Case Report

Different Endometrial Receptivity in Each Hemiuterus of a Woman with Uterus Didelphys and Previous Failed Embryo Transfers

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Abstract

The aim of this report is to describe the clinical case of a 31-year-old patient with uterus didelphys (double uterus) and primary infertility, who had been through several embryo transfers in the context of an *in vitro* fertilization (IVF) treatment with no success. In the case described, the patient is subjected to a new IVF treatment after an endometrial receptivity array (ERA) test performed in both hemiuteri, to assess endometrial receptivity. As a result, the test showed that the right-sided hemiuterus was receptive in 5 days since the beginning of progesterone administration while the left-sided hemiuterus was not receptive in that day. The IVF treatment is performed with vitrified oocytes and a single embryo in day-3 stage is transferred to the right hemiuterus. We concluded that the ERA analysis is a useful tool for IVF patients with uterus didelphys to choose the most appropriate hemiuterus and day to perform embryo transfer.

Keywords: *Assisted reproductive technologies, bicorporeal uterus, double uterus, endometrial receptivity, endometrial receptivity array, uterus didelphys*

Introduction

Uterus didelphys is a congenital malformation of the female genital tract, due to a complete fusion failure of the Müllerian ducts during fetal life. It is characterized by the presence of a double uterus and a double cervix. Besides, a longitudinal septum is also present in the vagina.[1,2]

To the best of our knowledge, this is the first reported case of a patient with double uterus where both endometrial cavities have been subjected to endometrial receptivity array (ERA) tests to study their receptivity, in the context of an *in vitro* fertilization (IVF) treatment. Remarkably, each hemiuterus showed a different implantation window.

Case Report

The patient and his partner attended our center in August 2009, after 8 months trying to get pregnant with no success. The woman was nulliparous and 28 years old at the time, while her partner was 31 years old. She was subjected to an ultrasound examination that revealed the presence of two uteri [Figure 1].

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The physician recommended a pelvic magnetic resonance imaging to further investigate this malformation and it was observed that the patient presented a double uterus with two independent endometrial cavities. A diagnosis of complete bicorporeal uterus was established (Class U3b according to the current ESHRE/ESGE classification system of female genital tract congenital anomalies).[3] The cervix also presented a double cavity (Class C2 according to the ESHRE/ESGE classification system). This congenital anomaly affecting the uterus and the cervix was formerly known as double uterus or uterus didelphys.

She presented a body mass index of 20.2 and had no significant medical history or relevant allergies. Relevant hormone levels were as follows: follicle stimulating hormone 5.79 mIU/mL, luteinizing hormone 4.44 mIU/mL, estradiol 70 pcg/mL, and prolactin 31.07 ng/mL.

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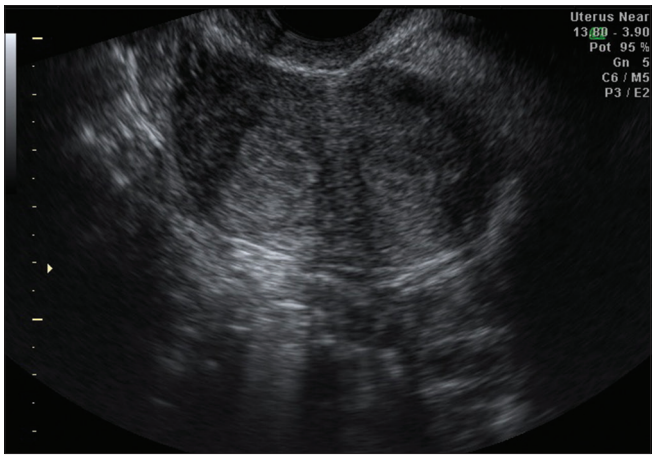

Figure 1: Ultrasound image showing the two uteri of the patient

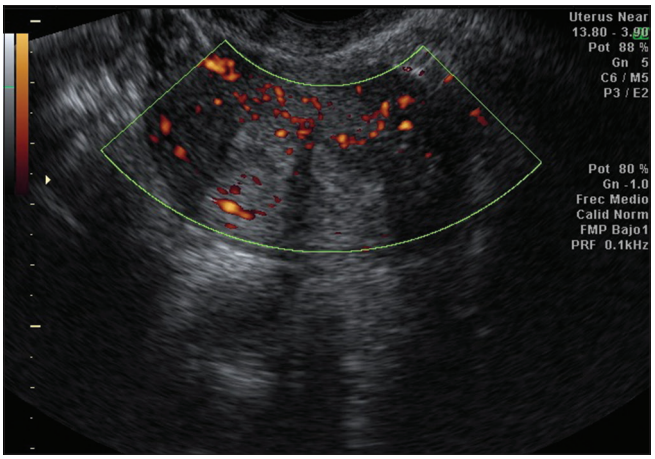

Figure 2: Doppler ultrasonography image showing a more intense Doppler signal in the right-sided uterus in comparison to the left one, meaning a higher frequency of subendometrial blood flow

