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Case Report

Nephritic syndrome complicating placental site trophoblastic tumour: a case report and review of the literature

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ABSTRACT

Placental site trophoblastic tumour (PSTT) is rarely associated with renal disorders and has been described only a few case reports so far. Authors report the case of a 27-year-old female who presented with abnormal uterine bleeding post vaginal delivery and developed nephritic syndrome, thereafter. Detailed evaluation revealed increased levels of human chorionic gonadotropin (beta subunit)-β-hCG, and imaging findings suggesting gestational trophoblastic disease. The patient underwent hysterectomy, which led to immediate remission of proteinuria, ascites and hypertension. Thus, the diagnosis was confirmed as PSTT and, following treatment, her β-hCG became normal and proteinuria gradually disappeared. This type of association of gestational trophoblastic disease with renal disorders is a rare entity. A thorough review of the literature was also performed by us, in order to explain the pathophysiology as well as the relation between these conditions so that these unusual findings can be interpreted appropriately to achieve the correct diagnosis.

Keywords: β-hCG, Nephritic syndrome, Gestational trophoblastic disease, Hysterectomy

INTRODUCTION

PSTT is a rare subtype of gestational trophoblastic neoplasms (GTNs) accounting for approximately 1% to 2% of all GTNs. It arises from placental intermediate trophoblasts (ITs), which are responsible for embryo implantation and is generally diagnosed within a few days to months after the event-labour/ miscarriage/ abortion.[1,2] According to the literature, this association of PSTT and renal disorders is very rare as evident from the scarce data of just 8 cases available.[3-10] In all these cases, hysterectomy led to the remission of the nephrotic syndrome, except for one patient who succumbed to the complications of PSTT. We report the case of a patient with nephritic syndrome in whom, an association between nephritic syndrome and PSTT was found.

CASE REPORT

A 27-year-old P1L1 female with spontaneous conception and uneventful antenatal course underwent caesarean section in April 2022, in view of foetal distress. She delivered an alive and healthy female baby weighing 2.2 kg with Apgar 9/9. Following delivery, she had continuous bleeding per vaginum on and off soaking 1 pad/day for 6 months. This was followed by 3 months of amenorrhea which was again followed by continuous spotting and abdominal distension. With these complaints, she visited a local hospital where her urine pregnancy test was performed which was positive. On examination, she had pallor, anasarca and blood pressure was also high. On abdominal examination there was ascites with no mass palpable and vaginal examination was suggestive of approximately 8-10 weeks anteverted uterus with fullness in bilateral fornices.

Investigations

The laboratory investigations were suggestive of moderate anaemia (Hb-10 g/dl) with a normal coagulation profile and platelet count. The renal function tests were also within normal limits with a serum creatinine of 0.6 mg/dl

and blood urea of 28 mg/dl. However, urinalysis results showed that glucose was 1+, protein was 4+, and erythrocytes were 3+, with an albumin to creatinine (A:C) ratio 2212 mg/gm and urinary proteins of 2.4g in 24 hours.

Serum human β-subunit of chorionic gonadotrophin (β-hCG) level was initially elevated at 1844 mIU/ml. In addition, serum proteins as well as serum albumin were low (4.6 g/dl and 2.2 g/dl, respectively). Serum cholesterol was normal. Serum complement levels were also normal. Viral markers including HbsAg, anti-hepatitis C antibodies and HIV were negative. Tests for rheumatoid factor, antinuclear antibodies, anti-double stranded DNA antibodies, antineutrophil cytoplasmic antibodies were also negative.

Laboratory findings demonstrated features consistent with renal involvement, including proteinuria, hypoalbuminemia, and elevated urine albumin-to-creatinine ratio, along with an increased β-hCG level are summarized in Table 1. Ultrasonography was suggestive of moderate ascites and mild right pleural effusion along with an ill-defined mass in the uterine cavity with normal sized bilateral kidneys. Her contrast-enhanced MRI was suggestive of a bulky uterus with enhancing endometrial mass of size 6.7×7.1×6.4 cm with myometrial infiltration with central and peripheral vascularity (Figure 1).

