(e) ISSN Online: 2321-9599

(p) ISSN Print: 2348-6805

CASE REPORT

MEMBRANOUS NEPHROPATHY IN PREGNANCY- A CASE REPORT AND REVIEW OF LITERATURE

Sushruti Kaushal[1], Poojan Dogra[2], Kapil Malhotra[3], Tanupriya [3], Reena Sharma[1], Anil Kumar[3]

[1]Assistant Professor, [2]Associate Professor, [3]Senior Resident

Department of Obstetrics and Gynaecology, Shri Lal Bahadur Shastri Govt. Medical College, Mandi (H.P.)

ABSTRACT:

Nephrotic syndrome occurs in 0.012-0.025% of all pregnancies. Membranous nephropathy is a major cause of nephrotic syndrome in adults (30-40%). We present a case of idiopathic membranous nephropathy (IMN) diagnosed during pregnancy. Pregnancy was complicated by the development of intrauterine growth restriction of fetus and oligohydramnios. Labour was induced at 36 weeks of gestation because of premature rupture of membranes. Patient delivered a female baby weighing 2 kg. The commonest presentation of idiopathic membranous nephropathy is nephrotic syndrome with preserved renal function. Nephrotic range proteinuria is abnormal for any trimester of pregnancy and needs evaluation by renal biopsy. Mainstay of treatment of IMN during pregnancy are steroids. Immunosupppressants used during pregnancy are cyclosporine and tacrolimus. Anticoagulation during pregnancy and postpartum should be considered.

Key words: Nephrotic, idiopathic membranous nephropathy, pregnancy, proteinuria.

Corresponding Author: Dr Kapil Malhotra, M.B.B.S. MD.(Obstetrics and Gynaecology), Senior Resident, Department of Obstetrics and Gynaecology, Shri Lal Bahadur Shastri Govt. Medical College, Mandi (H.P.), India

This article may be cited as: Kaushal S, Dogra P, Malhotra K, Tanupriya, Sharma R, Kumar A. Membranous nephropathy in pregnancy- A case report and review of literature. J Adv Med Dent Scie Res 2017;5(4):81-83.

Access this article online	
Quick Response Code	Website: www.jamdsr.com
	DOI: 10.21276/jamdsr.2017.5.4.17

INTRODUCTION:

Nephrotic syndrome occurs in 0.012-0.025% of all pregnancies[1]. Membranous nephropathy is a major cause of nephrotic syndrome in adults (30-40%)[2]. Pregnancy and its associated renal physiological adaptive changes unmask underlying renal diseases. Management of pregnancy with nephrotic syndrome requires a multidisciplinary approach and has risk of adverse outcome for both fetus and mother.

CASE REPORT:

34 yrs old Gravida 2 Para 1 presented at 15 weeks of gestation with complaints of pedal oedema and peri-orbital puffiness. Her first pregnancy, 7 yrs back, had been resulted in live birth of a 3 kg male child at term. She did not have hypertension or renal disease during that pregnancy. She had not undergone any medical examinations in the interim period.

On examination, her pulse rate was 90/min and BP was 110/70 mmHg. On urine analysis, she had nephritic range proteinuria(5.4g/24Hrs). Her haemoglobin was 13.9g%. Her serum Urea was 16mg/dl and serum creatinine was 0.5 mg/dl. Her liver functions, serum electrolytes, serum Calcium and serum Phosphate levels were normal. Serum cholesterol was raised to 304mg/dl which could be because of pregnancy or nephrotic syndrome. Renal biopsy was done because of nephrotic range proteinuria which showed diffuse thickening of capillaries with intramembranous mottling. There were no crescents, tufts or necrosed areas but a few hyaline casts were present. A diagnosis of membranous nephropathy was made. There was no evidence on history or clinical examination to suggest secondary membranous nephropathy. ANA, HBsAg, HCV and VDRL were non-reactive. MRI brain was normal. Her Anti-phospholipid A_2 Receptor antibody levels were increased (24.5pu/ml) supporting a diagnosis of primary membranous nephropathy. Obstetric ultrasound showed a live intrauterine fetus with no gross anomalies.

