

Case Report

Lupus nephritis associated with placental site trophoblastic tumor: A case report and review of the literature

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Introduction

PSTT usually follows a normal pregnancy or an abortion, and can be cured by surgery and chemotherapy (Scully and Young, 1981). The association of PSTT with kidney diseases is very rare. There is a single recorded case of thrombotic microangiopathy (TMA) (Mazzucco et al., 2011) and another of membranous glomerulonephritis (Batra et al., 2007; Bologna et al., 1994). Only 2 other cases of PSTT and kidney lesions have been reported. Both of these were described fully by Young et al. as showing a distinctive glomerular lesion (Young et al., 1985). We describe a case of lupus nephritis (LN) that occurred with PSTT. Kidney biopsy showed diffuse global proliferative LN. This unusual findings must be interpreted appropriately to achieve the correct diagnosis.

Case report

A 31-year-old female presented with amenorrhea lasting since full-term normal delivery 19 months previously and generalized anasarca for more than 1 month prior to presentation. One month before admission she had developed progressive edema of her face, lower

extremities. Upon examination there was mild pallor, facial butterfly erythema, anasarca and ascites. Her blood pressure was 140/90 mmHg. A diagnosis of nephrotic syndrome (proteinuria with 24-h urine specimen, >7 g/day) with normal kidney function was made (serum creatinine, 50 μmol/L and blood urea nitrogen 7.4 mmol/L). Her hemoglobin concentration was 117 g/L. Blood chemistry tests revealed levels of total serum protein of 42.2 g/L (normal ranges, 60–85 g/L), albumin 26 g/L (normal ranges, 35–51 g/L), triglyceride 1.96 mmol/L (normal ranges, 0.45–1.70 mmol/L), antistreptolysin-O 278 IU/ml, C4 complement 0.0716 g/L (normal ranges, 0.12–0.36 g/L). Tests for IgG type titer of antinuclear antibody were 1:320 (normal ranges, <1:40), but tests for C3 complement, anti-dsDNA antibody, rheumatoid factor, and C-reactive protein were within normal ranges.

Because of the persistence of edema, hematuria and nephrotic proteinuria, a kidney biopsy was performed to confirm the diagnosis of glomerulopathy. Light microscopy revealed the renal cortex containing 30 glomeruli. None was sclerotic. There were diffuse and global endothelial and mesangium proliferation, widespread wireloops, thickened basement membranes with focal and segmental subendothelial aggregates and some duplication formation. The tubule epithelial cells were granular and showed vacuolar degeneration. The capillary loops were even and thin. There was no evidence of pathologic changes in the interstitium. Immunofluorescence showed a full-house immunofluorescence pattern, immunoglobulin G (++) , IgM (++) , IgA (+++), C3 (+++), and C1q (+++) along the glomerular basement membrane. Pathologic findings suggested diffuse global proliferative LN (Class IV-G, active index 11 scores) (Fig. 1). Induction therapy using glucocorticoids and cytotoxic drugs was started and lasted for almost 1 year. However, nephrotic syndrome (NS) didn't improve, as indicated by the persistently elevated levels of the 24-h urine protein, which ranged from 2.76 g to 4.81 g and renal function became poor with the blood urea nitrogen elevation exceeding normal limits.

Because the patient's amenorrhea had persisted for more than 19 months with evidence of some uterine enlargement, serum human chorionic gonadotropin (β-hCG) levels were checked, which was elevated at 95.4 mIU/mL. Gynecological examination revealed a uterus of about 14 weeks gestation. An abdominopelvic magnetic resonance imaging (MRI) scan showed uterine expansion with a short T1 and long T2 signal. The uterine junction zone and myometrium were unclear, and the diffuse vascular flow void in myometrium and bilateral parametrium showed significant enhancement (Fig. 2). There was a

