Membranous glomerulopathy associated with placental site trophoblastic tumour: a case report

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Gestational trophoblastic disease is rarely associated with nephrotic syndrome. The most common renal complication in pregnant females is pre-eclamptic hypertensive nephropathy. Most cases have not been biopsied and thus the specific nature of renal involvement could not be ascertained. Only a few case reports exist in which gestational trophoblastic disease associated with nephrotic syndrome has been histologically documented [1–7]. We report a rare association of membranous nephropathy with gestational trophoblastic disease. Such an association has been documented in only one previously published report [1] to the best of our knowledge. We have also reviewed the literature available in cases of nephrotic syndrome occurring in patients of gestational trophoblastic disease in an attempt to explain the pathogenesis between the two conditions.

Case report

A 28-year-old female presented with periods of amenorrhoea followed by heavy bleeding for 14 months and generalized anasarca for 2 months. She had undergone medical termination of pregnancy 18 months previously. On examination there was marked pallor, severe anasarca, ascites and bilateral pleural effusion. Her blood pressure was within normal limits. The laboratory investigations showed a moderate anaemia (haemoglobin of 8 g/dl), and normal platelet count and coagulation profile. Renal function tests were within normal limits with blood urea of 13 mg/dl (4.64 mmol/l) and serum creatinine of 0.8 mg/dl (70.72 μmol/l). However, there was evidence of significant proteinuria (urinary proteins 2.8 g/24 h). Serum proteins were low (4.7 g/dl), albumin was 2.2 g/dl, and serum cholesterol was raised at 270 mg/dl (6.98 mmol/l). Serum complement level was within normal range (79.3 mg/ml). Tests for hepatitis B surface antigen, and antibodies against hepatitis C antigen and human immunodeficiency virus were negative. Tests for antinuclear antibody, anti double stranded DNA antibody, and rheumatoid factor were also negative. Serum human chorionic gonadotrophin (hCG) level was moderately elevated at 210 mIU/ml. Ultrasound abdomen revealed a thickened endometrium. An endometrial curettage was performed. The vaginal bleeding was not checked by the curettage. Therefore, the patient was prepared for total abdominal hysterectomy.

The hysterectomy specimen showed a nodular growth in the myometrium. The overlying endometrium was shaggy. The borders of the growth were well defined. The tumour on cut section was soft in consistency and tan in colour with areas of haemorrhage.

Sections from formalin fixed paraffin embedded tissue were stained for haematoxylin and eosin (H&E) stain and examined. The microscopic appearance of the tissue obtained from the endometrial curettage and hysterectomy specimen were similar. The tumour was primarily composed of a population of intermediate trophoblastic cells. The cells were polyhedral with a high nuclear cytoplasmic ratio and dense eosinophilic to amphophilic cytoplasm (Figure 1). Occasional cells showed cytoplasmic vacuoles. Nuclei were round to oval with vesicular chromatin. Some binucleate and multinucleate cells were also seen. The tumour cells were seen to invade into the myometrium singly and in sheets. Some cells showed multinucleate hyperchromatic nuclei (syncytiotrophoblasts).
Few vessels showed invasion of their walls by the tumour in the form of deposits of fibrinoid material and trophoblastic cells. Some areas of haemorrhage and necrosis were also identified within the tumour.

Sections were immunohistochemically examined for human placental lactogen (HPL) and human chorionic gonadotrophin (hCG) (pre-diluted Dako Cytomation A 0137 Ig fraction and A 0231 Ig fraction, respectively). These tumour cells showed strong cytoplasmic positivity for HPL and weak positivity for hCG. The diagnosis of placental site trophoblastic tumour (PSTT) was made.

Five days post-operatively, a renal biopsy was performed to investigate the cause of proteinuria. On light microscopy (H&E stain), the biopsy showed enlarged glomeruli with capillary loops displaying a stiff opened out appearance (Figure 2A). No proliferative activity was identified. PAS stain and silver methenamine staining demonstrated uniform thickening of the glomerular capillary walls (Figure 2B). However, no spikes were identified. Immunofluorescence study with fluoresceinated antisera to C3 and IgM revealed fine granular deposition of C3 (3+) (Figure 2C) and IgM (1+) along with focal deposition of IgG and IgA. Fibrinogen was negative. In view of the thickened basement membrane displaying linear deposition of C3 and IgM, the diagnosis of early membranous glomerulopathy (MGN) with PSTT was arrived at.

A post-operative beta hCG was performed two weeks after hysterectomy and was found to be within normal limits (<5 mIU/ml). The patient was put on diuretics, ACE inhibitors and haematinics and responded well. The generalized anaasarca subsided and proteinuria disappeared. She has been under regular follow-up for the last one and half years and is free of clinical symptoms.

**Discussion**

MGN is one of the commonest causes of nephrotic syndrome in adults. One-fourth of the cases of MGN are due to secondary causes like drugs, infections, tumours and connective tissue disorders such as systemic lupus erythematosus. Various studies have reported malignancy to be a cause of MGN in about 10% of cases [8,9]. Most of these cases were associated with epithelial malignancies.

Only a few case reports exist in which nephrotic syndrome occurring secondary to gestational trophoblastic disease has been documented [1–7]. Table 1 attempts to compile the review of literature available in this regard. In most of these cases, renal involvement was documented by examining 24 h urinary protein excretion, serum protein levels and lipid profile. Renal biopsy was occasionally performed.

Young et al. [2] reported two cases of nephrotic syndrome complicating placental site trophoblastic tumour. They described a classical renal lesion in the form of occlusive eosinophilic deposits in the capillary lumina of the glomeruli, staining brightly with fluoresceinated antisera to IgM and fibrinogen. Alvarez et al. [6] reported a similar lesion. However,
we did not encounter any such deposits in the renal biopsy in our case.

Altiparmak et al. [1] reported a case of MGN occurring in association with choriocarcinoma. In our case as well as in the above mentioned three cases, the appearance of features of nephrotic syndrome occurred concurrently with the symptoms related to uterine malignancy. This supports the interpretation that the tumour played a role in the pathogenesis of the renal disorder. The renal symptoms completely disappearing after hysterectomy further confirms the association.

The pathogenesis of glomerular abnormalities observed in the present case cannot be definitely elucidated. However, the immunofluorescence findings of deposition of IgM in the subendothelial space reflect the presence of antibodies bound to specific antigens. The nature of these antibodies could not be elucidated. These could have formed against tumour antigen deposited in the subendothelial space of glomeruli or may be formed against some alloantigen in the tumour which cross reacted with glomerular basement membrane antigens.

The fact that the clinical and biochemical features of nephrotic syndrome disappeared after hysterectomy provides conclusive proof that the membranous glomerulonephritis was secondary to the PSTT.

In conclusion, this case report serves to highlight the correlation between membranous nephropathy and placental site trophoblastic tumour and also highlights the renal complications of gestational trophoblastic disease.

Conflict of interest statement. None declared.

References


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