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A Case of Membranoproliferative Glomerulonephritis Associated with A Hydatidiform Mole

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Abstract

We treated a 54-year-old woman who was suffering from membranoproliferative glomerulonephritis associated with a complete type of hydatidiform mole. The renal manifestations were proteinuria and hematuria. A renal biopsy, performed before gynecologic management, disclosed focal and segmental subendothelial deposits with a proliferation of the mesangial cell and showed irregularly thickened capillary loops by light and electronmicroscoy. Genralized edema, proteinuria and hematuria were completely recovered by suction and curettage of the hydatidiform mole with prophylactic chemotherapy. The clinical manifestation of earlier presented 3 cases have been the nephrotic syndrome. The common feature of them was a complete remission of the nephropathy after the removal of the hydatidiform mole. The relationship between the hydatidiform mole and glomerulonephritis remains unresolved at present. But we concluded that the hydatidiform mole might be a cause of glomerulonephritis in this case.

Key Words: Glomerulonephritis, hydatidiform mole

INTRODUCTION

During normal pregnancy, the upper limit of urinary protein excretion ranges from 200 to 300 mg per day. Nephrotic syndrome in pregnancy is very rare and its incidence is 0.012−0.025% in all pregnancies.[1] The most common cause is preeclampsia associated with preeclamptic nephropathy. Preeclampsia may have a relation to the molar pregnancy. Twelve% of molar pregnancies are associated with preeclampsia.[2] To our knowledge, 3 cases of nephrotic syndrome associated with a molar pregnancy have been reported.[3-5] In this communication, a case of membranoproliferative glomerulonephritis associated with complete type of hydatidiform mole is described.

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CASE REPORT

A 54-year-old woman was referred to our section of nephrology because of generalized edema and voiding difficulty. Up until 2 months prior to our consultation, she was well until she first developed epigastric pain. At that time she noticed a generalized edema and complained of voiding difficulty. Two years prior to admission, a steroid had been administered for 6 months due to vitiligo in our hospital and urinalysis had showed no proteinuria and hematuria. Her obstetric history was $G_6P_6L_6D_0A_0$ and others were not remarkable.

On examination, her blood pressure was 150/90 mmHg with a regular heart rate of 90 beats per minute. No lymphadenopathy was present. A pretibial pitting edema (2 positive) was noted. The hemoglobin level was 8.5 g/dl, the white blood cell count was 5.18×10^9/L, and the platelet count was 108×10^9/L. The prothrombin time and partial thromboplastin time were within normal limits. The Wintrobe erythrocyte sedimentation rate was 30 mm/hr. Blood chemistry revealed total serum protein 5.7 g/dl, albumin 3.3 g/dl, AST 65 U/L, ALT 72 U/L, triglyceride 72 mg/dl, cholesterol 127 mg/dl, BUN 18.8 mg/dl, creatinine 0.9 mg/dl with normal serum electrolyte. The serum Ig A was 169 mg/dl, Ig G 757

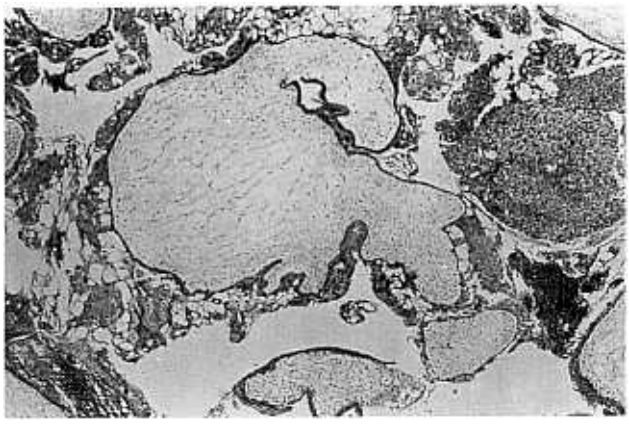

Fig. 1. Light micrograph of the intrauterine content. Multiple large villi show stromal edema and marked trophoblastic proliferation (H&E, ×100).

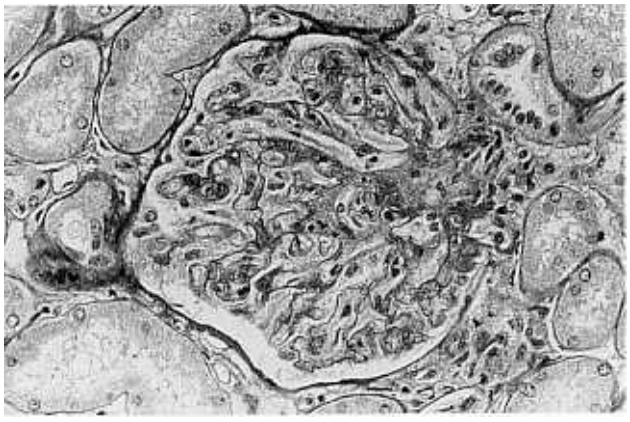

Fig. 2. Light micrograph of a glomerulus from this case. The glomerulus shows a slight increase of mesangial matrix and proliferation of mesangial cell. The capillary loops are irregularly thickened and reveal double line (PAS, ×200).

