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An unusual case of rapidly progressing glomerulonephritis in pregnancy; “triple positivity” or a co incidence?

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ABSTRACT

Background: Renal failure in pregnancy is usually due to acute kidney injury and very uncommonly due to rapidly progressing glomerulonephritis (RPGN). We describe here a case of RPGN in the first trimester of pregnancy.

Case Presentation: A 26 years old female patient in first trimester of pregnancy presented with RPGN. Investigations revealed dual serological positivity of anti-neutrophil cytoplasmic antibody (ANCA) and anti-glomerular basement membrane antibody (anti-GBM). The biopsy showed crescentic glomerulonephritis with linear with IgG deposition on GBM as well as mesangial IgA deposition. Despite aggressive therapy with cyclophosphamide and plasma exchange she continued to be dialysis dependent and developed end-stage renal disease.

Conclusions: RPGN is an uncommon cause of renal failure in pregnancy. While the dual ANCA and anti-GBM are common in RPGN and this concurrent occurrence is well-known, however, the association of ANCA and IgA nephropathy has been described rather uncommonly. This rare case has positivity of all three in pregnancy.

Implication for health policy/practice/research/medical education:

Rapidly progressing glomerulonephritis (RPGN) is an uncommon cause of renal failure in pregnancy. While the dual anti-neutrophil cytoplasmic antibody (ANCA) and anti-glomerular basement membrane antibody (anti-GBM) are common in RPGN and this concurrent occurrence is well-known, however, the association of ANCA associated glomerulonephritis and IgA nephropathy has been described rather uncommonly. This rare case has positivity of all three in pregnancy.

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1. Introduction

Rapidly progressing glomerulonephritis (RPGN) is an uncommon cause of renal dysfunction in pregnancy. RPGN with the dual anti-neutrophil cytoplasmic antibody (ANCA) and anti-glomerular basement membrane antibody (anti-GBM) are common and known. The association of ANCA and mesangial IgA deposition has been described rather uncommonly (1). This rare case has positivity of all three in first trimester of pregnancy.

2. Case Presentation

A 26-year-old woman, second gravida presented with 12 weeks of amenorrhea, generalized body swelling,

and decreased urine output for 2 weeks. No history of gross hematuria, hemoptysis, pain abdomen, fever, joint pain or skin rashes. The first pregnancy was uneventful and she had a 3-year-old apparently healthy child. On examination blood pressure was 150/100 mm Hg and she had mild pallor, facial puffiness and bilateral pedal edema. The urine examination revealed albumin 3+, plenty of RBCs/hpf, no casts. Other reports revealed Hb; 8 g/dL, total leucocyte count; 11 800/mm³ (N70%, L26%, M3% and E1%), platelets; 200 000/mm³, peripheral smear; normocytic normochromic, no schistocytes or abnormal cells. Serum creatinine; 8.69 mg/dL, urea; 96 mg/dL and uric acid was 3 mg/dL. Liver function tests, serum

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iron studies and B12 and folate levels were normal. Baseline renal function test was not available and history suggestive of chronic kidney disease was absent. Ultrasonography of the abdomen revealed single live intrauterine gestation of 12 weeks and normal kidneys with no evidence of hydronephrosis. In view of severe renal dysfunction, the fetal and maternal risks of continuing the pregnancy were explained and a decision to terminate the pregnancy was taken. The medical termination of pregnancy was done after two sessions of hemodialysis. Reticulocyte count and serial serum LDH levels showed no evidence of hemolysis. X-ray of chest was normal. As the clinical suspicion of proliferative glomerulonephritis was high she was given injection methyl prednisolone 500 mg pulse. Further evaluation showed p-ANCA (perinuclear - anti neutrophil cytoplasmic antibodies) positive with raised anti MPO titers (45.62 RU/mL [<20 /mL – Normal]). ANA was negative and the complement levels were in normal range. She was given injection cyclophosphamide 500 mg and started on plasma exchange (PEX) suspecting pauci-immune glomerulonephritis. She continued to be dialysis dependent with a urine output of about 200 mL/d. Anti-GBM titers sent after ANCA report also came positive (125.62 RU/mL [<20 RU/ml – Normal]). Repeat anti-GBM antibody levels came negative after seven sessions of PEX. High resolution contrast CT of the chest did not reveal lung involvement. Kidney biopsy was performed 1 week after PEX. The renal biopsy revealed crescentic glomerulonephritis (Figure 1) with mesangial IgA deposition (Figure 2) along with linear deposition of IgG along GBM on immunofluorescence (Figure 3). Hence a final diagnosis of dual anti GBM disease with ANCA positivity with IgA nephropathy (IgAN) was made. Immunosuppression and PEX was withdrawn in view of 100% glomerular involvement on biopsy with features of chronicity and no response to the initial therapy. She continued to be hemodialysis dependent at 24 weeks from diagnosis.

