Case Report

Good pasture's syndrome diagnosed in postpartum period: acute kidney injury severe enough to warrant renal transplant

Abstract

Objective: Goodpasture's syndrome (GPS) is the association of pulmonary haemorrhage with acute kidney injury (AKI) resulting from injury by auto-antibodies. Its de novo occurrence in pregnancy is extremely rare with only few cases reported. High risk of mortality and lack of consensus in treatment warrants its reporting.

Case report: A 24 year old primigravida, with no history suggestive of renal disease, presented to us in her third trimester with anuria. She was initially managed as sepsis or preeclampsia related AKI. However, even after delivery there was no improvement in kidney function with hemodialysis and she developed hemoptysis. Renal biopsy made a diagnosis of Anti-Glomerular Basement Membrane disease. With careful multi-disciplinary treatment, she delivered a live born baby and was discharged under stable condition on hemodialysis, currently awaiting a kidney transplant.

Conclusion: This case highlights that the current management for GPS should be revised to improve the outcome of AKI. Also, it determines how important it is for obstetricians to consider whether a pregnancy should be terminated to improve the outcome of AKI in pregnant patients with GPS.

Keywords: acute kidney injury, goodpature's syndrome, renal transplant, anti-glomerular basement membrane disease, hemodialysis

Volume 7 Issue 4 - 2021

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Received: May 02, 2021 | **Published:** July 16, 2021

Abbreviations: Anti-GBM, anti-glomerular basement membrane; AKI, acute kidney injury; ANA, antinuclear antibody; ANCA, antineutrophil cytoplasmic antibody; INR, International normalized ratio; GPS, goodpasture's syndrome; Pr-AKI, pregnancy-related acute kidney injury; RPGN, rapidly progressive glomerulonephritis; SGOT, serum glutamic oxaloacetic transaminase; SGPT, serum glutamic-pyruvic transaminase

Introduction

Anti-glomerular basement membrane (anti-GBM) antibody disease is associated with rapidly progressive glomerulonephritis (RPGN),[1] end-stage kidney disease and death.[2] Named after its discoverer in 1919,[3] Goodpasture's syndrome (GPS) is the presence of pulmonary haemorrhage with glomerulonephritis caused by an autoantibody to alveolar and glomerular basement membrane antigens.[4] Acute kidney injury (AKI) occurs in ~1:15000–1:20000 pregnancies annually.[5] Although a number of causes have been well established for pregnancy related AKI, there is limited data regarding de novo glomerulonephritis, and in particular de novo GPS in pregnancy. Incidence of GPS in the non-pregnant individuals is <1 case/1,000,000.[6] The etiology of GPS remains unknown; but, its occurrence following environmental exposures including hydrocarbon fumes, metallic dust or tobacco smoke has been reported.[7] GPS occurs due to antibody and T-lymphocyte reactivity to the NC1 domain of the α3 chain of type IV collagen.[8] Given the implications of systemic vasculitis and its management in maternal and fetal outcomes, literature on this topic is essential.

Case report

24 year old primigravida presented to our institute at 31+4 weeks period of gestation with complaint of anuria for 3 days. She was married for 1 year, had conceived spontaneously and was supervised adequately during this pregnancy with uneventful first and second trimesters.

Baseline investigations in pregnancy included a B positive blood group, not reactive for HIV, Hepatitis B and C and syphilis. Urine routine microscopy was normal and she had mild anemia with hemoglobin of 10.1 gm%. Early trans-abdominal ultrasound had confirmed her dating while second trimester scan had ruled out any malformations in the fetus (Figure 1).

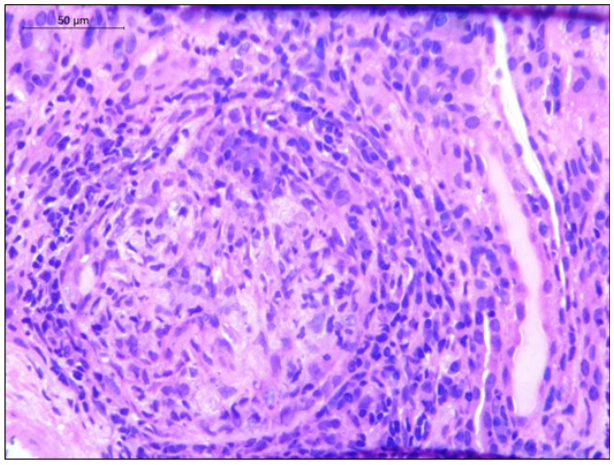

Figure 1 Glomerulus (H&E stain) showing cellular crescent (extracapillary proliferation) with ruptured Bowmans capsule(arrow) and periglomerular infilammatory infiltrate.

