

Twin Sisters with Unique Septate Uterus and Longitudinal Vaginal Septum

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Abstract: The septate uterus is the most common form of structural uterine anomalies. A rare developmental variant is a complete septate uterus with cervical duplication and a complete vaginal septum. Experiences with these unique uterine anomalies are limited only to case reports. Although there have been a few families in which members are affected similarly, there are no reports in the literature describing dizygotic twins with the same congenital uterine malformation, as seen in our cases.

A 28-year-old woman and her dizygotic twin sister who had spontaneous abortion history were identified in our practice with complete septate uterus, cervical duplication and a complete vaginal septum. After excision of the septum, both patients conceived spontaneously and delivered healthy term babies.

Although occurrence of Müllerian anomalies in the same family supports genetic tendency, no information exists on the number and chromosomal location of the responsible genes. The aim of this case is to share our experience about this unique Müllerian anomaly, which was detected and treated successfully in twin sisters, and also to discuss the possibility of the genetic tendency of this congenital anomaly.

Key Words: Septate uterus, cervical duplication, familial tendency, twin sisters

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İkiz Kızkardeşlerde Septat Uterus ve Longitudinal Vajinal Septum

Özet: Septat uterus yapısal uterin anomalilerin en sık görülen formudur. Servikal duplikasyon ve komplet vajinal septumun komplet septat uterus ile birlikteliği nadir görülen bir gelişimsel anomalidir. Bu tip nadir uterin anomalilerle ilgili çalışmalar vaka takdimleri ile sınırlıdır. Literatürde aynı aile bireylerinde benzer uterin anomalilerin tespit edildiği vaka takdimleri mevcutken, henüz dizigotik ikizlerde aynı konjenital uterin malformasyonların varlığı ile ilgili bir vaka sunulmamıştır.

Bu çalışmada, her ikisinde de spontan abortus hikayesi olan, servikal duplikasyon ve komplet vajinal septum ile birlikte komplet septat uterus tanısı almış 28 yaşındaki dizigotik ikiz kız kardeşin durumu sunulmuştur. Her iki hasta da, septum eksizyonundan sonra spontan olarak gebe kalmış ve sağlıklı, term bebekler dünyaya getirmişlerdir.

Müllerian anomalilerin aynı aile bireylerinde görülmesi genetik eğilimi düşündürmesine rağmen sorumlu genlerin sayısı ve kromozomal yerleşimi ile ilgili herhangi bir bilgi bulunmamaktadır. Bu vaka, ikiz kardeşlerde tespit edilen ve başarıyla tedavisi verilen Müllerian anomalili olgulardaki deneyimimizi paylaşmak ve bu konjenital anomalideki genetik eğilim olasılığını tartışmak amacıyla sunulmaktadır.

Anahtar Sözcükler: Septat uterus, servikal duplikasyon, ailesel eğilim, ikiz kız kardeşler

Introduction

Congenital uterine anomalies in the general population are estimated to have an incidence of 0.001%-10% (1). Differences in diagnostic methods, classification systems, patient selection factors and clinical experience all contribute to difficulties in estimating the true prevalence of congenital uterine malformations. Septate uterus is the most common pathology seen in the patients who are evaluated for repeated abortion and found to have uterine anomaly. A rare developmental variant is a complete septate uterus with cervical duplication and a complete vaginal septum (2). This anomaly is inconsistent with the classical theory of unidirectional Müllerian duct anomalies; the alternative bidirectional theory is proposed instead (3).

The aim of this case is to share our experience about this unique Müllerian anomaly, which was detected and treated successfully in twin sisters, and also to discuss the possibility of the genetic tendency of this congenital anomaly.