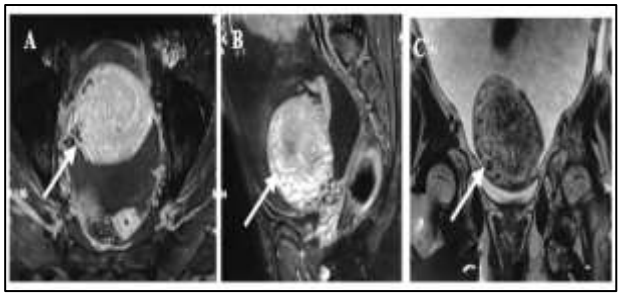

Figure 1: MRI images (A) T1 post-contrast axial. (B) T1 post-contrast sagittal and (C) T2 FS coronal showing the uterine mass (marked with white arrows).

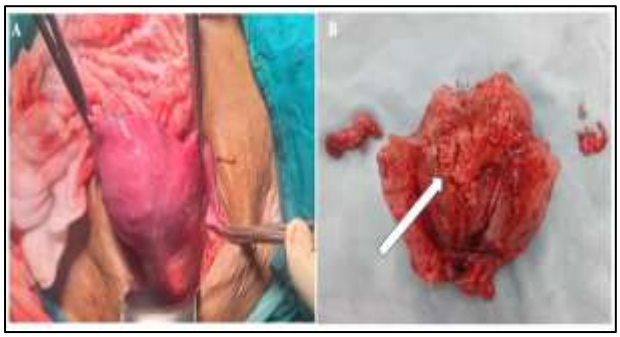

Figure 2: Intraoperative and gross specimen findings. (A) Intraoperative finding of an enlarged uterus (12 weeks size). (B) Gross specimen following hysterectomy showing 6×6 cm growth arising from posterior wall >50% myometrial invasion and calcified area in the growth.

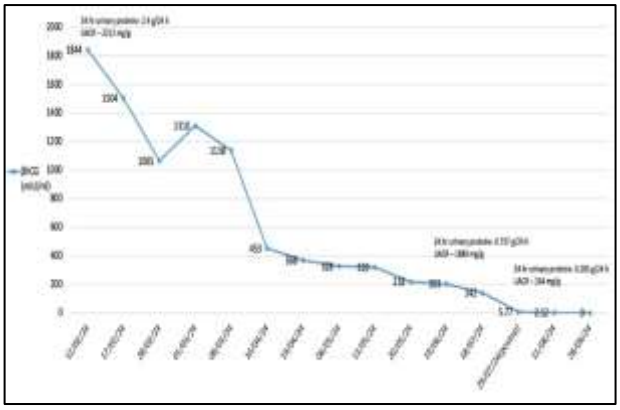

Figure 3: β-hCG and proteinuria trend.

Trend of serum β-hCG (mIU/ml) over time with corresponding 24-hour urinary protein levels and urine albumin-to-creatinine ratio (UACR) during follow-up. The graph illustrates a steady decline in β-hCG, paralleled by improvement in proteinuria parameters. Ascitic fluid analysis revealed high SAAG, low protein ascites and was negative for tuberculosis and malignant cells. The serial serum β-hCG levels trend was decreasing, so we decided to monitor her while evaluating the cause of ascites and proteinuria. Interestingly, her proteinuria showed spontaneous regression (proteinuria of 737 mg/24 h, UACR–1880 mg/gm) and β-hCG decreased to 142 IU/ml. Furthermore, her BP records also improved not requiring antihypertensives.

Treatment

Subsequently, follow-up imaging studies were suggestive of similar findings and plateau low levels of β-hCG. Thus, a suspicion of chemo resistant trophoblastic tumour was elicited. Total abdominal hysterectomy and bilateral salpingectomy was performed. Intraoperatively, approximately 300 cc of straw-coloured ascitic fluid was present. The uterus was enlarged to 12 weeks' size, soft in consistency, with bilateral tubes and ovaries appearing healthy. No evidence of disease was noted elsewhere in the abdomen, and pelvic lymph nodes were not enlarged (Figure 2A).