At about 28 weeks of gestation, she developed fever which lasted for 5 days. She was hospitalized, managed as typhoid with intravenous

antibiotics and discharged under stable conditions. At 31 weeks of gestation, she had multiple episodes of vomiting and anuria of 1 day, was readmitted to a private hospital, where catheterization confirmed anuria. Renal function tests showed a blood urea of 165 mg/dL and serum creatinine of 7.2 mg/dL. An ultrasound for fetal wellbeing at this time showed a fetus of about 30+2 weeks weighing about 1542gm with Amniotic Fluid Index of 11cm and a posterior, upper placenta. There was no significant past or family history and she was referred our institute for further care.

At admission to our institute, she was well oriented, afebrile, with pallor but no pedal edema, icterus or anasarca. Her vitals showed a pulse rate of 86/min, blood pressure in left arm of 140/90 mmhg, respiratory rate of 16/min with no abnormalities detected in the respiratory and cardiovascular systems. Uterine height corresponded to 28-30 weeks with a live fetus in cephalic presentation. Urine examination showed traces of albumin, nil sugar and 25-30 pus cells/hpf. Her hemoglobin was 6.2gm/dl, total leucocyte count was 25,200 per microliter, platelets were 2.26 lakh per microliter, normal liver functions, with grossly deranged RFTs in the form of blood urea of 185 mg/dL and serum creatinine of 13.7 mg/dL but normal blood gases. She had only 40 ml urine output in the 24 hours following admission. Ultrasound kidney and urinary bladder showed bilateral raised renal echogenicity with kidney sizes of 9.5cm and 10.3cm. A provisional diagnosis of Acute Kidney Injury secondary to Sepsis or Pre-eclampsia was made. A multi-disciplinary team made the decision for renal replacement therapy along with intravenous broad spectrum antibiotics (Ceftriaxone and Metronidazole). Biophysical profile for the fetus scored 8/8 (Figure 2).

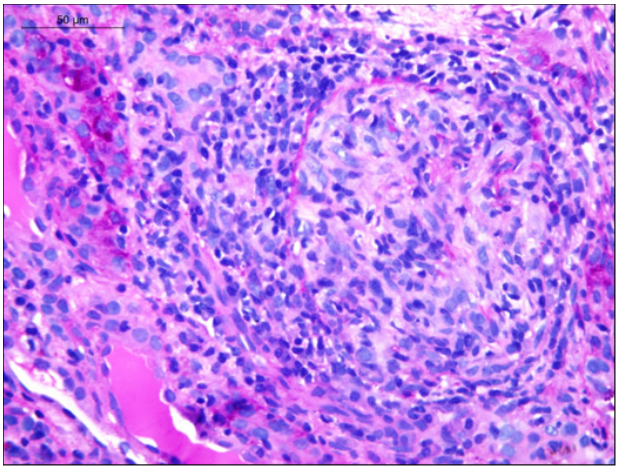

Figure 2 Glomerulus (PAS stain) showing cellular crescent (extracapillary proliferation) with ruptured Bowmans capsule (arrow) and periglomerular infilammatory infiltrate.

After first cycle of hemodialysis, she developed tachycardia, tachypnea, bilateral coarse crepts in lungs with oxygen saturation falling down to 70%. Endo-tracheal intubation was done and she was placed on mechanical ventilation. Antibiotics were hiked to Inj Piperacillin-Tazobactam and she was given a second cycle of hemodialysis with one unit of packed red blood cells. 2D echo showed mild mitral regurgitation, mild tricuspid regurgitation, global left ventricular hypokinesia, ventricular ejection fraction of 30-35%. A diagnosis of renal disease related dilated cardiomyopathy was made and she was started on diuretics. She was managed in the intensive care unit where her antibiotics were further hiked up to intravenous Meropenem and Vancomycin. She continued to be anuric and kept on renal replacement therapy till she was extubated at 32+2 weeks of gestation (Figure 3).