She was started on oral steroids – Tab prednisolone 50 mg/day. Calcium and vitamin D were supplemented. A low sodium diet was recommended. She was started on prophylactic doses of low molecular weight heparin. She responded to steroids and went into partial remission. 24 hour urine protein levels decreased to 624mg/24 hrs at 24 weeks period of gestation. She remained normotensive throughout pregnancy. Intrauterine growth restriction with mild oligohydramnios appeared at 32 weeks of gestation. She was subsequently admitted for maternal and fetal

monitoring. 24 hour urine protein levels increased to 2.4g/24 hrs at 34 weeks of gestation. At 36 weeks of gestation, she had preterm premature rupture of membranes. Labour was induced with misoprostol and she delivered a live female baby weighing 2 kg. During labour she was given 50 mg hydrocortisone iv 6 hourly. In post-partum period, her renal functions were normal and she was normotensive.

DISCUSSION AND REVIEW OF LITERATURE:

The commonest presentation of idiopathic membranous nephropathy is nephrotic syndrome with preserved renal function[3]. Nephrotic range proteinuria is abnormal for any trimester of pregnancy and needs evaluation by renal biopsy. Diagnostic features on renal biopsy include capillary wall thickening, normal cellularity, IgG and C3 along capillary walls on immunofluorescence and subepthelial deposits on electron microscopy. In idiopathic membranous nephropathy (IMN), deposition of IgG4 subclass of IgG is dominant whereas other subclasses dominate in secondary forms of membranous nephropathy[4]. Idiopathic membranous nephropathy(IMN) is an organ specific autoimmune disease and there is increasing evidence to suggest M type Phospholipase A2 receptor as target antigen in IMN[5]. Common secondary causes of membranous nephropathy include systemic lupus, chronic hepatitis-B infection, drugs such as NSAIDS, Gold and Mercury compounds and malignancy. These causes need to be ruled out in every patient with membranous nephropathy using history, examination and appropriate serological and radiological investigations; as was done in our patient.

Patients with membranous nephropathy are divided into three categories based on the model developed using data derived from Metropolitan Toronto Glomerulonephritis registry. Patients with normal creatinine clearance, proteinuria less than 4g/24hrs and stable renal function have low risk of progression to End Stage Renal Disease (ESRD) over next 10 years. Patients with proteinuria 4-8g/24 hrs with stable renal function have 55% probability of developing ESRD in 10 yrs. Patients with proteinuria > 8g/day have 66-80% probability of progressing to ESRD within 10yrs, independent of the degree of renal dysfunction.

Pregnancy in patients with membranous nephropathy is associated with maternal and fetal complications. Iris de Castro et al studied pregnancy outcomes in 26 pregnancies complicated by nephrotic syndrome. Maternal complications included pre-eclampsia in seven, acute kidney injury in six, premature rupture of membranes in two and cellulitis in three[6]. Some studies have shown good neonatal outcomes in patients with nephritic syndrome[7], while others have demonstrated fetal loss rates upto 24-35%. Most of these are attributed to first trimester spontaneous abortions. In a study conducted by Jungers et al that reviewed 43 pregnancies associated with impaired renal function. 5 ended in first trimester abortions and 8 ended in fetal death beyond 20 weeks[8]. In a systemic review of six studies, Lindheimer and Katz concluded that the average live birth rate in patients with membranous glomerulonephritis was 86.3%. Out of 14% losses, 10% were first trimester losses and 4% were second trimester losses.

The presence of hypertension at the time of conception or in early pregnancy is a major factor influencing fetal prognosis , increasing relative risk of fetal loss 10.6 times[9].

Patients with membranous nephropathy should be advised dietary sodium restriction and diuretics should be used to manage oedema.

The Kidney disease –Improving clinical outcomes (KDIGO) clinical practice guidelines for glomerulonephritis published in 2012 suggest that initial therapy of membranous nephropathy should consist of 6 month course of alternating monthly cycles of steroids and oral alkylating agents. The preferred agent is Cyclophosphamide. As alkylating agents are contraindicated in pregnancy, immunosuppressants of choice, if required, are cyclosporine and tacrolimus[10]. Both of these are FDA category C for use in pregnancy. Azathioprine is safe in pregnancy but is not effective in patients with IMN[3].