Her partner had β-thalassemia minor. Sperm analysis showed a concentration of 29.5 million of sperm cells per mL, 18% of progressive motile sperm cells (asthenozoospermia according to the WHO criteria[4]), 9% of nonprogressive motile sperm cells, and 73% of immotile sperm cells. Eight percent of spermatozoa presented normal morphology.

Both couple members were seronegative for hepatitis B and C as well as for HIV.

The patients underwent four artificial insemination cycles and two IVF cycles (with three embryo transfers) with no success. Two transfers were performed in the right-sided uterus (the most accessible one) and one transfer was performed in the left-sided uterus.

After these negative results, the physician decided to perform ERA tests in both uteri. The tests were performed in April 2012, while the patient underwent hormone replacement therapy (HRT). We observed that the right-sided uterus had an endometrial thickness of 9 mm, while the left-sided uterus had a thickness of 8.9 mm. Both uteri presented a three-layer pattern. During biopsy procedure, we confirmed that the access to the left-sided uterus was more difficult. The two uterine cavities showed different implantation windows: while the right-sided cavity was receptive in 5 days since the beginning of progesterone administration ($P + 5$), the left one was not receptive in that day.

A third IVF cycle was performed in January 2013 with HRT, mimicking the previous ERA cycle. Before the beginning of progesterone administration, endometrial thickness was 12.1 mm in the right uterus and 8.1 mm in the left one. Assessment of subendometrial blood flow with Doppler ultrasonography (as an indicator of endometrial receptivity) showed a higher frequency of subendometrial flow in the right-sided uterus in comparison to the left-sided one [Figure 2].

As the patient still had 12 vitrified oocytes from her second cycle, those were thawed and subjected to intracytoplasmic sperm injection. Eight oocytes were correctly fertilized, and one embryo was transferred in day-3 to the right-sided uterus, within its implantation window. The β-hCG test result for this transfer was of 576.6 mIU/mL.

Ultrasound examination was performed in February 2013 revealing a gestational sac of 10 mm in the right-sided uterus, with an embryo of 1 mm presenting heartbeat. Pregnancy evolved correctly and a female healthy baby was delivered through C-section after 39 weeks (in October 2013), weighing 3050 g. To date, she has not experienced any remarkable health issue.

Medical records of the patient were used, and consent from the patient was obtained for the publication of the findings.

Discussion

The prevalence of uterus didelphys in the general population is 0.3% (95% confidence interval [CI], 0.1–0.6). This prevalence is significantly increased in women with miscarriage in association with infertility (2.1%; 95% CI, 1.4–3.2).[5] Patients with uterus didelphys do not seem to have a reduced fertility, but this anomaly is associated with altered pregnancy outcomes. Modest increases in the risk of preterm labor (relative risk [RR] 3.58; 95% CI, 2.00–6.40) and fetal malpresentation (RR 3.70; 95% CI, 2.04–6.70) have also been reported. Miscarriage rate does not seem to be altered in these women.[6]

Since a few years ago, ERA tests can be applied in IVF treatments to analyze the receptivity of the endometrium and to determine the optimal day to

perform embryo transfer. These tests consist on taking an endometrium biopsy in the context of either a natural cycle, a controlled ovarian stimulation cycle, or an HRT cycle. Then, a transcriptomic profile of this sample is generated, allowing us to establish if the endometrium is receptive for the embryo the day of the cycle in which the biopsy was taken.[7,8]

ERA tests are of particular interest in this case since they allow us to study the receptivity of both hemiuteri.[9] In our case, we found that one of the endometrial cavities was receptive in day $P + 5$ while the other was not. This allowed us to plan a better clinical approach to this case.

From the methodological point of view, it would have been optimal to transfer one embryo to each hemiuterus at the same time. However, elective single embryo transfer is especially mandatory in patients with uterine pathologies since risks associated to multiple pregnancy are even more serious.[10]

We consider that this case report can be useful for the scientific community, clinicians, and patients in a similar situation.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patients have given their consent for their images and other clinical information to be reported in the journal. The patients understand that name and initials will not be published and due efforts will be made to conceal identity, but anonymity cannot be guaranteed.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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