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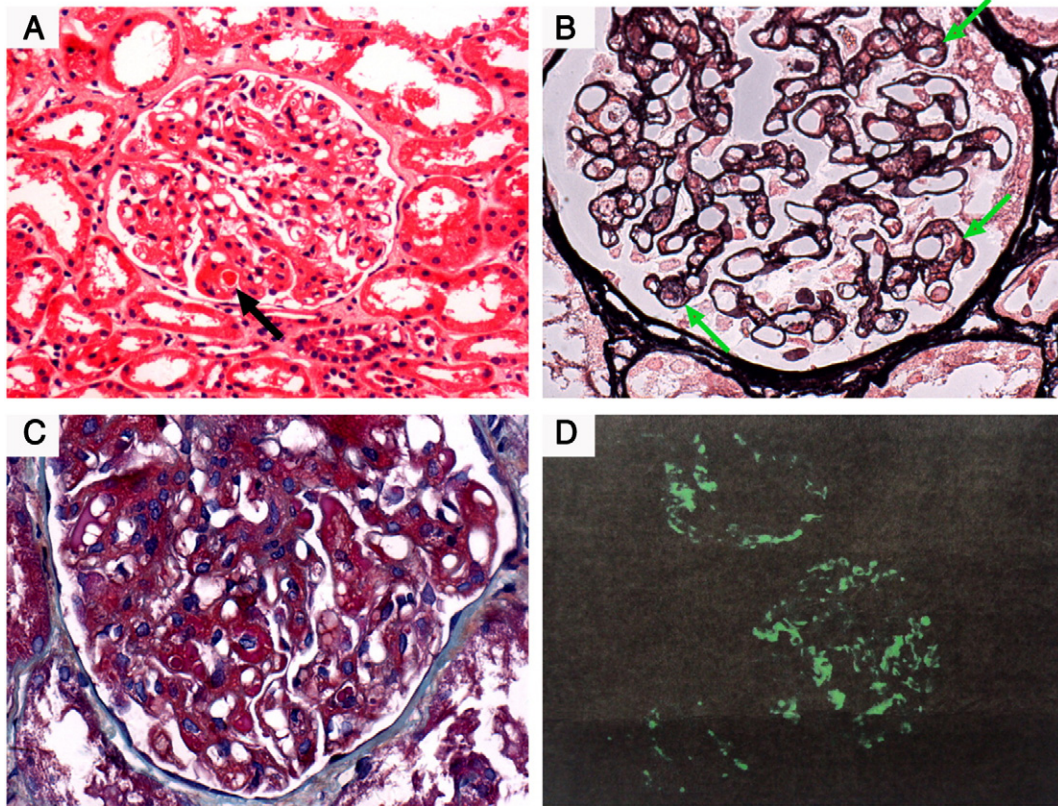


Fig. 1. (A) H&E staining shows increases in the number of glomerular cells, and visible thrombosis (arrow) (200 \times). (B) Periodic acid-Schiff staining shows a glomerulus with diffuse endothelial and mesangium proliferation (arrow) (400 \times). (C) Masson staining shows thickened basement membranes with focal and segmental subendothelial aggregates (400 \times). (D) Immunofluorescence photomicrograph displaying diffuse deposition of C1q along basement membranes (200 \times).

little fluid in the pelvic cavity. Given the slightly elevated β -hCG level, enlarged uterus of about 14 weeks gestational size and diffuse lesions of the uterus by MRI scan, PSTT was highly suspected. But she was not suitable for chemotherapy with poor kidney function. A total abdominal hysterectomy with a bilateral salpingo-oophorectomy was performed. Pathologic investigation showed typical features of PSTT deeply infiltrating the whole layer of uterine corpus wall to the serosa (Young et al., 1985). Sections were immunohistochemically evaluated for β -hCG and human placental lactogen (HPL). These tumor cells

showed strong cytoplasmic positivity for HPL and negative for β -hCG. Because of the patient's poor kidney function, she was not given chemotherapy.

Two weeks later, a post-operative β -hCG reduced to 0.5 mIU/ml, which is just within normal limits (WNL, <5 mIU/ml). The quantity of the 24-h urine protein decreased to 0.40 g/L (normal ranges from 0 to 0.20 g/L). One month after operation the β -hCG level of this patient was WNL with no proteinuria. Additional follow-up visits for the subsequent 15 months showed no evidence of recurrence or metastasis of

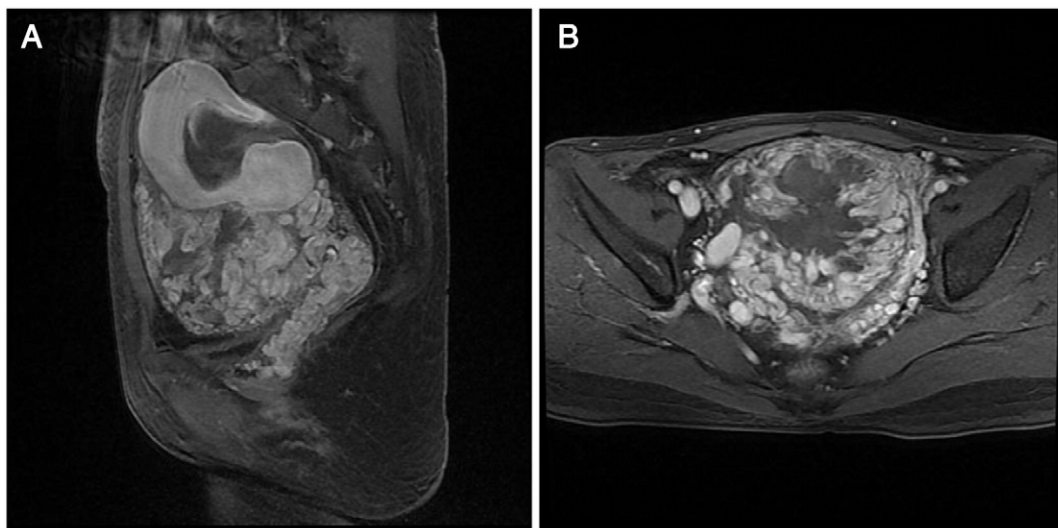


Fig. 2. Pelvic MRI scan showing uterine cavity expansion. (A) Scan showing diffuse vascular flow void in myometrium and (B) bilateral parametrium with a significant enhancement.