3. Discussion

The patient in our case presented with features of RPGN in first trimester of pregnancy. She had no evidence of any extra renal features. In view of normal C_3 and C_4 , IgA nephropathy was a possibility but further investigations showed positivity to p-ANCA (anti-MPO) and anti-GBM antibodies.

Vasculitides are commoner in men than women and tend to occur in an older age group, so they rarely complicate pregnancy (2). Our patient also had anti-GBM disease which is even more uncommon in

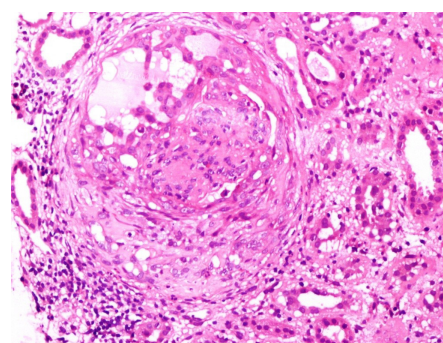


Figure 1. Hematoxylin and eosin stain showing fibrocellular crescent and areas of necrosis in the glomerulus

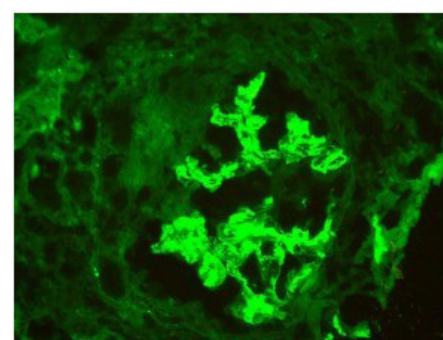


Figure 2. Immunofluorescence stain showing mesangial IgA deposition.

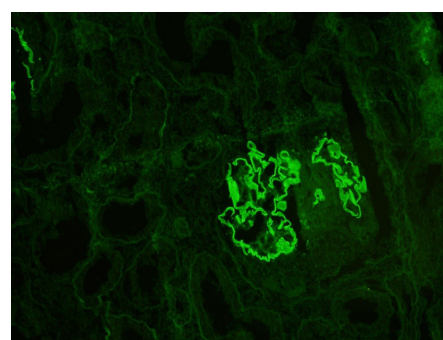


Figure 3. Immunofluorescence stain showing linear deposition of IgG along the glomerular basement membrane.

pregnancy and is associated with poor maternal and fetal outcomes. The reported time of presentation varies from 13 to 28 weeks of gestation (3).

Another unusual feature of this case was the presence of IgA on renal biopsy. While dual ANCA and anti-GBM is not uncommon (other than in the setting of pregnancy) the concurrence of mesangial IgA deposits with p-ANCA is uncommon (1). This entity is different from the IgA-ANCA positivity. Less is known about the prognosis of this ‘dual positivity’ (ANCA serology and mesangial IgA deposits). Some of the available reports suggest a rather guarded prognosis while others suggest a favorable prognosis

(3,4). Though IgAN itself can present with crescentic glomerulonephritis the deposition of IgAN in severe cases is mesangial as well as over capillary walls (5).

4. Conclusions

This case has a curious conglomeration of antibodies in pregnancy. The one possible reason for the coexistence of dual ANCA and anti-GBM disease with IgAN could be due to the higher incidence of milder forms of IgAN (which remained asymptomatic) which was superimposed by the dual ANCA and anti-GBM disease. The possibility of an interrelated pathogenesis however cannot be completely ruled out.

Authors' contribution

SD and VT were involved in case management and manuscript preparation. MP first identified the case. CM, TDB, AB, KB and AR helped in literature search. RP has been a mentor and also provided critical insights while manuscript preparation. All authors read, revised, and approved the final manuscript.

Conflicts of interest

The authors have no conflicts of interest to declare.

Informed consent

A written informed consent was obtained from the patient to report this case.

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The management of the case was carried out at IPGMER, a tertiary care government hospital and all the expenses of treatment and investigations were born by the institute as a part of patient care. No other funding sources.

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