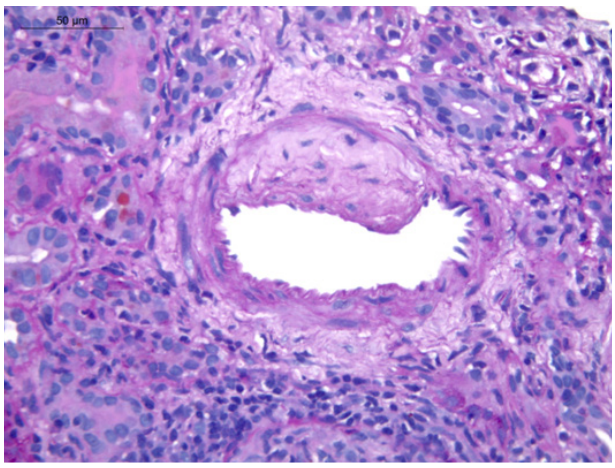

Figure 3 Blood vessels showing organised and recanalised thrombus .Tubules showing rbc casts and pus cell casts (PAS stain).

4 doses of Injection Dexamethasone 6 mg 12 hours apart were given for fetal lung maturation. At 32+4 weeks she had two episodes of hemoptysis with a fall in oxygen saturation and she was kept on non-invasive ventilation. Chest X ray was suggestive of bilateral alveolar infiltrates. She continued to improve clinically on hemodialysis but biochemical parameters were suggestive of microangiopathy with evidence of hemolysis, a decreasing hemoglobin, deranging liver function tests and increasing serum uric acid. A decision was taken to terminate the pregnancy by a multi-disciplinary team as pre-eclampsia induced acute kidney injury was considered the most likely diagnosis. Induction of labor was done after cervical ripening; however after 4 hours of Pitocin infusion, she de-saturated requiring emergency hemodialysis. As cervical findings did not improve, she underwent LSCS under general anaesthesia delivering a live born girl of 1265gm with normal APGARs. After delivery she continued to be anuric and was kept on alternate day hemodialysis. 4 days after delivery, a contrast enhanced computerized tomography of kidneys and bladder showed bilateral renal parenchymal disease and no evidence of renal cortical necrosis (Figure 4).

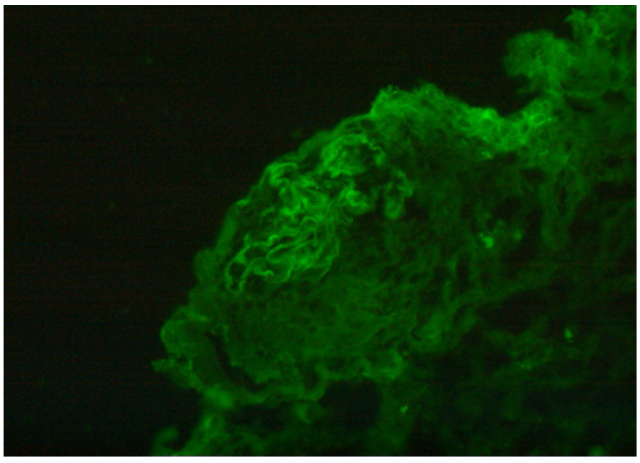

Figure 4 Immunofluorescence showing linear positivity in the capillary walls for IgG.

With no improvement in urine output and continued requirement for hemodialysis, decision was taken for renal biopsy 20 days after delivery, which showed acute pyelonephritis, anti-glomerular basement membrane glomerulonephritis of the crescentic variety and vascular thrombotic microangiopathy, thus making a diagnosis

of Anti-GBM disease and correlating the episodes of hemoptysis, a diagnosis of the rare Goodpasture's syndrome.

After 31 days of hospital stay, she was discharged with a serum creatinine of 3.8 and nil urine output. She remained afebrile throughout her stay. On Follow-up, she was on bi-weekly hemodialysis with urine output of 50-100 ml/day. Further investigations such as c-ANCA, p-ANCA were negative, complement C3 was normal, complement C4 was elevated, ANA and Glomerular Basement Membrane IgG Antibody were found to be negative.

Considering the advanced stage of her disease, a multi-disciplinary team concluded that the usual treatment of choice of repeated plasmapheresis and immune-suppressants was unlikely to be effective. So decision was made to spare her the clinically significant risks of aggressive treatment and give supportive care and eventual renal transplantation.

