

## A CASE REPORT: A MOTHER WITH SECONDARY INFERTILITY

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### ABSTRACT

**Aims:** Secondary infertility is a disease where women with a firstborn are not able to have a child again. In this case report, we wanted to observe a whole process of a patient with secondary infertility and investigate the causes and whether there are any solutions for it.

**Case Report:** A 41-year-old female patient presented to the clinic with the complaint of not being able to get pregnant. First thoughts about the patient were focused on infertility however, she had a child before. Therefore, further investigations were needed. After the investigations, she was diagnosed with secondary infertility because no rational reasons were able to clarify her disease.

**Conclusion:** Nowadays, secondary infertility is still a major health problem and no medications or treatments are enough to resolve this problem. The most common theory is the H-Y antigen hypothesis, but still, there is not enough evidence for this theory to be proven.

**Keywords:** Infertility, pregnancy, immune system

### INTRODUCTION

Infertility is the failure of achieving a clinical pregnancy after 12 months or more of unprotected sexual intercourse. Infertility can be divided into two major categories: physiological and pathological. Physiological - process is where a woman can not get pregnant due to her biological timing or pregnancy. Pathological - condition has two types; primary and secondary infertility. A woman who never got pregnant in spite of having repetitive intercourse is diagnosed with primary infertility. Unlike this situation, women with secondary infertility get diagnosed after giving birth to a child (1).

Secondary infertility is the disability of the mother to get pregnant following the birth of her first child that was conceived without any reproductive technologies or fertility treats. Secondary infertility could also be defined as a process which includes recurrent miscarriages. This medical problem mostly comes out after birth, where cells of the fetus are able to pass through maternal circulation (2). During pregnancy placenta becomes permeable to fetal cells and even, after pregnancy, male DNA becomes sensible in the maternal

circulation. Women which are suffering from secondary recurrent miscarriages (SRM) are mostly mothers of boys where their immune systems are against a protein called male-specific minor histocompatibility (H-Y) antigens (2).

A specific gene on Y chromosome that encodes H-Y antigen; male, fetal and trophoblast cells express them in a ubiquitous manner (2). These antigens are very specific for H-Y immunity which becomes functional and is seen mostly after stem-cell transplantation.

In this case report it is aimed to present a forty-one-year-old female patient who had subsequent miscarriages after having given birth to her first son, thus was diagnosed with secondary infertility after the examinations.

### CASE REPORT

A forty-one-year-old female patient admitted to the Department of Gynecology and Obstetrics in Trakya University Hospital with unexpected and continued abortions is presented. According to her anamnesis,

she had two miscarriages and one medical abortion. She was healthy, not on any medication and had no known allergies. She did not have a history of alcohol or any other substance abuse.

Patient has an eight-year-old boy. For her previous pregnancy, no fertility medications or reproductive technologies were used. The patient stated that since her first born she has been trying to get pregnant, but she could not. Some genetic tests were needed to determine her diagnosis and treatment.

Polymerase Chain Reaction analysis was performed using genomic gene-specific DNA primers derived from the peripheral blood sample of the patient, which was later on directed to the Genetic Disease Diagnosis Center of Trakya University. 8 polymorphisms in 8 different gene regions were evaluated by the Pyrosequencing technique.

Prothrombin, factor V leiden, MTHFR C677T, beta fibrinogen genes were considered as normal; MTHFR A1298C homozygous mutant, factor XIII and GPIIIa heterozygous mutant, PAI-1 homozygote 5G.

The peripheral blood sample has been also sent to Istanbul Genetic Diagnosis Center for her chromosomal analysis. In the cytogenetic analysis report, no anomaly was detected performed on the metaphases obtained from the peripheral blood but pericentric inversion was detected in the region of p11q13 of chromosome 9. This change was evaluated as polymorphism and the phenotypic effect was not expected. Still, genetic counseling was suggested to the patient.

Simultaneous chromosome analysis of the patient's partner was also seen necessary and no numerical or structural anomaly was detected in the chromosome analysis performed on peripheral metaphases. With the results gathered together, it was decided that the patient did not have any disability for having a child and the patient was discharged.

After 4 years, the patient was presented again to Trakya University Hospital Department of Gynecology with the same complaints she had 4 years ago. Patient's husband was also admitted to the clinic for in-vitro fertilization treatment. For their microbiological evaluation venous blood samples were taken. The patient's AMH, Anti tox. IgM and CMV IgM levels were examined and the values according to the laboratory test results were found to be within normal limits. The ELISA

test was used to detect AntiHIV, HBsAg and AntiHCV values on patients' partner which were found to be negative.

## DISCUSSION

Secondary infertility is an unaccountable health problem. Still to this day, reasons for secondary infertility remain unclear while studies on possible causes continue.

This type of infertility is also characterized by having a male child. Resolving patients with secondary infertilities are much more difficult than patients with primary infertility, which often leads to discharge with an undefined cause of infertility diagnosis (3, 4).

Usually, patients have very similar complaints as Primary Recurrent Miscarriage (PRM) patients. Research shows that there are similar discomforts between PRM and secondary infertility patients (5). Another research found that immunotherapy method used for treating infertility did not affect PRM patients. On the other hand, it was observed that patients with SRM had a significant increase in birth rate (2).

Studies on the cause of secondary infertility are mostly focused on the H-Y hypothesis. According to this hypothesis immune reactions lead to a male-specific histopathological disorder. The role of gender in SRM was found 20 years ago. Based on the data and the information obtained from the study, a male-specific factor can be found in a woman with a male fetus (2).

Maternal carriage of HLA-class II alleles causes the production of H-Y antigens in patients with a first-born. Especially HLA-DRB1 is a part of the family gene called the human leukocyte antigen (HLA) complex which helps the immune system distinguish the body's own proteins from the ones made by foreign invaders. Providing instructions for building a protein that plays an important in our immune system (6).

It is also thought that recurrent miscarriage patients, in contrast to PRM, are carrying the immunological high responder alleles HLA-DR1 \*03 and HLA-DRB1 \*15 times more frequently (2). So SRM patients immune system is more selective and aggressive than normal peoples. This information predicts that H-Y antigens passing to blood after the first-born child may reduce the chances of having a healthy pregnancy. However,

this still remains an issue to be researched further considering the fact that the effects are not seen in every woman who has had a male child before.

In conclusion, we are hoping that this case report will lead to an increase in further research about this topic and be a path for the treatment of this condition.

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**Informed Consent:** Written informed consent was obtained from the participants of this study.

**Conflict of Interest:** The authors declared no conflict of interest.

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