A 27-year-old Japanese female developed nephrotic syndrome and impaired renal function during pregnancy. A renal biopsy performed at 21 weeks of gestation revealed crescentic IgA nephropathy. She was treated with steroid pulse therapy followed by conventional steroid therapy. Although the nephrotic syndrome was persistent, the impaired renal function did not deteriorate after the treatment. A live infant was delivered by cesarean section at 37 weeks of gestation. After the delivery, both the nephrotic syndrome and renal insufficiency improved gradually. The indications for renal biopsy and treatments for active IgA nephropathy during pregnancy are discussed.

Key words: crescentic IgA nephropathy, nephrotic syndrome, pregnancy, renal biopsy
and nontender uterus was palpable in the lower median part of the abdomen, about 5 cm from the superior aspect of the pubis. The neurologic findings were negative. There was no edema in either leg.

The erythrocyte sedimentation rate was 70 mm/h, erythrocyte count 284×10⁴/µl, hemoglobin 8.9 g/dl, hematocrit 26.5%, leukocyte count 11,900/µl (neutrophils, 74%; eosinophils, 3%; monocytes, 1%; lymphocytes, 22%), and platelet count 29.9×10⁴/µl. The total urinary protein for 24 hours was 8.3 g, and the urine sediment showed 10–25 red blood cell casts per high power field. The serum total protein was 5.2 g/dl, albumin 2.7 g/dl, blood urea nitrogen 15 mg/dl, creatinine 0.9 mg/dl, and uric acid 3.9 mg/dl. 24h-Ccr was 62 ml/min. Liver function tests were normal. Serum IgG was 395 mg/dl, IgA 134 mg/dl, and IgM 209 mg/dl. Anti-streptolysin O titer was 25 Todd. Rheumatoid factor and antinuclear antibodies were negative. Serum C3 was 55 mg/dl (normal range: 60–116 mg/dl), C4 21 mg/dl (15–44 mg/dl), and CH50 35 CH50U/ml (30–45 CH50U/ml). Neither perinuclear-antineutrophil cytoplasmic antibodies nor cytoplasmic-antineutrophil cytoplasmic antibodies were detected with indirect immunofluorescence staining.

A percutaneous renal biopsy was performed on October 20 (at 21 weeks of gestation). Light microscopic examination demonstrated slightly enlarged glomeruli with diffuse and moderate mesangial cell proliferation; more than 50% of the glomeruli (eight of 15 glomeruli) were accompanied by cellular crescent formations (Fig. 1A). In addition, segmental necrotic lesions and segmental sclerotic lesions were found in some glomeruli (Fig. 1B). The glomerular capillary walls showed no appearance of endotheliosis. The interstitial architecture was relatively well preserved, although focal tubular atrophy and infiltrates of small round cells were observed. Proximal tubular epithelial cells frequently showed vacuolar degeneration, and red blood cells were occasionally observed in the tubular lumen. Immunofluorescence microscopy revealed 3+ staining for IgA, 2+ staining for κ and λ, and 1+ staining for IgG, IgM, and C3 over the mesangial area and along the peripheral capillary walls in a granular pattern (Fig. 2). Electron microscopy of ultrathin sections stained with uranyl acetate and lead citrate revealed electron dense deposits mainly in the mesangial area, and to a lesser extent in the subendothelial space of the glomerular capillary walls. Attenuation of the glomerular basement membrane was occasionally observed (Fig. 3).

Based on these findings, the patient was diagnosed as having crescentic IgA nephropathy. She was treated with m-PSL pulse therapy (500 mg/day for 3 days) followed by conventional prednisolone therapy (40 mg/day for 4 weeks, gradually tapered to 15 mg/day) and dipyridamole (150 mg/day). Thereafter, the 24h-Ccr remained over 50 ml/min until delivery, although the nephrotic syndrome persisted. The growth of the fetus was stable until 35 weeks of gestation. Fetal weight gain stopped after 36 weeks of gestation and the patient was transferred to our Department of Gynecology and Obstetrics on February 12, 1993. A live male infant weighing 2,200g was delivered by cesarean operation at 37 weeks of gestation. The infant showed no apparent physical abnormalities. In August
Pregnancy in Active IgA Nephropathy

Discussion

This woman with chronic glomerulonephritis developed nephrotic syndrome and progressive renal impairment during pregnancy. A renal biopsy performed at 21-weeks gestation demonstrated crescentic IgA nephropathy. She was successfully treated with steroids and successfully delivered a live infant.