Table 1
Review of literature of cases of renal lesions associated with GTD.

Diagnosis of renal lesion	GTD	Author	Renal biopsy performed	No.	Year
Thrombotic microangiopathy	PSTT	Mazzucco Mazzucco et al. (2011)	Yes	1	2011
Membranous glomerulonephritis	Invasive mole	Yang Yang et al. (2010)	Yes	1	2010
Membranous glomerulopathy	PSTT	Batra Batra et al. (2007)	Yes	1	2007
Membranous glomerulonephritis	Choriocarcinoma	Altiparmak Altiparmak et al. (2003)	Yes	1	2003
Membranoproliferative glomerulonephritis	Hydatiform mole	Komatsuda Komatsuda et al. (1992)	Yes	1	1992
Occlusive eosinophilic deposit in capillary lumen	PSTT	Young Young et al. (1985)	Yes	2	1985

GTD: Gestational trophoblastic disease, PSTT: Placental site trophoblastic tumor.

PSTT. The patient currently remains free of clinical symptoms of LN. Tests for C3, C4, anti-dsDNA antibody, antinuclear antibody, rheumatoid factor, and C-reactive protein were all within normal ranges.

Discussion

Gestational trophoblastic disease (GTD) is used to refer to a variety of gynecological tumors arising from the trophoblastic cells, including hydatidiform mole (complete or partial), choriocarcinoma, PSTT, and ETT. The malignant transformation of trophoblastic tissue can cause a paraneoplastic syndrome (Yang et al., 2010), which were thought to be mediated by an immune response to malignant cells. Sometimes, the clinical manifestations from the paraneoplastic syndrome are noted prior to the diagnosis of malignancy. A number of different types of glomerular disease, nephrotic or nephritic, may be associated with malignancy (Jhaveri et al., 2013). Effective treatment of the tumor generally leads to remission of the glomerular injury in these situations (Lefaucheur et al., 2006).

The association of renal lesions and GTD is very rare. Only a few case reports have reported the association of NS with GTD (Altiparmak et al., 2003; Batra et al., 2007; Komatsuda et al., 1992; Mazzucco et al., 2011; Yang et al., 2010; Young et al., 1985), which were summarized in Table 1. In these cases, membranoproliferative glomerulonephritis (Komatsuda et al., 1992) has been found to be associated with hydatidiform mole, and membranous glomerulonephritis has been observed with invasive mole and choriocarcinoma (Altiparmak et al., 2003; Yang et al., 2010). For PSTT, there has been one reported case of TMA and another of membranous glomerulonephritis (Batra et al., 2007; Mazzucco et al., 2011). Only 2 other cases of PSTT and kidney lesions have been reported (Young et al., 1985). These glomerular lesions have also been observed in the present patient, although similar features may be observed under different circumstances. The present case suggests a diagnosis of a variant of LN. This conclusion is supported not only by light microscopy but also by immunohistochemistry findings. Conclusive evidence of LN comes from clinical and laboratory evidence. According to diagnostic criteria for SLE by the American College of Rheumatology in 1997, LN must be considered first. The mechanism may involve an immunologic process associated with LN, specifically the presence of complement and immunoglobulin on immunofluorescence and large subendothelial and smaller subepithelial and mesangial deposits, as indicated by light microscopy. Because there are several types of glomerulonephritis reported in association with epithelial and hematologic neoplasia, a relationship with the PSTT may exist (Jhaveri et al., 2013).

In the present case, LN was considered secondary to PSTT, because this patient had presented with NS having amenorrhea for 19 months

without a clear etiology. She had no previous history of systemic lupus erythematosus. She had received induction therapy with glucocorticoids and cytotoxic drugs for almost 1 year until PSTT was discovered when the clinical symptoms of LN didn't resolve with medical therapy. The fact that the clinical and biochemical features of nephrotic syndrome disappeared completely after the hysterectomy provides strong evidence that LN was secondary to PSTT, although the pathogenesis of this disease process is still unclear at this point.

In conclusion, this case provides a highlight of the correlation between LN and PSTT and also highlights the nephritic complications of GTD.

Written informed consent was obtained from the patient for the publication of this case report and the accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Conflict of interest statement

We declare that we have no conflict of interest.

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