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Case Report

A 28-year-old woman, gravida (G) 1, parity (P) 0, admitted to our institution at 6 weeks of gestation according to her last menstruation period with vaginal bleeding. Gynecological evaluation revealed a longitudinal vaginal septum and two separate cervixes with cervical bleeding. The uterus was normal in size and contour. Transvaginal sonographic examination (TV-USG) demonstrated two uterine cavities: one had irregular gestational sac and fetal heart rate was not seen, which was demonstrated before. The patient was taken to the operating room for carman curettage to complete the evaluation for abnormal uterine bleeding. Diagnostic laparoscopy and hysteroscopy were planned after curettage in two months. Diagnostic laparoscopy confirmed the presence of a single, smooth uterine fundus with normal appearing tubes and ovaries. Before starting hysteroscopy, vaginal septum was excised and hysteroscopy revealed a complete uterine and cervical septum. The uterine septum resection was then started at a point above the internal cervical os with microscissors and/or electroscurgically with a loop until the hysteroscope could be moved freely across the top of the endometrial cavity and both tubal ostia could be visualized. Increased bleeding at the fundus signaled that the junction of the septum and myometrium had been reached. The cervical septum was protected during this procedure. The patient conceived spontaneously two months after the operation, and delivered vaginally at 40 weeks of gestation. Investigation of the family showed that she had a dizygotic twin sister who had spontaneous abortion history, suggesting familial tendency for the same malformations. We invited her sister to our institution for a complete evaluation. She was 28 years old, G 1, P 0, abortion 1. Gynecologic examination and TV-USG confirmed the same uterine-vaginal anomalies. Diagnostic laparoscopy and hysteroscopy were planned similarly. After confirming a complete uterine septum with double cervix and vaginal septum, the complete vaginal septum was resected to improve access to the cervix, and then operative hysteroscopy was performed. The uterine septum was incised in a cephalad direction with electrocautery until the uterine cavities were united. In order to avoid risk of iatrogenic cervical incompetence, the cervical septum was preserved. She also conceived spontaneously three months later and delivered at term. Intravenous urography revealed normal findings in both sisters. No additional pathology such as skeletal abnormality or neurosensorial hearing loss was detected in either sister.

Discussion

A failure of reabsorption of the midline uterine septum between the two fused Müllerian ducts results in defects that range from a partial midline septum to complete septum in the uterine cavity. Müllerian anomalies might contribute to poor fetal outcomes such as first trimester losses and preterm labor. Septate uterus with cervical duplication and longitudinal vaginal septum is a very rare variant of the septate uterus in gynecologic practice (2). Experiences with these unique uterine anomalies are limited only to case reports. In 2004, Saygılı-Yılmaz et al. (4) reported clinical features of 9 new cases, suggesting that this atypical septate uterus type is probably more frequent than reported.

In patients with no history of a poor reproductive outcome, a conservative approach may be considered. Some investigators have reported better reproductive outcome among women with a septate uterus not subjected to surgical interventions (5,6). In one study, Heinonen et al. (7) evaluated gynecologic complaints, fertility and obstetric outcomes in 67 patients with a complete septate uterus and longitudinal vaginal septum. They reported that complete septate uterus and longitudinal vaginal septum is not associated with primary infertility, and that pregnancy may progress successfully without surgical treatment. The results do not support elective hysteroscopic incision of the septum in asymptomatic patients or before the first pregnancy.

Significant pregnancy wastage, obstetric complications and dyspareunia are commonly observed with a complete uterine septum, double cervix and vaginal septum, which make metroplasty and vaginal septum removal advisable (8). Hysteroscopic division of the uterine septum (metroplasty) is one method of choice in treating uterine septum (7) because of its simplicity and low associated morbidity. In our cases, at the time of the operation, we preserved the cervical septum to avoid the risk of iatrogenic cervical incompetence. Actually, at the time of the hysteroscopic division of the uterine septum, excision of the tissue between the two cervixes is controversial. Some investigators excise, while others have stated that excision may lead to cervical incompetence during pregnancy (8-10). Çalışkan et al. (11) reported a case of a leiomyoma localized in the septum of a septate uterus that had cervical duplication and a longitudinal vaginal septum. Restoration of normal anatomy was achieved after correct diagnosis and a two-

