Case Report

DOI: 10.7860/JCDR/2018/36044.11836

Childhood Onset Nephrotic Syndrome- A Journey Through Two Pregnancies

Obstetrics and Gynaecology Section

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ABSTRACT

Nephrotic Syndrome (NS), a unique renal disease complex associated with heavy proteinuria (protein excretion >3.5 gm/day), hypoalbuminemia (<30 gm/L) and peripheral oedema. It is a rare entity in pregnancy, with an incidence of about 0.012-0.025%. There have been very few reports of pregnancy with co-existing NS. We hereby report a case of steroid sensitive childhood onset NS, due to minimal change disease and her course through two pregnancies. While she had a relapse of NS during her first pregnancy, she sailed through her second pregnancy without relapse. Women with NS can have a good maternal and perinatal outcome with multidisciplinary approach. Pregnancy does not always worsen the existing NS by causing a relapse or disease progression.

Keywords: Hypertension, Pregnancy, Proteinuria, Renal disease, Steroids

CASE REPORT

First Pregnancy

A 25-year-old female presented in 2012 with 16 weeks amenorrhoea, and recent onset of rapidly progressive, gross oedema. She was a known case of steroid sensitive NS, from the age of three years. At the age of 10, she was diagnosed to have minimal change disease based on renal biopsy (the patient's histopathology report was available to the authors). She has had many episodes of relapse that would respond to treatment with prednisolone. Married for about one year, she did not have any problems with conception. Her last relapse was about one year before her pregnancy.

Her renal functions were normal (serum creatinine 0.6 mg/dL), and she had hypoalbuminemia with massive proteinuria (serum total protein 62 gm/L, albumin 30 gm/L, urine protein 3.6 gm/day). Other haematological and biochemical tests, including thyroid function tests, were normal. She was diagnosed to have a relapse of her NS during the second trimester of pregnancy.

Treatment was initiated in consultation with Departments of Internal Medicine and Nephrology, using prednisolone 1 mg/kg body weight, along with salt and fluid restriction. The patient had a gradual reduction of oedema and proteinuria, and the dose of prednisolone was gradually reduced by about 0.25 mg/kg body weight every 2-4 weeks with close medical and obstetric monitoring. At 30 weeks, she developed gestational hypertension, while on 10 mg/day of prednisolone that was managed with oral labetalol, starting with 50 mg twice daily (100 mg of tablet labetalol, half tablet twice daily). By 35 weeks, her requirement for prednisolone was stable at 10 mg per day, and labetalol requirement was 200 mg twice daily.

She underwent emergency caesarean delivery at 35 weeks of gestation, due to severe pre-eclampsia and intrauterine growth restriction. Birth weight of the baby was 1800 grams. Her blood pressure was very high perioperatively and required continued usage of parenteral antihypertensive agents for 24 hours in the postoperative period. The baby had neonatal hypoglycaemia and needed neonatal intensive care for six days. She went into remission of NS postnatally, and steroids, as well as antihypertensives, were tapered and stopped about four weeks after delivery.

Second Pregnancy

Though she was advised to avoid conception for at least two years, she conceived during lactational amenorrhea. She had no significant oedema or proteinuria during this pregnancy and was not started on prednisolone this time. She was under close fortnightly follow-up. She showed trace proteinuria; however, renal functions and serum protein levels were within normal ranges. In consultation with internal medicine and nephrology services, she received a total fluid intake of less than 1.2 L/day and salt <5 gm/day. She developed gestational hypertension at 24 weeks of gestation and started on labetalol 50 mg twice daily (100 mg of tablet labetalol, half tablet twice daily). She was also found to be hypothyroid and started on levothyroxine 50 µg once daily.

She neither had a relapse of NS during second pregnancy nor did she develop pre-eclampsia. However, there was foetal growth restriction during this pregnancy too, and elective caesarean delivery with bilateral tubal ligation was done at 38 weeks. The birth weight was 2100 grams. There were no perioperative complications. She did not need antihypertensives in the postnatal period after the second delivery, and there were no neonatal problems.

DISCUSSION

Preconceptional counselling is of utmost importance in females with kidney disease, as there could be worsening during pregnancy, especially if the disease is active. In women with advanced renal insufficiency, and if the woman is on cytotoxic alkylating agents, fertility may be a concern. At least six months of remission is considered optimal before conception [1]. This patient had consulted the nephrologist and was counselled to plan the first pregnancy as she was in remission for more than a year and her renal function tests were normal.

