**Title**: Favourable Pregnancy Outcome in a Patient with Granulomatosis with Polyangiitis with Renal Insufficiency

**Author:** Dr. Arpana Verma, Dr. Sarita Rajbhar, Dr.(Prof) Sarita Agrawal, Dr. Pushpawati

**Institution:** All India Institute of Medical Sciences, Raipur

**Introduction**: Granulomatosis with Polyangiitis (GPA), previously known as Wegener’s Granulomatosis (WG) is an idiosyncratic clinico-pathological disease, characterized by necrotizing granulomatous vasculitis of the upper and lower respiratory tract, pauci-immune segmental necrotizing glomerulonephritis, and small vessel vasculitis.

The aetiology of GPA remains unidentified, while evidence supports an Autoimmune cause. Presence of Antineutrophil cytoplasmic antibodies (ANCA) has been established in most patients with active disease. Treatment consists of Immunosuppressive drugs, essentially Cyclophosphamide (CYC) in combination with High-dose Corticosteroids.

The peak incidence of the disease is in the 4th and 5th decades, and that makes the association of GPA with pregnancy rare. We describe a case of successful term pregnancy outcome in a patient with known GPA.

**Case Summary**

22 year, Gravida 2 Para1 Living 1 with 35 weeks of gestation with previous 1 Lower segment cesarean section (LSCS) was referred to our department owing to 1 year diagnosis of GPA with nephritic syndrome. Her disease course started as painless skin lesions over upper and lower limbs, on & off bilateral flank pain with few episodes of syncopal attack. On evaluation, she was found to be hypertensive and Antihypertensive treatment (Amlodipine and Losartan) was started. Few months later she developed hemoptysis and breathing difficulties for which she was admitted under intensive care unit, evaluated for autoimmune cause, P-ANCA was found to be positive, her renal function test (RFT) was impaired, chest x-ray was abnormal, based on above findings, diagnosis of ANCA associated vasculitis(AAV) with Pneumonia with Acute kidney injury was made. Skin Biopsy was taken from new lesions over lower limb. However histopathological report of skin biopsy had no features of vasculitis. She received pulse therapy of injection Methyl Prednisolone 500mg for 3 days and injection CYC 500mg for 2 doses, given 2 weeks apart , to which the patient responded well and was discharged on oral Azathioprine (AZA) and Prednisolone on tapering doses and Antihypertensives were continued. 10 months later, she conceived during partial remission phase and was continued on AZA and Amlodipine, patient herself stopped medications at around 30-32 weeks, later at 35 weeks she was referred to AIIMS nephrology unit in view of nephritic syndrome and AZA was restarted and was sent to OBGYN outpatient department for further evaluation and obstetric management. She was admitted in view of high risk pregnancy, her blood pressure was found to be normal. ANCA was repeated and was negative, Growth scan was suggestive of Fetal Growth Restriction, investigations showed raised Blood Urea Nitrogen, Albumin Creatinine Ratio, serum urea and creatinine. Dexamethasone was given for fetal lung maturity. LSCS was done at 37 weeks in view of previous 1 LSCS and worsening renal profile with outcome being live female baby of birth weight 2.05 kg with APGAR of 10 in 1 min & 5 min. Post op period was uneventful and was discharged on day 10 on oral AZA. Presently Mother and Baby both are doing well.

**Discussion:** GPA is now a well-recognized clinical entity in India. Prevalence among female population has been seen in the Indian scenario.

The Diagnosis of GPA is made on the basis of American College of Rheumatology criteria and recently, a modified class which, in addition to the original four criteria (nasal or oral inflammation, an abnormal chest radiograph, urinary sediment and granulomatous inflammation on biopsy) also incorporates a positive serum enzyme immunoassay for antibodies to proteinase-3. Diagnosis can be made if at least two of these five criteria are present.

ANCA are a sensitive and specific marker for ANCA-associated systemic vasculitis. Using indirect immunofluorescence, two prime fluoroscopic patterns can be identified: a diffuse cytoplasmic staining (C-ANCA), and a perinuclear/nuclear staining (P-ANCA). ANCA levels are useful to monitor disease activity. A significant rise in titers, or the reappearance of ANCA, is alarming for the clinicians and calls for intense patient monitoring.

 Cutaneous lesions are found in 50% of patients but may be the presenting symptoms in up to 10% of case. There is no single lesion specifically associated with the disease. Skin lesions are usually indicative of an active systemic disease and are typically located on the lower extremities. Topical steroids are the commonest treatment modality in use. Surgery is only required in cases of severe tissue damage due to fibrosis or necrosis. In our case, the disease started as multiple painless pin head sized lesions over upper and lower limbs which later increased in size (approx 5\*5cm), became ulcerated and healed on its own, forming scar. (figure1)

Pulmonary involvement was seen in 49–84% of cases manifesting as cough, hemoptysis and dyspnoea. Pulmonary nodules are the most common chest radiographic manifestation of GPA; occurring in 40-70% of cases. Cavitations occur in approximately 25%. Lung ground-glass attenuation and consolidation often occur in up to 50% of patients with active GPA, these are mostly the consequences of alveolar hemorrhage, although pulmonary edema secondary to renal involvement may also occur.

In our case, during the active phase of disease, patient had few episodes of hemoptysis and breathing difficulties, chest X-ray showed multiple scattered radio-opaque shadows in bilateral lung fields suggestive of patchy pneumonic consolidation and homogenous opacities in bilateral lung fields suggestive of pulmonary edema (figure 2). High-resolution computed tomography showed ground glass opacities in bilateral lung fields involving all segments with interlobular septal thickening suggestive of organizing pneumonia, from which she recovered after intensive treatment.

Glomerulonephritis (GN) occurs in 70-85% of GPA patients during the disease course, but renal insufficiency (serum creatinine >2.0mg/dl) occurs in only 11-17% of patients at presentation. On renal biopsy, the characteristic renal lesion seen in cases of GPA is segmental focal GN. Immune complexes are absent or infrequent, consistent with “pauci-immune GN”. Our patient had history of acute kidney injury 1 year preceding the index pregnancy and received treatment for the same. She was referred in view of disease flare up, presenting as renal dysfunction. Her RFT was found to be deranged(BUN-34mg/dl, serum creatinine-2.57 mg/dl, urea-52 mg/dl, uric acid-8.3mg/dl, ACR-1525.76 mg/gm, urine creatinine-21.19 mg/dl and urine microalbumin-323.52 mg/L . further testing showed worsening of renal parameters and the decision for LSCS was made.

**Conclusion**

Pregnancy in patients with GPA requires Multidisciplinary approach including preconceptional planning, careful clinical judgment, and vigorous treatment of active disease. The best time to plan conception is a minimum of six months after entering remission. Multiple relapses also occur in some patients. Substantial organ damage due to disease complications and adverse effects of treatment is known to occur, leading to long-term sequelae.

**Acknowledgement**

**Informed Consent:** Informed consent was obtained from the patient.

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**Legends**

**FIGURE 1** – Atrophic scars present on medial side of Right knee joint (1a) and above the Ankle joint (1b)

**FIGURE 2** – chest X ray (PA view) showing Multiple scattered radio opaque shadows and homogenous opacities in bilateral lung fields.