Pregnancy in a Patient with Wegener’s Granulomatosis
A Case Report

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Abstract

Background: Pregnancy in patients with Wegener’s granulomatosis (WG) is rare, and differential diagnosis of WG flare and preeclampsia is difficult.

Case: A pregnant 35 year old with WG was referred with diagnosis of severe preeclampsia; caesarean section was performed. Intubation of the patient was difficult due to subglottic stenosis. Because of the clinical symptom, the case was considered preeclampsia, but p-ANCA of the patient was positive. In pregnancies with WG, differential diagnosis of WG flare-ups from preeclampsia should be made from clinical symptoms and laboratory findings. Serum ANCA titers are not useful in the differential diagnosis of WG flare-ups and preeclampsia because it may be positive in preeclampsia.

Conclusion: Differential diagnosis of WG flare-up and preeclampsia should be made by clinical features. In the patients with subglottic stenosis, general anesthesia should not be preferred due to the probability of difficult intubation.

Wegener’s granulomatosis (WG) is a rare disease characterized by a triad of necrotizing granulomas in the upper and lower respiratory tracts, small vessel vasculitis, and glomerulonephritis. It usually presents in the fourth and fifth decades of life1, 2 with a wide range of clinical presentations. The etiology is unknown, but antineutrophil cytoplasmic antibodies (ANCA) that target neutrophils have been shown to play a significant role. Prognosis is poor with a mortality rate of 82%.1-3 Pregnancy in patients with WG is rare.1 This report presents a case of pregnancy with WG referred to our clinic with a diagnosis of severe preeclampsia and placental abruption.

Case Report

A 35-years-old nulliparous patient in her 34th week of pregnancy was referred to our clinic due to vaginal bleeding. She had WG for three years. Her blood pressure was high (160/100 mmHg), and she had severe vaginal bleeding with a board like uterus. She had no cervical effacement or dilation. Ultrasonography revealed a large hypoechoic area behind placenta and fetal bradycardia about 80 beats per minute. An emergency cesarean section was planned with the diagnosis of placental ablation and fetal distress.

Intubating the patient was difficult because of subglottic stenosis. A male newborn weighing 2,700 g was delivered with APGAR scores of 1 at both the 1st and 5th minutes. There was a large retro-placental hematoma and couvelliar uterus. The operation was ended with no further complication.

Laboratory findings of the patient revealed hypoalbuminemia (2.8 g/dL), elevated liver enzymes (AST: 338 IU/L ALT: 206 IU/L), thrombocytopenia (117,000/mm3), hemoconcentration (Hb: 14.8 g/dL) and proteinuria on urinary stick (++). In addition, C-reactive protein, erythrocyte sedimentation rate, glomerular filtration rate, and 24 hour urine proteinuria were 0.45 mg/L (normal range: 0 to 0.8), 48 mm/hour, 90 mL/min, and 1,000 mg, respectively. Perinuclear staining ANCA (p-ANCA) directed against myeloperoxidase (MPO-ANCA) was positive, but cytoplasmic staining ANCA (c-ANCA) against proteinase-3 (PR-3) was negative. Prednisolone (4 mg/day) and antihypertensive medication was given during the postoperative period with the diagnosis of HELLP syndrome.

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(hemolysis, elevated liver enzyme levels and low platelet count). The patient was discharged from the hospital on 7th postoperative day when her laboratory and clinical conditions returned to normal. The newborn stayed 7 days in the intensive care unit and was discharged from the hospital on the 14th postpartum day.

The history of the patient revealed that 3 years ago she had been admitted to a clinic with breathing difficulty and hoarseness. The tracheoscopic examination revealed subglottic stenosis, edema, and inflammation at the level of second and third tracheal rings. The patient was diagnosed as WG because a giant cell granuloma and necrotizing leucocytoclastic vasculitis were observed on the pathologic examination of the biopsy specimens obtained from these lesions. To diagnose WG as a localized or generalized form, renal biopsy and thorax computerized tomography (CT) were performed. No abnormal finding was observed on the CT. There were no abnormal pathologic findings in renal biopsy. Based on these results, the diagnosis of localized WG was made.

The patient had been treated by methotrexate and prednisolone therapy for two years due to localized WG, which affected only the upper respiratory tract. Methotrexate was stopped before conception because the disease was in remission. Prednisolone treatment was maintained until labor. The pregnancy was uneventful. Routine visits were performed, and fetal growth was normal, and screenings for congenital anomalies and diabetes revealed no abnormal results.

Discussion

Wegener’s granulomatosis is an inflammatory disease of variable clinical presentation. Usually the disease progresses from a localized to a generalized form over the course of weeks to years; however, it may also remain localized. There are three subgroups of WG defined according to the European Vasculitis Study Group based on clinical and pathologic considerations: 1. localized (i.e., affecting the upper or lower respiratory tract); 2. early systemic, including any organ involvement except renal or imminent organ failure; and 3. the generalized form, including renal involvement or imminent organ failure. In present case, the disease was localized during the first two years and remitted before conception.

The standard medications of localized WG are corticosteroids, and the most commonly used drugs are prednisone, prednisolone, and hydrocortisone. Methotrexate is administered as the maintenance therapy but not during pregnancy due to its high teratogenic potential. Prophylactic treatment with trimethoprim-sulfamethoxazole reduces infections and the risk of relapses during remission but is contraindicated during pregnancy.

The IgG auto antibodies against cytoplasmic components of neutrophils, granulocytes, and monocytes have an immunodiagnostic potential for WG. Also, clinical activity of the disease showed positive correlation with the titers of ANCA. Positive c-ANCA results were determined in 87% of those with severe disease and in 90% of those with limited disease. Ten percent of patients with limited disease were p-ANCA positive.

When pregnancy is complicated with preeclampsia, it should be distinguished from a flare-up of WG. Auzary and colleagues reported on five cases of pregnancy with WG and put forward that the differential diagnosis of WG from preeclampsia should be made by the absence of hypertension (which is rare in a WG flare), the presence of extra-renal manifestations, especially upper and lower airways, and positive ANCA titers. However, Shaarawy and associates reported results of 92 pregnancies in late third trimester and demonstrated the positivity of both c-ANCA and p-ANCA levels in mild and severe preeclampsia (38.5% and 69.3%, respectively). They also showed that the serum titers of these markers correlated well with the severity of the disease and concluded that these markers might play role in the pathophysiology of the preeclampsia.

In present case, there were no symptoms of upper or lower airway disease. Blood pressure and liver enzymes were elevated, and the patient had proteinuria, hemococoncentration, thrombocytopenia, and placental abruption. The c-ANCA titer was negative, but p-ANCA was positive. The absence of WG signs and symptoms and the presence of clinical and laboratory findings supported the diagnosis of preeclampsia but not a flare-up of WG.

Upper and lower airways are involved in the clinical picture of WG characterized by granulomatous inflammation, and it may cause scar tissue formation leading to permanent subglottic stenosis. Therefore, intubation of these patients may be difficult in emergent cesarean operations as in the presented case. General anesthesia should be avoided if there is a permanent upper airway stenosis.

In conclusion, conception should be delayed until remission for women with WG. It is incorrect to presume that positive ANCA titers can help in the differential diagnosis of WG flare-up and preeclampsia. Because of high mortality and morbidity risk during pregnancy, patients with WG require multidisciplinary management and close follow-up.

References