Discussion

Anti-GBM disease is an immune complex, small vessel vasculitis.[9] The disease is characterized by the development of antibodies directed against an antigen intrinsic to the glomerular basement membrane and shared by the alveolar basement membrane. When these anti-GBM antibodies bind to the basement membrane, they activate the classical pathway of the complement system and start a neutrophilic inflammation that results in a crescentic glomerulonephritis.[9] Anti-GBM disease associated with both glomerular and alveolar capillaries is labelled as Goodpasture's disease, which generally produces a rapidly progressive glomerulonephritis that, despite modern treatment, results in renal failure or death in greater than two thirds of patients.[9]

Anti-GBM disease of pregnancy is uncommon with its incidence being restricted to case reports. Crescent formation is the histopathologic hallmark of Anti-GBM disease with almost 95% of patients having evidence of crescent formation on kidney biopsy and in 80% of these patients more than 50% of glomeruli will be affected.[10] The proportion of crescents has been observed to correlate strongly with the degree of renal impairment at presentation.

Based on the various case reports, be it postpartum or ante partum, anti-GBM disease that presents during or after pregnancy is typically severe enough to cause oliguric renal failure. Treatment of anti-GBM disease causing rapidly progressing glomerulonephritis generally consists of plasma exchange, high-dose steroids, and cytotoxic agents such as cyclophosphamide. It is unusual to have renal recovery if kidney failure is severe enough to require dialysis to maintain electrolyte equilibrium and euvolemia.

Thomson et al.,[11] performed a systematic review to identify maternal, pregnancy and fetal outcomes in de novo anti-GBM disease in pregnancy. Data from eight patients were derived from seven case reports and one unpublished case. Most (6/8) patients presented after the first trimester. Markedly elevated serum creatinine was reported in 5 of the 8 cases while serum anti-GBM titer was elevated at presentation in 6 of 7 cases where it was performed. When hemodialysis was required antepartum (5/8), renal function recovery to independence of renal replacement was unlikely (2/5). While pulmonary involvement was common (5/8) with chest X-ray commonly (3/4) showing evidence of pulmonary hemorrhage, no permanent damage was reported (0/8). Renal biopsy was performed in most (7/8) cases and every kidney biopsy was diagnostic for anti-GBM disease (7/7). Immunosuppressive therapy was given in all 8 patients and in 4/8 during pregnancy, corticosteroids were used. Cyclophosphamide was used in some patients during pregnancy (2/8) and postponed to postpartum period in some (3/8). The majority of cases ended in livebirths (6/8) although prematurity (6/6), intrauterine growth restriction (2/6), small for gestational age (4/6) and complications of prematurity (1/6) were common. When anti-GBM levels were tested in the living newborn, they were detectable (2/5), but no newborn renal or lung disease was reported (0/6). Complications in pregnancy included gestational diabetes (3/8), hyperemesis gravidarum (2/8) and preeclampsia (2/8).

We treated our patient with supportive therapy and hemodialysis, deciding against aggressive immunosuppression considering the severity of her disease. As renal biopsy was deferred till 3 weeks after delivery, diagnosis was delayed and anti-GBM antibodies were found to be negative after they were tested almost a month after the onset of the disease. Nevertheless biopsy findings were diagnostic and with careful renal replacement therapy, fatality could be avoided and our patient was discharged with a live baby while awaiting a kidney transplant.

Conclusion

The prognosis of this disease is good if the disease is identified promptly and the treatment is started efficiently. A careful coordination of several specialities is required in the management of good pasture's syndrome. This case highlights that the current management for GPS should be revised to improve the outcome of obstetric AKI. Also, it determines how important it is for obstetricians to consider whether a pregnancy should be terminated to improve the outcome of AKI in pregnant patients with GPS.

Acknowledgments

None

Conflicts of interest

The authors have no conflict of interest to declare

Funding

None.

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Citation: Veeramalla SR, Arora A, Thakur G, et al. Good pasture's syndrome diagnosed in postpartum period: acute kidney injury severe enough to warrant renal transplant. *Int J Pregn & Chi Birth.* 2021;7(4):93–96. DOI: 10.15406/ipcb.2021.07.00235