCr 2.2 mg/dl), hematocrit (30%) and severe hypertension (170/120 mm Hg). The next week (33nd), sCr was 3.1 mg/dl, hematocrit 26%, and hypertension persisted with fundi examination grade III (K-W). A cesarean section

was undertaken at this point and a premature, viable female infant of low weight (1,530 g) was born. A tubal ligation was also performed. In the postoperative course, diazoxide was prescribed and an increase of anemia (Hb 8.1 g/dl, hematocrit 23%) was observed. Signs of hemolytic activity were present: absent haptoglobin level, reticulocyte count $109 \times 10^9/l$ (40%) and schistocytes 6–10%. White cell count ($10 \times 10^9/l$), platelet count ($138 \times 10^9/l$) and coagulation factors were normal, with plasma fibrin degradation products 10 mg/l. Tests for LE cells, Latex and Coombs were negative. C3 in the serum was 150 mg/dl and C4 53 mg/dl.

As a rapid increase of sCr to 5.8 mg/dl was observed, a renal biopsy by lumbar puncture was obtained 3 days after delivery. Most of glomeruli showed lesions of thrombotic microangiopathy, with thrombi in glomerular capillary and focal necrosis. In afferent arterioles there were intimal deposition of fibrin, swelling, cell proliferation and decreased vascular lumen with thrombi inside. Similar lesions as those in the first biopsy were observed in less affected glomeruli. A diffuse tubular necrosis and moderate interstitial fibrosis were also seen. Immunofluorescence studies disclosed scattered aggregates of C3 at the glomerulus periphery, and glomerular and vascular deposits fibrinogen in a granular pattern.

Dipyridamole 300 mg/day and fresh-frozen plasma (20 ml/kg/day for 1 month) was associated to oral antihypertensive drugs (minoxidil, prazosin and propranolol). Arterial pressure was controlled; however, dialysis was initiated by progressive uremia 10 days after delivery. Between May and August 1984, while staying in hemodialysis regimen, she had an episodic pericarditis and minoxidil was withdrawn. At this late date, a partial recovery of renal function (sCr 4.7 mg/dl, Cr clearance 16 ml/min) was proved when arterial pressure was well controlled.

Reticulocytosis persisted in peripheral blood but platelet counts were normal and schistocytes absent. Dialysis was discontinued.

In June 1987, renal function was stable (sCr 4.4 mg/dl), hematocrit reduced to 30% and no signs of hemolytic activity were observed (reticulocyte count 1% and schistocytes absent). In urinalysis, mild proteinuria 0.7 g/day and microscopic hematuria persisted. Arterial pressure had remained well controlled with captopril, propranolol, hydralazine and furosemide.

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Discussion

Acute renal failure due to hemolytic uremic syndrome may occur in healthy women while taking oral contraceptives, after delivery and also in early [1] and late [2] pregnancy in association with preeclamptic signs. In women with previous MPGN, pregnancy appears to cause more obstetrical, fetal and renal complications than in other nephropathies [3]. Specifically, acute worsening of renal function caused by superimposed rapidly progressive (crescentic) glomerulonephritis upon MPGN has been referred, with [4] or without [5] ultimate recovery. On the other hand, enhanced capacity to produce fibrin and decreased fibrinolytic activity has been reported in normal and especially in complicated pregnancy (preeclampsia) [2], and a depressed prostacyclin (PGI₂) production has also been suggested [6].

In our case, this hypercoagulable state upon a predisposed renal microvasculature (MPGN) and consequent severe hypertension could explain the resultant renal thrombotic microangiopathy. Factors such as prerenal azotemia, drug toxicity or sepsis were otherwise absent.

In relation to the evolution, a beneficial effect of initial plasma infusion and subsequent intermittent heparinization by need of dialysis appears as a remote possibility. Rather, the active

control of arterial pressure by combined dialysis and antihypertensive drugs may, in part, be the cause of late and partial renal function improvement.

Together with previous experiences, the present case, who revealed a different renal course during each pregnancy, should be borne in mind when women with glomerular diseases, particularly MPGN, seek counseling.

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