step operation procedure. A normal cervical length was measured at 26 weeks of gestation after cervical unification. In their study, Le Ray et al. (12) reported their experience with 10 patients with complete septate uterus, in whom they performed a hysteroscopic section of the cervical, uterine and vaginal septum at discovery of the anomaly. Although they could not draw a conclusion about the obstetrical benefit of this surgical technique, they reported that complete surgical section of the cervical and uterine septum in case of complete septum uterus is safe. In another study, Rock et al. (13) reported that surgical correction of complete uterine septum with preservation of the cervical septum is associated with low morbidity and satisfactory postoperative obstetric outcome. This large series spanning 13 years of clinical data demonstrated a 5.2% incidence of cervical incompetence. Actually, the presence of a cervical septum is not associated with a higher incidence of dystocia since the cervical septum is usually displaced to one side by the descending fetal head (14). However, the incidence of cervical incompetence in general is small, estimated at 2.9% of treated patients in one large metroplasty review (15), and one recent study showed no cervical incompetence among seven women who underwent both cervical and fundal septal division (16).

Occurrence of Müllerian anomalies in members of the same family and the association with other somatic anomalies support genetic linkages. Many investigations have been undertaken to determine a genetic relationship in the development of disorders of the Müllerian ducts. The study of Adamian et al. (17) analyzed 624 patients with various malformations of the uterus and vagina, and genetic analysis of genealogical trees of patients with malformations of the uterus and vagina revealed the recessive type of inheritance. Recently apoptosis was the mechanism proposed for the resorption of the uterine-cervical-vaginal septum during fetal life. Lee et al. (18) theorized that resorption of the uterine septum may be regulated by Bcl-2. Bcl-2 is a protein that protects cells from apoptosis and promotes cell survival. Bcl-2 protein was localized in the endometrium, and in the superior, lateral and inferior myometrium of 4 fetuses in a study observing 8 fetuses. However, Bcl-2 protein was consistently absent from the septum. It has been suggested that presence of Bcl-2 in the above elements protects them from apoptosis during growth. The septum, however, in the absence of Bcl-2, is not protected from

apoptosis and therefore undergoes resorption. It is theoretically possible that it may be caused by the rare situation in which Bcl-2 is present in most of the septum.

Multiple malformation syndromes with anomalies of the uterus or vagina are associated with some genetic origin. For example, single mutant genes are responsible for McKusick-Kaufman syndrome and hand-foot-genital syndrome. Although no information exists on the number and chromosomal location of the responsible genes, HOX gene mutations have been reported in several families with multiple Müllerian anomalies (19).

Familial aggregates of the most common disorders of Müllerian differentiation are best explained on the basis of polygenic or multifactorial inheritance. Indeed, this is the usual mode of inheritance for anomalies affecting either a single organ system or a single embryologically related organ system. In polygenic or multifactorial inheritance, recurrence rates among first-degree relatives are usually 1% to 5% (20). Unlike Mendelian traits, polygenic or multifactorial inheritance traits are compatible with discordance among monozygotic twins; however, concordance rates are still higher in monozygotic than in dizygotic twins. The other possible explanation is genetic heterogeneity. A dominant or recessive gene could explain some cases, whereas nongenetic factors or polygenic/multifactorial inheritance could explain most (21).

To date, there have been a few families in which members are affected by similar Müllerian disorders (22,23). In 1997, Ergun et al. (24) reported a case that included multiple affected siblings as well as mother and daughter. We have identified twin sisters in our practice with an uncommon variance of uterine septum. To our knowledge, there are no reported similar Müllerian anomalies consisting of a complete uterine septum with cervical duplication and a longitudinal vaginal septum in dizygotic twins delivering a full-term infant after resection of the uterine septum. Although no information exists on the number and chromosomal location of the responsible genes, the genetic mechanism most likely to explain familial tendencies will be considered. The ideal study may be very difficult to perform because asymptomatic relatives would need to be assessed. Nevertheless, relatives of a woman with a Müllerian fusion defect should be examined in future studies, in order to improve our understanding of the genetic aspect of this anomaly.

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