Venous, systemic and pulmonary artery thrombosis have been reported to occur with increased frequency in nephrotic syndrome. Renal vein thrombosis develops in 25-30% patients with nephritic syndrome while Deep vein thrombosis is seen in 15% patients. The underlying mechanisms of 'thrombophilia' of the nephrotic syndrome are multiple but seem to be related to imbalance of prothrombotic factors, antithrombotic factors and impaired thrombolytic activity[11].As pregnancy is in itself a hypercoagulable state, pregnant female with IMN is at further increased risk and should be given prophylactic anticoagulation during pregnancy and post-partum period.

Long term use of steroids, as is common in patients with autoimmune diseases including IMN, leads to suppression of Hypothalamo-Pituitary- Adrenal axis. Steroid response during periods of stress is blunted and acute stress can precipitate adrenal crisis. Steroid replacement during periods of stress is required to prevent this catastrophe. Labour and delivery require additional steroids in doses of peri-operative steroids recommended for moderate-major surgery[12].ACE Inhibitors can reduce proteinuria and slow progression of renal disease and thus, are preferred agents to treat hypertension in patients with IMN. ACE Inhibitors are contraindicated in pregnancy but Enalapril and Captopril are safe during lactation. In the modification of diet in renal disease study, patients with proteinuria greater than 1g/day had significantly better outcome when BP was reduced to lower target 125/75 mmHg compared to those with higher BP targets.

Patient needs to be kept in strict follow-up in postpartum period for maternal renal functions and proteinuria. Anticoagulation can be continued with warfarin or heparin. ACE Inhibitors can be stared in hypertensive patients.

REFERENCES:

1. Cohen AW, Burton HG. Nephrotic syndrome due to pre-eclamptic nephropathy in a hydatidiform mole and co-existant fetus. Obstet Gynaecol 1979;53:130-134.
2. Julia B. Lewis, Eric G. Nelson. Glomerular Diseases. In: Dennis L. Kasper, Stephen L Hauser, J Larry Jameson, Anthony S Fauci, Dan Congo, Jaseph Loscalzo(eds). Harrison's Principles of Internal Medicine 19th Edition. New York: Mc Graw Hill Education;2015.p.1831-1850.
3. Eknoyan G, Lameire N et al. Idiopathic membranous nephropathy. In: KDIGO clinical practice guideline for Glomerulonephritis. Kidney international Supplements (2012)2,186-197.
4. Kuroki A, Shibata T, Honda H et al. Glomerular and serum IgG subclasses in diffuse proliferative lupus nephritis, membranous lupus nephritis and idiopathic membranous nephropathy. Intern Med 2002;41:936-942.
5. Laurence H Bk, Ramon GB Bonegio, David J Salant. M-type Phospholipase A2 Receptor as Target antigen in Idiopathic Membranous Nephropathy.N Eng J Med 2009 jul 2;361(1):11-21.
6. Iris de Castro, Easterling TR, Bansal N et al. Nephrotic syndrome in pregnancy poses risks with both maternal and fetal complications. IJ. Kint 2016.12.019.
7. S.Abe, Y. Amagasaki, K. Konishi, E. Kato, H. Sakaguchi, S. Iyori. The influence of antecedent renal disease on pregnancy. American Journal of Obstetrics and Gynaecology.1985:153(5);508-514.
8. P.Jungers, D Chauveau, G. Choukroun et al.pregnancy in women with impaired renal function. Clinical nephrology 1997;47(5):281-288.
9. Ope-Adenuga S, Moretti M, Lakhi N. Management of Membranous Glomerulonephritis in pregnancy- A multidisciplinary challenge. Case Reports in Obstetrics and Gynaecology2015http://dx.doi.org/10.1155/2015/839376.
10. Kun S C, Diaz SH. Safety of immunosuppressive drugs in pregnant women with systemic Inflammatory diseases. Arthritis Rheumatol 2014feb66(2):246-249.
11. Glasssck RJ. Prophylactic anticoagulation in Nephrotic Syndrome: A clinical conundrum. J Am Soc Nephrol 18;2221-2225,2007.
12. Elliot D. Clinical guideline for peri-operative Steroid Replacement.2015. NHS Trust.

Source of support: Nil **Conflict of interest:** None declared

-