mg/dl and Ig M 56.1 mg/dl. The serum C3 and C4 were 75.8, 16.8 mg/dl, respectively. The antithrombin III was 22.2 mg/dl. The urinalysis was reported as showing 150 mg/dl of proteinuria and 10−29 red blood cells per high-power field. In a 24-hour specimen of urine, protein was 574 mg, microalbumin 464 mg and creatinine 683 mg. The tests for antistreptolysin O, ANA, VDRL, hepatitis B surface antigen and antibody, hepatitis C virus antibody and rheumatoid factor were all negative. The chest roentgenogram and abdominal ultrasonogram taken on admission were normal. There was no evidence of heart or liver disease. A pelvic ultrasonogram for palpable mass on the lower abdomen showed vesicular sonographic

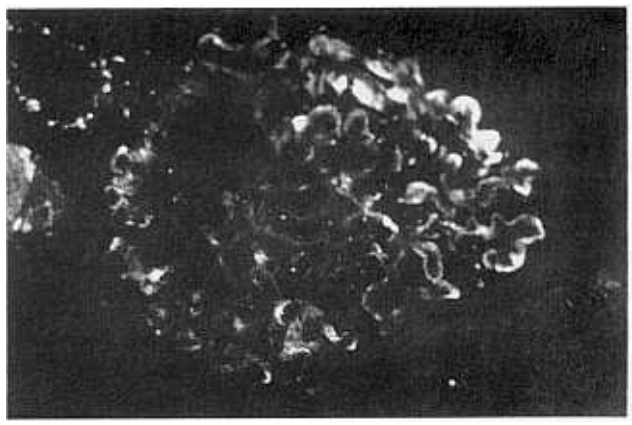

Fig. 3. Immunofluorescence micrograph demonstrates an IgM deposit in the mesangium and capillary loops (IF, ×400).

pattern with 14×8.6 cm size and suggested the hydatidiform mole. The pregnancy test was positive and the serum β-HCG was 1,975,000 mIU/mL. A renal biopsy was performed, and suction and curettage was brought to completion 3 days later.

A specimen evacuated from the intrauterine cavity consisted of a multiple thin walled grape-like, pale pink, soft to friable mole tissue and was consistent with the diagnosis of "hydatidiform mole" (Fig. 1). Light microscopy of the kidney demonstrated a mesangial cell hyperplasia and slight widening of mesangial matrix. The capillary loops were irregularly thickened and showed a double-lined appearance. AFOG stain showed focal and segmental subendothelial and paramesangial fuscinophilic deposits. Focal minimal interstitial mononuclear cell infiltration was noted. The tubules were relatively normal. The blood vessels were unremarkable (Fig. 2). Immunofluorescent findings were minimal deposits of Ig M, C4 and fibrinogen in the mesangium and minimal deposits of C3 in the tubules, blood vessels and Bowman's capsule (Fig. 3). By electronmicroscopy, two glomeruli were noted. A glomerulus demonstrated conglomeration by a subendothelial electron dense deposit and another glomerulus showed relatively normal architectures with a focal mesangial increase of the matrix and a small subendothelial electron dense deposit. The basement membrane thickness was normal. There was a diffuse loss of foot processes and a villous transformation (Fig. 4). The pathologic findings suggested membranoproliferative glomerulonephritis.

One month later, the serum β-HCG was 1086

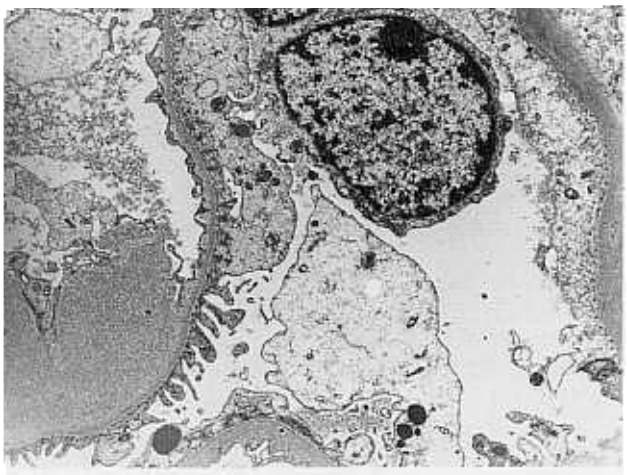

Fig. 4. Electron micrograph of a portion of a glomerulus shows relatively preserved glomerular architecture with a focal increased mesangial matrix and subendothelial electron dense deposit (× 4,000).

mIU/mL and then she took a prophylactic Kür chemotherapy (Actinomycine-D 500 μg, 5 times). Urinalysis revealed no proteinuria, but the RBC was 5−9 per high-power field. Four months later, the serum β-HCG was below 2 mIU/mL with no proteinuria and hematuria. The generalized edema had also disappeared. The serum C3 was 111.6 mg/dl and C4 29.0 mg/dl. She had completely recovered from the renal manifestations. Two years later, there was no evidence of recurrence or metastasis of the hydatidiform mole.

