



Case report

Flare of eosinophilic granulomatosis with polyangiitis related to pregnancy: Case report and review of the literature

Osamu Matsuno*, Seijiro Minamoto

Department of Medicine for Allergic Disease, Osaka Habikino Medical Center, 3-7-1 Habikino, Habikino City, Osaka, 583-8588, Japan

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ABSTRACT

Eosinophilic granulomatosis with polyangiitis (EGPA) is characterized by excessive eosinophil accumulation in the peripheral blood and affected tissues with development of granulomatous vasculitic organ damage. It is strongly associated with asthma and ear-nose-throat disease. It often affects patients between the ages of 40 and 60 years. It is unknown whether pregnancy impacts the disease activity of EGPA, including initial diagnosis or relapse. Because of its rarity and age of susceptibility, there are few reported cases describing pregnancy in women with quiescent or active EGPA. Here, we describe a young woman who experienced EGPA relapse during pregnancy and subsequently underwent an elective caesarean section for non-reassuring fetal status at 37 weeks without complication.

1. Introduction

Eosinophilic granulomatosis with polyangiitis (EGPA), also known as Churg-Strauss syndrome, is a rare eosinophil-rich disorder characterized by necrotizing granulomatous inflammation affecting small to medium-sized vessels. Extrapulmonary manifestations can be life-threatening when the heart, central nervous system (CNS), gastrointestinal tract, or kidneys are affected [1]. EGPA is strongly associated with asthma and ear-nose-throat disease. EGPA belongs to the spectrum of antineutrophil cytoplasm antibody (ANCA)-associated vasculitis. However, while ANCA are consistently found in 70–95% of patients with granulomatosis with polyangiitis (GPA) and microscopic polyangiitis (MPA), their prevalence in EGPA is much lower (around 40%) [1,2]. EGPA can affect women of childbearing age. However, reports of the disease during pregnancy are limited. It is unknown whether pregnancy impacts EGPA disease activity, including initial diagnosis or relapse. In this report, we describe a patient who experienced EGPA relapse related to pregnancy and was successfully treated with oral corticosteroids. In addition, we have reviewed the English-language literature on pregnancies in patients affected by EGPA.

2. Case report

A 32-year-old woman was admitted during the 15th week of her

first pregnancy because of an episode of hemoptysis and paresthesia of the left arm. A diagnosis of bronchial asthma was made when the patient was 13 years old.

Her past medical history was remarkable for ANCA-positive EGPA, diagnosed 6 years earlier, which manifested as recurrent asthma exacerbations, hemoptysis, pulmonary infiltrations, mononeuritis multiplex, palpable purpura, and elevated blood eosinophil counts of up to 2740/ μ l. There were histopathological findings of intestinal eosinophilic infiltrates of the skin. The patient was treated with 50 mg prednisone daily. Her symptoms improved rapidly, the prednisone were reduced gradually. The patient took 5 mg prednisone daily and twice-daily inhaled corticosteroids and long-acting β 2 antagonists (fluticasone propionate, 500 μ g \times 2; salmeterol, 50 μ g \times 2).

Until admission, the course of gestation had been uneventful with normal blood pressure, renal function, and fetal growth. Her blood pressure was 103/62 mmHg, her pulse rate was 99/min, and she had no fever. Laboratory studies showed an elevated white blood cell count (11,500/ μ l with 19.9% eosinophilic cells). Hemoglobin was 10.6 g/dL. A chest X-ray image highlighted diffuse hazy opacities in the left lung. The results of indirect immunofluorescence testing for anti-neutrophil cytoplasmic antibodies against myeloperoxidase (MPO-ANCA) were negative. Her forced expiratory volume in one second (FEV1) was 101.6% of predicted. Asthma control test was 20 indicating well controlled asthma.

Abbreviations: EGPA, eosinophilic granulomatosis with polyangiitis; CNS, central nervous system; IVIG, intravenous immunoglobulin; MPO-ANCA, anti-neutrophil cytoplasmic antibodies against myeloperoxidase

* Corresponding author

E-mail address: matsunoo@ra.opho.jp (O. Matsuno).

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Table 1
Onset and exacerbation of EGPA during pregnancy: review of the literature.