It is controversial whether IgA nephropathy influences the outcome of pregnancy, or whether pregnancy has any adverse effect on the course of IgA nephropathy. Packham et al (2) reported that the rate of fetal loss in 70 women with IgA nephropathy examined between 1971 and 1986 was 30% (35 of 118 fetuses). Surian et al (5) described that perinatal death occurred in three (10%) of 29 pregnancies in 21 patients with IgA nephropathy encountered between 1970 and 1981. On the other hand, Abe (3) recently reported a more favorable outcome, i.e., only seven of 168 pregnancies (4%) resulted in fetal loss in 118 women with IgA nephropathy. Moreover, while the rate of perinatal death in the 1970’s was 9%, it was 0% in the 1980’s (3). Abe also stated that IgA nephropathy without hypertension and impaired renal function (glomerular filtration rate less than 70 ml/min) did not adversely influence the outcome of pregnancy. The different perinatal death rates in these reports may be due to differences in the patient populations as well as to advances in prenatal and neonatal care.

Concerning the influence of pregnancy on IgA nephropathy, there is general agreement that pregnancy does not affect IgA nephropathy if the woman is normotensive and has normal or slightly impaired renal function (6). Abe (3) compared the natural course of renal function in pregnant patients suffering from IgA nephropathy with that of non-pregnant women with IgA nephropathy, and demonstrated that there was no significant difference between the two groups. He therefore concluded that pregnancy has no general influence on the course of IgA nephropathy when the patient is normotensive and has a pre-pregnancy glomerular filtration rate of more than 70 ml/min. Since the present case was also normotensive and her 24h-Ccr before gestation was more than 70 ml/min, the deterioration of renal function with nephrotic syndrome which developed seems unlikely to have been associated with the pregnancy itself. The patient might have suffered from crescentic IgA nephropathy during the pregnancy coincidentally. We also consider that this event did not have superimposed on preeclampsia, since the patient had been normotensive during the pregnancy, the level of proteinuria increased to the nephrotic range at 12 weeks of gestation, and the renal biopsy performed at 21 weeks of gestation showed no appearance of glomerular endotheliosis.

In general, the performance of renal biopsies in pregnant women is limited. Packham and Fairley (7) reported 111 consecutive renal biopsies performed in 104 pregnant women, and concluded that renal biopsies during the first two trimesters do not appear to be associated with an increased rate of complications. Lindheimer and Davison (8) proposed the following two indications for renal biopsy in pregnant women: a sudden impairment in renal function before 32 weeks of gestation with no apparent cause, and symptomatic nephrotic syndrome of unknown origin observed before 32 weeks of gestation. As these two indications were present, we performed a percutaneous renal biopsy in the present patient at 21 weeks of gestation, and we were therefore able to treat the crescentic IgA nephropathy at an early stage. Since crescentic IgA nephropathy is a rapidly progressive glomerulonephritis of the primary immune-complex type (9), we treated the patient with steroid pulse therapy. Although the effectiveness of treatment with steroids in active IgA nephropathy remains controversial (10–13), several authors have reported that steroids are effective for crescentic IgA nephropathy (12, 13). D’Amico (12) stated that the use of intravenous steroid pulses is warranted in patients with oliguric renal failure in whom renal biopsy reveals cellular crescents in the majority of the glomeruli. Yoshimura et al (13) also demonstrated that mPSL pulse therapy improves the renal function of patients with crescentic IgA nephropathy. In their eight patients, follow-up biopsies performed after the pulse therapy revealed complete disappearance of cellular crescents in six patients and a marked decrease (from 73% to 33%) in the other two. In the present patient, although the nephrotic syndrome was persistent, the 24h-Ccr was greater than 50 ml/min at 35 weeks of gestation, and the patient was successfully delivered of a live baby without complications. The persistent nephrosis during pregnancy may be accounted for by the presence of IgA deposits in the glomerular capillary walls (14). After the delivery, her renal function gradually improved (24h-Ccr of 70 ml/min), and the nephrotic syndrome reached partial remission. We therefore consider that steroid pulse therapy followed by conventional steroid therapy was effective in the

1993, prednisolone was tapered (10 mg/day), and the patient’s 24-hour proteinuria was 0.8 g, serum total protein 6.0 g/dl, albumin 3.9 g/dl, and 24h-Ccr 70 ml/min.

Fig. 3. Electron microscopy disclosed electron dense deposits in the mesangial area (arrows) and to a lesser extent in the subendothelial space of the glomerular capillary walls (arrow heads). Focal attenuation of the glomerular basement membrane was noted (uranyl acetate and lead citrate stain, ×2,500).
Regarding the effect of steroids on pregnancy, it is generally considered that steroid pulse therapy and conventional steroid therapy have few adverse effects. Since placental 11 β-dehydrogenase oxidizes glucocorticoids to inactive 11-keto forms, the fetus is protected from a large proportion of the glucocorticoids in the maternal circulation (15). Steroids are used in pregnant women with systemic lupus erythematosus; there have been no reports of fetal abnormalities caused by steroid administration (16). Indeed, the baby in the present case showed no physical abnormalities.

In conclusion, in the pregnant patient suffering from active glomerular disease, renal biopsy may be a useful aid for the evaluation of renal histological changes and for determination of the steroid treatment, as in non-pregnant patients.

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References