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Pregnancy in a patient with hypereosinophilic syndrome

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Abstract

Hypereosinophilic syndrome (HES) is a rare entity of unknown etiology that may cause a multitude of problems, from skin rash to organ failure, due to eosinophil infiltrate of tissues. Information on the interaction of hypereosinophilia and pregnancy in patients with established HES is very limited. Here we report a case of a woman with a seven year history of HES whose pregnancy resulted in the delivery of a healthy infant without complications, and no evidence of elevated eosinophils in the infants blood. During pregnancy the patient experienced significant reduction of eosinophils in her blood and resolution of signs and symptoms related to hypereosinophilia.

Keywords

Pregnancy; Hypereosinophilic Syndrome

Introduction

Hypereosinophilic syndrome (HES) encompasses a wide range of clinical manifestations and its course may vary from relatively indolent to aggressive and rapidly fatal.¹ Diagnosis, as defined by Chusid et al,² includes 1) peripheral blood eosinophil count of greater than $1.5 \times 10^9/L$ for 6 months or longer, 2) evidence of organ involvement, thus excluding benign eosinophilia, and 3) an absence of other causes of eosinophilia, such as parasitic infections, allergy, malignancy, and collagen vascular disease. Multiple cytokines stimulate eosinophil production, including interleukins 3 and 5, and granulocyte-macrophage colony-stimulating factor.¹ Treatment of HES varies widely. Steroids are the most common initial treatment, with good control of the disease and associated symptoms and signs in the majority of patients. Long term steroid use is associated, however, with undesirable side effects and other medications are then utilized, including hydroxyurea, interferon and imatinib.¹

For more than a century clinical observations have recognized the ameliorating effect of pregnancy on inflammatory disorders in such patients.³ A number of factors have been suggested as immunomodulating factors capable of modifying inflammatory disorders during pregnancy, including cortisol, progesterone, and pregnancy associated α_2 -glycoprotein.³ In a healthy subject pregnancy is accompanied by leukocytosis and a

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decrease in circulating eosinophils; eosinopenia is statistically significant.⁴ These changes may represent increased adrenal cortical activity since during pregnancy physiologic increase in pituitary activity results in increased production of adrenal corticotrophic hormone (ACTH) which stimulates the adrenal cortex to secrete more steroids.⁵ Interestingly, it has been reported that a component of maternal ACTH in pregnancy is not only of pituitary origin, but also of placental origin.⁶ The placenta releases ACTH autonomously, not subject to feedback control.⁷ Due to these physiologic mechanisms associated with pregnancy it is of interest to describe an effect of pregnancy on hypereosinophilia, and associated signs and symptoms, in patients with established HES.

Review of the available English literature revealed a number of case reports of a pregnancy associated with an acute eosinophilic disorders, with pulmonary involvement as a primary problem. These disorders include pulmonary eosinophilic granuloma/eosinophilic granulomatosis of lungs,^{8,9} idiopathic eosinophilic pneumonia,¹⁰ Churg-Strauss syndrome,¹¹ and eosinophilia-associated hypermeability syndrome (with pericardial and pleural effusions, and ascites).¹² One case described an elevation of blood eosinophils in a newborn, in a patient with HES.¹³ We found only one case report of a pregnancy in a patient with established HES, in whom blood eosinophil count during the pregnancy was monitored and reported.¹⁴

The case involved a 22-year-old woman with established hypereosinophilia (preceding pregnancy for 14 months) and associated skin rash and itching.¹⁴ Daily dose of prednisone (15mg) controlled the symptoms well. The diagnosis of HES was made by exclusion of parasitic, collagen-vascular and allergic diseases. The patient presented at 11 weeks gestation for antenatal assessment and ultrasound examination showed a twin pregnancy. The WBC was $29.2 \times 10^9/L$, with >70% eosinophils (absolute eosinophil count $\sim 21 \times 10^9/L$). A rise of blood eosinophils to $35 \times 10^9/L$ required augmentation of a daily prednisone dose to 75mg for a period of 5 weeks. This was then reduced in steps over 4 weeks to a daily maintenance dose of 25mg. Despite monitoring the patient closely she presented at 30 weeks gestation with premature rupture of membranes resulting in Cesarean delivery under general anesthesia. The two male infants did well; neither showed hypereosinophilia within their first six months of life. At 10 months postpartum the mother's WBC count stabilized at $15\text{--}20 \times 10^9/L$ with 50–70% eosinophils, on immunosuppressive regimen.

Case Report

A 30 year old female was found to have hypereosinophilia on a routine blood count in 1996. She was asymptomatic but over next three years developed dyspnea on exertion, easy bruising and tingling sensation in legs. She was then referred to our institution for evaluation and treatment suggestions. The EKG and chest x-ray were normal, and testing for parasitic infection and autoimmune disorders were unrevealing. The patient received antiparasitic antibiotic therapy anyway, without response in blood eosinophilia. In 1999, a bone marrow aspiration and biopsy showed hypoplastic marrow with 10% cellularity, no lymphoid infiltrates, adequate trilineage maturation, no blast, and 19% eosinophils. The cytogenetic analysis revealed diploid female karyotype (46, XX) with inversion 9(p11q12) in all metaphases (constitutional abnormality). Molecular testing (PCR), performed recently on

archived material, was negative for FIP1L1-platelet derived growth factor receptor alpha (PDGFR α). The complete blood cell count revealed WBC of $9.1 \times 10^9/L$ with 29% eosinophils, normal hemoglobin and platelets. The patient was treated with H1 and H2 blockers and anti-asthmatic medications. In 2002 she was seen again, and enrolled on a clinical study with imatinib mesylate. The starting dose was 100 mg daily; after one month of therapy and no response, the dose was escalated to 400mg a day. After further two months and a lack of response she was taken off the study.

In April 2005 the patient presented to the clinic for the follow up and was found to be pregnant. WBC was $7.1 \times 10^9/L$ with 41% eosinophils. She was closely monitored with regular blood cell count check (Figure 1). During the pregnancy the percent and total number of eosinophils in patient's blood steadily decreased with a resolution of signs and symptoms related to high eosinophil count. At the delivery WBC was $7.7 \times 10^9/L$ with 9% eosinophils. Upon delivery the eosinophils rapidly increased in patient's blood to the pre-pregnancy levels. The patient delivered healthy infant without complications. There was no elevation of eosinophils in infant's blood.

Discussion

While HES is rare disease we were surprised to find only one case report of a pregnancy in a patient with HES, where an interaction of hypereosinophilia and pregnancy was subject of the report.¹⁴ It is very likely that great majority of HES cases are uneventful and physicians therefore do not report them. However, this case report describes interesting clinical experience with pregnancy in a HES patient, where the eosinophil number significantly decreased in patient's blood during the pregnancy, with the elimination of signs and symptoms of the disease. Such a development may be result of immunomodulatory/hormonal changes known to happen in pregnancy.⁴⁻⁷ In the only case reported so far in the literature, however, such an improvement was not observed but neither was a significant aggravation of the disease. Based on this very limited experience with one case, it seems that the eosinophilia in patients with chronic HES could be a subject to positive effects of the pregnancy associated immune/hormonal changes.

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Figure 1.