A pathological examination of the hysterectomy specimen showed an infiltrative greyish white tumour measuring 6×6×3 cm reaching up to the lower uterine segment and occupying >50 % of myometrial thickness (Figure 2B). The tumour was primarily composed of a population of large polygonal, round to oval pleomorphic cells with abundant amphophilic cytoplasm having hyperchromatic, pleomorphic nuclei and conspicuous nucleoli.

Few cells also showed binucleation and multinucleation. Tumour showed necrosis in few areas however occasional mitosis accounting up to 1-2/10 HPF is noted. These cells were immune-positive for MUC4, CD10 and GATA 3 but were immune-negative for p63. Ki67 labelling index was

approximately 15-20%. The features were those of placental site trophoblastic tumour.

Outcome and follow-up

A post-operative β-hCG performed immediately and 1 month after hysterectomy was found to be 5.77 and <1.20 mIU/ml respectively. The generalized anasarca subsided and proteinuria decreased to 285.6 mg/day and urine ACR to 264 mg/g. She has been on follow-up for the last two months and remains asymptomatic. Serial monitoring demonstrated a progressive decline in serum β-hCG levels with corresponding improvement in proteinuria parameters (Figure 3).

Table 1: Laboratory findings at presentation.

Parameter	Patient result	Reference range	Remarks
Hemoglobin (g/dl)	10	12.0-15.0	Moderate anemia
Serum creatinine (mg/dl)	0.6	0.5-0.9	Within normal limits
Blood urea (mg/dl)	28	17-49	Within normal limits
Serum total protein (g/dl)	4.6	6.4-8.3	Low
Serum albumin (g/dl)	2.2	4.0-4.9	Low
Serum cholesterol (mg/dl)	110	<200	Within normal limits
Serum complement levels C3 (mg/dl)	102	88-201	Within normal limits
Serum complement levels C4 (mg/dl)	28	15-45	Within normal limits
Serum β-hCG (mIU/ml)	1844	<5 (non-pregnant)	Elevated
Urinalysis: Glucose	1+	Negative	Abnormal
Urinalysis: Protein	4+	Negative	Abnormal
Urinalysis: Erythrocytes	3+	Negative	Abnormal
Albumin-to-creatinine ratio (mg/g)	2212	<30	Elevated
24-hour urinary protein (g/24h)	2.4	<0.14	Elevated
Viral markers (HBsAg, anti-HCV, HIV)	Negative	Negative	Normal
Autoimmune profile (RF, ANA, anti-dsDNA, ANCA)	Negative	Negative	Normal

Table 2: Clinical-pathological features of cases presenting with renal diseases in relation to trophoblastic tumours.

Authors	Age (in year)	Presentation	Proteinuria (g/day)	S-Alb (g/dl)	S-Cr (mg/dl)	Max b-HCG (mIU/ml)	Therapy	Outcome
Zhao et al[3]	28	10 months post-partum	Unknown	1.93 - 2.36	0.49 - 1.01	1983	Hysterectomy	Remission
Sawamura et al[4]	32	6 months post-partum	4 g/day	2.1	0.46	289.2	Chemotherapy→ Hysterectomy	Remission
Xiao et al[5]	31	19 months post-partum	>7 g/ day	2.6	0.57	95.5	Hysterectomy	Remission
Mazzucco et al[6]	42	days after incomplete abortion	12.3 g/day	2.1	72*	1685	Methotrexate→ Hysterectomy→ EMACO	Remission
Batra et al[7]	28	18 months after abortion	2.8 g/day	2.2	0.8	210	Hysterectomy	Remission
Young et al[8]	30	11 months postpartum	>4 g/day	2.1	ND	413	Hysterectomy →Chemotherapy	Died
Eckstein et al[9]	21	24 months post molar pregnancy	5 g/day	2.4	0.68	362	Chemotherapy →Hysterectomy	Remission
Lely et al[10]	38	4 months pregnant	>4 g/day	ND	0.62	1000	Hysterectomy	Remission
This case	27	8 months post-partum	2.4 g/day	2.2	0.6	1844	Hysterectomy	Remission

