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Case Report

Successful Pregnancy after Donor Oocyte *In Vitro* Fertilization in a Woman with Systemic Lupus Erythematosus Treated with Belimumab

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ABSTRACT

According to recent evidence, autoimmunity cannot be considered as the cause of primary infertility. Except for cyclophosphamide-mediated ovarian failure, fertility in patients with Systemic Lupus Erythematous (SLE) and other systemic autoimmune disease is not different from the general population. Herein, we present the first case of successful donor oocyte *In Vitro* Fertilization (IVF) in a patient with SLE treated with belimumab a monoclonal antibody that specifically recognizes and inhibits the biological activity of B-Lymphocyte Stimulator (BLyS). This case supports the feasibility, efficacy and safety of donor oocyte IVF in patients with SLE in remission. Hence, donor oocyte IVF might be a further option for SLE patients to achieve successful pregnancies.

Keywords: Pregnancy; Systemic lupus erythematosus; Endometriosis; Primary ovarian failure; Donor oocyte

INTRODUCTION

Systemic Lupus Erythematosus (SLE) mostly affects women of childbearing age and female hormones are involved in its pathogenesis [1]. According to recent evidence, autoimmunity cannot be considered as a cause of primary infertility, excluding cyclophosphamide-mediated ovarian failure, fertility in patients with SLE and other systemic autoimmune disease is not different from the general population [2-4]. Assisted Reproductive Technology (ART) procedures, including *In Vitro* Fertilization (IVF), do not seem to elevate the risk of disease flares or thrombosis in patients with SLE [5]. Even though ART can be considered successful in SLE patients, the rate of maternal and fetal complications is high, so that candidates for ART should have a quiescent disease for at least 6 months before attempting pregnancy to achieve the best possible outcome for mother and child [6,7]. Donor oocyte IVF has enabled many women diagnosed with primary or secondary ovarian failure, diminished ovarian reserve, multiple IVF failure or genetic conditions to conceive successfully [8]. The B-Lymphocyte Stimulator (BLyS) inhibitor belimumab (Benlysta) is a human immunoglobulin G1λ monoclonal antibody, is the only biological therapy currently approved for the treatment of non-renal SLE. Belimumab is approved as add-on therapy in adult patients with active, autoantibody-positive SLE despite standard therapy [9]. We report a case in which a patient with SLE treated with belimumab in clinical and serological remission successfully conceived with a donor oocyte IVF.

CASE PRESENTATION

Herein, we present the first case of successful IVF in a patient with SLE. A 39-year-old woman developed SLE at the age of 28 years. Manifesting with polyarthritis, pleuritis, oral ulcers, hemolytic anemia, leucocytopenia, hypocomplementemia, positive antinuclear and positive anti-dsDNA autoantibodies. Antiphospholipid syndrome markers, such as lupus anticoagulant, anti-cardiolipin and anti-β2GPI IgG/IgM were consistently negative. In the course of disease, she has been treated with methotrexate, which was discontinued because of family planning, Hydroxychloroquine (HCQ) which triggered a skin reaction and Chloroquine (CQ) plus low-dose prednisolone (5 mg/d) which was well tolerated. Because of recurrent malar rash, mucosal ulcerations, arthritis, hypocomplementemia and leucopenia (SLEDAI:8) intravenous belimumab at standard dosages (10 mg/kg/4 weeks) was added to the treatment.

Until diagnosis of SLE her gynecological history was unremarkable, with a menarche at age 12 followed by regular menstruation intervals. With SLE, amenorrhea appeared and after 4 years of unsuccessful attempts to conceive, she was diagnosed with endometriosis and primary ovarian failure. SLE

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was in remission by treatment with belimumab, chloroquine and low-dose prednisolone (SLEDAI:2). Our patient opted for assisted reproductive technology procedures including multiple cycles of controlled ovarian stimulation for ovulation induction to perform *in vitro* fertilization (IVF). The procedures did not lead to SLE exacerbation, ovarian hyperstimulation syndrome or thrombosis related to the excess of hormones, as it had been previously described [10,11]. However, ART did also not yield any success in oocyte retrieval in this patient.

Having exhausted her options, she decided to undergo donor oocyte IVF in Spain, since such procedure is not permitted in Germany. The first IVF attempt with donor oocytes, performed according to the state-of-the-art techniques, with multiple embryo transfer in a natural cycle and hormone support of the luteal phase, resulted in pregnancy. Belimumab and chloroquine were discontinued but low-dose prednisolone (5 mg/d) was continued. Due to SLE, her pregnancy was classified as high-risk. Low-molecular weight heparin was given until the end of pregnancy, although this is not indicated in the absence of antiphospholipid antibodies. Monthly follow up by rheumatologists and bi-weekly follow up by the gynecologists were done, following the recommendations of the European league against rheumatism [12]. SLE remained in remission during the entire pregnancy. The patient delivered a healthy baby at week 39 of gestation with normal body weight, height and maturation. After delivery, the patient resumed chloroquine and continued low-dose prednisolone treatment. After 10 months belimumab has not been started because of complete remission (SLEDAI:0).

RESULTS AND DISCUSSION

According to recent evidence, autoimmunity cannot be considered as the cause of primary infertility but current evidence demonstrates the association between endometriosis and autoimmune diseases [4-13]. Except for cyclophosphamide-mediated ovarian failure, fertility in patients with SLE and other systemic autoimmune disease is not different from the general population [2]. Hence, we do not think that failure of conception in this patient was based on SLE. Furthermore, ovarian stimulation to induce ovulation in the context of IVF has shown to be safe and successful in patients with SLE, if the disease is in remission and under adequate treatment [4-6]. However, nothing was known about the efficacy and safety of donor oocyte IVF in patients with SLE. Women undergoing such procedure should be carefully counseled regarding pregnancy complications, including hypertension and premature delivery [8]. This case supports the feasibility, efficacy and safety of donor oocyte IVF in patients with SLE. Hence, donor oocyte IVF might be a further option for SLE patients to achieve successful pregnancies. Albeit, considering all published information on ART in SLE, this procedure should not be expected to be more dangerous or challenging.

CONCLUSION

Donor oocyte IVF might be a safe option for SLE patients in remission to achieve successful pregnancies.

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