Pt	Age	Age at EGPA onset (years)	Onset or exacerbation at gestational age (weeks)	Asthma duration (years)	Symptoms	Eo (/μl or %)	MPO-ANCA	Treatment	Fetal outcome	Patient outcome	Reference
1	33	32	24	15	PN, S, L	4000	NA	PSL	Labor induced at 37th gestation because of growth retardation	Good response	Debby et al.
2	30	27	6 (Third)	3	A, S, PN, C, L	3400	NA	Pulse mPSL, PSL, IVCY	First: healthy infant, Second: spontaneous abortion, Third: fetal death	Died from myocardial infarction	Connolly et al.
3	30	19	14	17	A, L, S, PN, HT, PU	560	-	PSL	First: elective termination, Second: IUFD at 30th gestation, Third: healthy infant	Good response	Ogasawara et al.
4	32	29	22	10	PN, C, L, AR, A	18%	NA	PSL	Healthy infant	Good response	Commio et al.
5	25	25	23	0.66	L, PN, S, HT, PU	4515	NA	PSL, Azathioprine → IVCY	Emergency caesarean section for membrane rupture at 30th week. Twin two required early minimal ventilatory support.	Good response after IVCY	Barry et al.
6	26	24	10 (Second)	Since childhood	1st: none 2nd: GLS, A, PN, Si	1st: 9% 2nd: NA	+	1st: PSL, IVCY, Azathioprine. 2nd: PSL, Azathioprine	First and second pregnancies: Healthy infant	Good response	Lima et al.
7	37	37	16	3	A, PN, L, Si, TA	5200	NA	PSL	Caesarean section at 36th week for membrane rupture. Healthy infant	Good response	Priori et al.
8	19	17	21	2	A, L, S, C, Si	20%	NA	PSL, CPA, IVIG	Elective caesarean section at 34th weeks. Healthy infant.	Good response after IVIG	Rutberg et al.
9	31	NA	5	NA	S, GI, BA, PN, L, C	4844	+	PSL, IVIG	Termination of pregnancy at 20th week for trisomy 13	Good response after IVIG	Hot et al.
10	32	25	11	19	PN, L	2300	+	PSL	Elective caesarean section for non-reassuring fetal status at 37 weeks. Healthy infant.	Good response	Our case

EGPA, eosinophilic granulomatosis with polyangiitis; Pt, patient; Eo, eosinophils; MPO-ANCA, anti-neutrophil cytoplasmic antibodies against myeloperoxidase; PSL, prednisolone; mPSL, methylprednisolone; PN, peripheral nervous system; S, skin; L, Lung; A, asthma; C, cardiovascular; HT, hypertension; PU, proteinuria; AR, allergic rhinitis; Si, sinusitis; GI, gastrointestinal; TA, temporal arteritis; IUFD, intrauterine fetal death; CPA, cyclophosphamide; IVCY, intravenous cyclophosphamide; IVIG, intravenous immunoglobulin.

The prednisolone dosage was increased to 50 mg/day. The eosinophil count and chest X-ray findings were normal 6 days after initiation of therapy. Steroid therapy was slowly tapered and then administered at 10 mg/day.

The patient underwent an elective caesarean section for non-reassuring fetal status at 37 weeks without complication. A healthy female infant weighing 2520 g was delivered with Apgar scores of 8 at 1 min and 9 at 5 min. The postpartum course was uneventful; the patient was discharged on day 15. After delivery, the patient was symptom-free, with laboratory test results within normal ranges.

3. Discussion

We have presented a case of EGPA aggravated during pregnancy. During pregnancy, profound modifications of the hormonal and cytokine microenvironments occur. Flares of EGPA may occur due to immunological or hormonal changes, increased physiological stress reactivating latent disease. Asthma is present in 96–100% of EGPA patients [1,2]. Asthma is the most common respiratory disorder complicating pregnancy, and it is associated with a range of adverse maternal and perinatal outcomes [3]. Over the years it has been widely stated that approximately one-third of asthmatic women experience worsening of the disease during pregnancy [4]. EGPA is an uncommon and potentially fatal primary systemic vasculitis. EGPA is a rare condition in pregnancy, because it often affects patients between the ages of 40 and 60 years [1]. It is unknown whether pregnancy impacts EGPA disease activity, either at initial diagnosis or relapse. Because of its rarity, there are few reported cases describing pregnancy in women with quiescent or active EGPA.