Pregnancy is a state of altered haemodynamic and hormonal physiology [2]. These changes have significant implications for renal function too. Patients with pre-existing renal diseases pose a unique challenge. Management of such patients requires a multidisciplinary approach and close supervision [3].

Kidney disease has the propensity to affect fertility as well as pregnancy outcome [4]. Two related aspects here are the effect of gestation on kidney and effect of kidney disease on pregnancy.

Renal plasma flow and GFR increase by 35-50% during pregnancy. The rise in GFR is gradual, it starts after conception and reaches a peak by 12 weeks [5]. As a result, serum creatinine and urea values reduce during normal pregnancy; accompanied by an elevated urinary protein excretion. Random urinary samples for estimating creatinine clearance or proteinuria are inaccurate, 24-hour urine collection is the gold standard in pregnancy. In the non-pregnant woman, daily protein excretion is less than 150 mg/day, consisting of about 20 mg/day of albumin and the remaining proteins of tubular origin. However, up to 260-300 mg/day of proteinuria is considered normal in pregnancy [6,7].

In patients with glomerular disease, the histologic type of glomerulonephritis may not be as important as clinical parameters like impaired renal function, hypertension and nephrotic range proteinuria in determining the pregnancy outcome. However, while the overall rate of foetal loss in glomerular disease is 21%, the worst foetal loss rate and low birth weight are seen in focal glomerulosclerosis [2].

Pregnancy outcome is good if the patient has only mild renal dysfunction (serum creatinine <1.4 mg/dL), no nephrotic range proteinuria and mild or no hypertension. As serum creatinine increases, there is worsening of hypertension and proteinuria too, and most of the studies have shown poor outcome at serum creatinine values >2.5 mg/dL [8,9].

Since the present case was already diagnosed to have minimal change disease based on renal biopsy, there was no indication for a repeat biopsy. Renal biopsy is generally considered safe in pregnancy, however, it is required only when the patient has rapidly progressive renal failure or has symptomatic NS at less than 30-32 weeks of pregnancy [10]. However, there are reports of biopsies done in advanced gestation too.

There is a case reported in the literature of a woman who had relapses of NS in both pregnancies [11]. However, the present case report is unique because NS behaved differently in two pregnancies in the same patient. This patient did not have fertility issues too and conceived even during the lactational amenorrhoea after the first pregnancy.

While in the first pregnancy there was a relapse of NS requiring initiation and maintenance of prednisolone therapy, she was in complete remission throughout the second pregnancy. First pregnancy was associated with severe pre-eclampsia which prompted us to terminate the pregnancy at 35 weeks itself, however, the second pregnancy was associated with well-controlled gestational hypertension alone, allowing the pregnancy to continue until 38 weeks. She required two antihypertensives for a prolonged post-natal period after first delivery and needed none after the second delivery. After the first delivery, the neonate required NICU care for hypoglycaemia in a late preterm baby with intrauterine growth restriction. However, the newborn after second delivery had an uneventful neonatal period. The patient did not have elevated blood glucose values during the first pregnancy despite steroid therapy.

Patients with NS are at an increased risk of thrombotic and thromboembolic events, especially in pregnancy [12]. Patients with membranous nephropathy causing NS are at the highest risk, while all other aetiologies impose a much lesser risk, especially with serum albumin >20 gm/L [12]. We did not use thromboprophylaxis in both pregnancies as the present case was at minimal risk with NS due to minimal change disease and serum albumin well above 20 gm/L; she did not develop any thrombotic complications too. However, she was advised adequate ambulation and managed with close follow-up.

CONCLUSION

Without pre-existing hypertension and renal failure, pregnancy in patients with NS may have favourable outcomes when managed by a multidisciplinary team.

ACKNOWLEDGEMENTS

We thank the patient for consenting to be part of this case report.

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FINANCIAL OR OTHER COMPETING INTERESTS: None.

Date of Submission: **Feb 18, 2018**
Date of Peer Review: **Apr 23, 2018**
Date of Acceptance: **May 11, 2018**
Date of Publishing: **Jul 01, 2018**