ND=not described *Cr clearance (ml/min)

DISCUSSION

In general, trophoblastic tumours are very rare and develop either after a completed pregnancy or may be reported after few days up to many years (2 decades in some cases) after the pregnancy or hydatidiform mole. In our case, suspicion of PSTT was roused 8 months post-delivery. Interestingly, patient had proteinuria, ascites and hypertension. This has been described in similar cases. (Young RH). Trophoblastic tumours complicated by renal involvement resembling a paraneoplastic syndrome have been previously described. The clinicopathological features of placental site trophoblastic tumour (PSTT) from eight reported cases, together with the present case, are summarized in Table 2.[3-10]

The age of these patients ranged from 21 to 42 years. Most of them presented with normal renal function but with proteinuria in nephrotic-range and hypoalbuminemia. In almost all of these cases, the involvement of the kidney was discovered by examining serum protein levels, lipid profile and 24-hour urinary protein excretion. Renal biopsy was performed only in a few cases. In all of these reported cases, management was in the form of hysterectomy, which was performed within a few months of onset of symptoms and which led to the remission of the nephrotic syndrome. Immunohistochemistry supported the diagnosis of PSTT, with tumour cells showing positivity for MUC4, CD10, and GATA3, and negativity for p63. The Ki-67 proliferation index was 15-20%, consistent with the typically low mitotic activity of PSTT.

Additional markers such as Mel-CAM and HLA-G could not be performed due to unavailability at our centre, which we acknowledge as a limitation. In this case also, the symptoms related to uterine malignancy were concurrent with the appearance of features of nephritic syndrome, thus, supporting the interpretation that the tumour is actually responsible for the occurrence of the renal dysfunction. The proteinuria disappeared in all cases after successful therapy, except for 1 patient who died of sepsis.[4] The disappearance of biochemical as well as clinical features of the renal dysfunction after hysterectomy is strongly suggestive of a paraneoplastic etiology secondary to the tumour.

Further, it must be known that many autoimmune diseases can also be an early manifestation of an occult malignancy. Although the reasons are not exactly known, it has been postulated that the breakdown of self-tolerance against the tumour antigens lead to immune activation which further leads to the formation of auto-antibodies. These auto-antibodies cause a syndrome that is indistinguishable from the “true” SLE (systemic lupus erythematosus). Another hypothesis states that the toxins that are produced by the tumour cells could also trigger the autoimmune reaction.

Renal involvement in PSTT is rare, with mechanisms likely immune-mediated. Proposed pathways include immune complex deposition, antigenic cross-reactivity, and cytokine-induced glomerular injury. Cytokines such as interleukin-6 and TNF-α may increase glomerular permeability and inflammation.[13] Aberrant antigen expression by tumour cells could also trigger autoantibody production with renal effects. Though speculative in PSTT, these mechanisms are consistent with other paraneoplastic glomerulopathies. The resolution of proteinuria after tumour resection in our case supports a paraneoplastic origin.

CONCLUSION

In conclusion, this case report highlights the correlation between PSTT and renal diseases. The discovery of similar cases in future, is required for getting more conclusive evidence. In general, these types of symptoms could be predictive of malignancy and thus, help in early diagnosis and treatment, when recognized as paraneoplastic manifestations. This case emphasizes the need for coordinated care across specialties, with oncologists, nephrologists, and radiologists working together to address rare tumour-related systemic effects. Enhancing clinician awareness of such atypical presentations can contribute to earlier recognition and better outcomes. Ongoing, long-term surveillance is also essential to track disease progression and ensure timely detection of recurrence.

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