DISCUSSION

In this old patient with a generalized edema, a palpable mass noticed on the lower abdomen and pregnancy test was positive. She was compatible with hydatidiform mole by pelvic ultrasonography which is a reliable and sensitive technique for the diagnosis. The hydatidiform mole developed in old age and serum β-HCG over 100,000 mIU/mL showed poor prognosis.[6] She had a poor prognostic factor and then treated with Kür chemotherapy regimen for prophylaxis. There was no evidence of recurrence or metastasis of the mole and she remained in complete remission of the nephrotic syndrome.

Generally, the upper limited range of urinary protein excretion, 200 to 300 mg per day, was informed as normal during pregnancy.[7] Percentage of preeclamptic nephropathy is about 80% in nephrotic syndrome during pregnancy. Other cases occur because of membranous nephropathy, focal glomerulosclerosis, minimal change nephropathy, diabetic nephropathy, systemic lupus erythematosus, and other renal diseases.[7]

The renal pathologic features in preeclamptic nephropathy are bloodless glomerular enlargement and the narrowing the capillary lumen due to swelling of the endothelial, mesangial and epithelial cells with an expansion of the mesangial matrix. The glomerular capillary walls may be thickened but a hypercellular change rarely occurs.[8-10] Akhtar's case[3] was a preeclamptic nephropathy associated with a transitional mole with a coexistent fetus. Cohen's case[4] was not performed renal biopsy but the nephrotic syndrome was clinically related to a preeclamptic nephropathy. In his case, the hydatidiform mole was incomplete type coexisting fetal tissue. Komatsuda[5] reported an older patient revealed a membranoproliferative glomerulonephritis like lesion by renal biopsy. His case was a nephrotic syndrome associated with a complete type of hydatidiform mole. Prior to this report, there was a similar case reported in a Korean journal.[11] In our case, the hydatidiform mole was a complete type and the renal biopsy was compatible with membranoproliferative glomerulonephritis. The precise pathogenetic relationship between the hydatidiform mole and glomerulonephritis is not clear, because the reported cases were extremely rare. The production of immune complexes and the activation of intravascular coagulation by the hydatidiform mole are the supposed pathogenetic mechanisms.[3] As in previously reported cases,[3-5] our patient remained renal symptom free for 2 years after the removal of the tumor. These several interesting cases linking the pathogenesis of the glomerulonephritis directly to the gestational trophoblastic disease provide a challenge for future research.

In summary, we concluded that the hydatidiform mole might be a cause of the glomerulonephritis in this case.

REFERENCES

1. Marcus SL. The nephrotic syndrome during pregnancy. Obstet Gynecol Surv 1963;18:511-42.
2. Curry SL, Hammond CB, Tyrey L, Creasman WT, Parker

RT. Hydatidiform mole. Obstet Gynecol 1975;45:1-8.
3. Akhtar M, Bunuan H, Mcdonald DJ. Nephrotic syndrome due to preeclamptic nephropathy associated with a transitional mole with coexistent fetus. Am J Clin Pathol 1981;76:109-12.
4. Cohen AW, Burton HG. Nephrotic syndrome due to preeclamptic nephropathy in a hydatidiform mole and coexistent fetus. Obstet Gynecol 1978;53:130-4.
5. Komatsuda A, Nakamoto Y, Asakura KI, Yasuda T, Imai H, Miura AB. Case report: Nephrotic syndrome associated with a total hydatidiform mole. Am J Med Sci 1992;303: 309-12.
6. Berokowitz RS, Goldstein DP. Gestational Trophoblastic disease. In: Berek JS, Adashi EY, Hillard PA, editors. Novak's Gynecology. 12th ed. Baltimore: Williams & Wilkins; 1996. p.1261-82.
7. Paller MS, Ferris TF. The kidney and hypertension in pregnancy. In: Brenner BM, editor. The kidney. 5th ed. Philadelphia: Saunders; 1996. p.1731-63.
8. Roy First M, Ooi BS, Jao W, Pollak VE. Preeclampsia with the nephrotic syndrome. Kidney Int 1978;13:166-77.
9. Roy First M, Pollak VE. Pregnancy and renal disease. In: Schrier RW, Gottschalk CW, editors. Diseases of the kidney. 5th ed. Boston: Little Brown; 1993. p.2287-310.
10. Fisher KA, Luger A, Spargo BH, Lindheimer MD. Hypertension in pregnancy: Clinical-pathological correlations and remote prognosis. Medicine 1981;60:267-76.
11. Cheong HJ, Lee TW, Ahn JH, Ihm CG, Kim MJ, Hong JK, et al. A case of membranoproliferative glomerulonephritis associatd with H-mole. Korean J Nephrol 1994; 14:917-23.