Our review of the literature has yielded 9 previous reports with a total of 15 pregnancies, plus our case, describing active EGPA in subjects during pregnancy (Table 1) [5–13]. The final diagnosis was made during pregnancy in three cases in onset or relapse (30%) and before pregnancy in seven (70%). All pregnancy-related EGPA cases developed before the third gestational trimester (four patients in the first gestational trimester and six patients in the second trimester). In GPA, complication or vasculitis flares occur in about 25% of the pregnancy, sometimes post-partum. The onset of GPA during pregnancy was usually in the second and trimester [14]. There are only two reports of patients developing MPA during pregnancy. In addition, no flare-up of MPA was reported in already diagnosed MPA patients [15].

Hemoptysis was observed in only our patient. The most common reported symptoms were lung infiltration (9/10) and peripheral neuropathy (9/10). Although EGPA is commonly classified as an ANCA-associated vasculitis, in about 60% of the cases ANCA test results are negative [1]. Three of four patients were ANCA-positive, although the data were not available for six patients.

Our patient had an excellent response to glucocorticoids, which are the mainstay of EGPA treatment and can dramatically improve the prognosis [16]. Extensive studies involving the therapeutic use of steroids during pregnancy have shown a remarkable lack of harmful effects on the human fetus, although an increase on the order of 3.4-fold in the risk of oral cleft has been suggested [17] following high-dose long-term therapy. On the other hand, corticosteroids have been shown to enhance fetal lung maturation [18]. Although glucocorticoids are the basis of EGPA treatment, other immunomodulating agents are used as adjunct therapy in severe cases. Cyclophosphamide (CPA) is contraindicated during the first and second trimesters of pregnancy but may be considered during the third trimester for the treatment of severe disease [19]. However, it has been argued that aggressive immunosuppression may be less toxic to the fetus than an insufficiently treated vasculitis flare [19]. The rapid and aggressive onset of EGPA, despite high doses of corticosteroids, is thought to justify the use of CPA. Azathioprine has been used safely during pregnancy in patients with systemic lupus erythematosus and renal transplant [19]. Intravenous immunoglobulin can be used in pregnancy [20], and no fetal

adverse effects have been reported. Thiel et al. reported that Rituximab (RTX) was effective in inducing remission and during long-term follow-up in patients with EGPA, even when previously refractory to standard immunosuppressive therapy including CYC [21]. However, the evidence for treatment of EGPA in pregnancy is lacking. Harris et al. reported that RTX can be considered for the ANCA vasculitis during pregnancy [22].

It is difficult to determine whether adverse obstetric outcomes are solely due to the severity of underlying EGPA or whether the medication plays a role. There were five fetal deaths reported (one due to his mother's death, one spontaneous abortion, one intrauterine fetal death, and two elective terminations). Among the ten other pregnancies not involving fetal death, four were complicated in terms of fetal outcome: one growth retardation; two membrane rupture, and one non-reassuring fetal status. Maternal mortality was fortunately not high in these cases. Of ten patients, only one died, from myocardial infarction.

This case highlights a rare occurrence of EGPA in pregnancy. The principle in the management of women who present with or experience a relapse of EGPA is early diagnosis and treatment with the least toxic agent appropriate to effectively treat the mother and protect the fetus. The rarity of this disease in young women and the limited number of reports describing pregnancy outcomes has made it difficult to give clear advice to women contemplating pregnancy in this context. All pregnancy-related EGPA cases flared before the third gestational trimester. Few non-teratogenic agents can be used for disease flare: corticosteroids, IVIG, and AZA. Maternal mortality is relatively rare. Women with EGPA who become pregnant should be followed by multidisciplinary teams managing their EGPA.

Declarations

Authors' contributions

All authors provided clinical care to the patient and edited the manuscript. All authors read and approved the final manuscript.

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Competing interests

The authors declare that they have no competing interests.

Consent for publication

Written assent and consent to publish this report were obtained from the patient. A copy can be made available if required.

Ethics approval and consent to participate

The presented data are part of our clinical work and there are no ethical conflicts.

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