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Phenotypic and clinical aspects of Mayer-Rokitansky-Küster-Hauser syndrome in a Chinese population: an analysis of 594 patients

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Objective: To analyze the phenotypic and clinical aspects of Mayer-Rokitansky-Küster-Hauser (MRKH) syndrome.
Design: Cross-sectional study.
Setting: University hospital.
Patient(s): Five hundred and ninety-four patients with MRKH syndrome.
Intervention(s): Clinical examination, abdominal or perineal/rectal ultrasound, magnetic resonance imaging, hormonal profile, karyotype, and laparoscopy.
Main Outcome Measure(s): Clinicopathologic data, VCUAM (vagina cervix uterus adnex-associated malformation) classification, types with cycle phase, and karyotype.
Result(s): We identified associated malformations in 43 out of 594 (7.2%) cases of MRKH. The 594 patients could be grouped into hormone phases: 53.7% follicular, 35.2% luteal, and 11.1% ovulatory. The major karyotype of MRKH patients was 46,XX; abnormal karyotypes were found in two cases.
Conclusion(s): A lower proportion of associated malformations were found when compared with those provided in the current literature. Renal anomalies were the most frequent associated malformations, and most of the patients presented with a normal karyotype. Given the large cohort of this study, the lower malformation rates might be related to geographic or referral patterns, so further investigation is warranted. (Fertil Steril® 2016;■:■–■. ©2016 by American Society for Reproductive Medicine.)
Key Words: Abnormal karyotype, malformations, MRKH syndrome, pituitary and steroid hormones, VCUAM classification

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Mayer-Rokitansky-Küster-Hauser syndrome (MRKH; OMIM 27700), also known as Rokitansky syndrome, is characterized by congenital aplasia of the uterus, cervix, and upper two-thirds of the vagina during fetal development. The incidence of the syndrome is 1 in 4,500 female newborns (1, 2). Women with MRKH syndrome typically have normal ovarian function and a 46,XX karyotype; thus, these patients typically present with primary amenorrhea (3). The association of malformations in müllerian duct development with other organ systems suggests that crucial genes involved in fetal development and sex differentiation are potential candidates for these congenital malformations. However, the etiology of MRKH syndrome remains unknown (4).

The patient's history, clinical examination, ultrasound, magnetic resonance imaging, and laparoscopy can assist in the initial diagnosis of MRKH (5–7). The syndrome can be classified into type I (isolated) or Rokitansky syndrome, and type II (associated with malformations of organs of the renal, skeletal, cardiovascular, and other systems) (8). Patients with MRKH syndrome can also be classified by the vagina cervix uterus adnex-associated malformation (VCUAM) genital classification system according to phenotypes associated with each of these anatomic structures. The VCUAM system, developed in 2005, aids in providing an accurate description of the phenotypes of female genital malformations (9). Recent publications have described patients with MRKH syndrome using the VCUAM classification system, but there are few detailed descriptions of the expected findings in patients within a large cohort.

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Single case studies and small cohort investigations indicate that steroid and pituitary hormone levels in individuals with MRKH fall within the normal limits (10, 11). However, some studies have revealed that hormone deregulation could exist in some MRKH patients, as hyperprolactinemia, high progesterone levels, dysregulation of antimüllerian hormone levels, differences in luteal phase estrogens, and hypergonadotrophic hypogonadism have been observed (11–14). Our study used the VCUAM classification system to describe the spectrum of congenital malformations in a large cohort of 623 patients with MRKH syndrome.

MATERIAL AND METHODS

Patients

The cohort included 623 patients who presented initially with primary amenorrhea before MRKH syndrome was diagnosed. The women, who came from all areas of the People's Republic of China, presented between July 2006 and November 2014 in the Department of Obstetrics and Gynecology at the University Hospital of Shenzhen (People's Republic of China).

The majority of the patients had data collected, including personal and family history, gynecologic examination, abdominal ultrasonography, X-rays, hormone profiling, karyotype testing, magnetic resonance imaging of the pelvis, and surgical reports. All serum samples of hormones were collected at the time of initial diagnosis and were analyzed using DxI800 analyzers (Beckman Coulter). The same operator evaluated all 623 patients according to the VCUAM classification using laparoscopy, as a part of an improved laparoscopic peritoneal vaginoplasty (15–17). The final classification of each malformation was performed using the new VCUAM classification. This classification makes it possible to descriptively record the pathologic anatomy of genital developmental disturbances.

All the patients were informed that the data were to be analyzed in the context of a research study outlining the key objectives and research outcomes. All participants provided written consent upon request. Approval for the study was obtained from the ethics committee at the University of Shenzhen.

Statistical Analysis

The data captured followed a full patient record-review process using a standardized score form, recorded on an Excel database (Microsoft). Where necessary, patients with incomplete data were excluded from the study to ensure that the statistics were accurate and consistent with our identified hypothesis.

RESULTS

Clinicopathologic Data

The patient files of 623 patients with diagnosed MRKH syndrome who were treated during the study period were analyzed. We deemed 594 cases eligible for inclusion in the analysis. Twenty-nine patients were excluded from this study due to undetermined abdominal or perineal/rectal ultrasound, magnetic resonance imaging, hormone profile, and karyotype data.

All 594 patients were Chinese; all the patients underwent a clinical examination as well as ultrasound and laparoscopy examinations. Patients with skeletal, neuronal, or cardiac malformations were further examined using thoracic X-ray, echocardiography, audiometry, or visual tests. All cases in our research group were sporadic. The mean age at the time of the diagnosis was 24.7 ± 4.5 years (range: 12–43 years). Table 1 gives the characteristics of the study participants. The mean interval between the diagnosis of malformation and surgical treatment was 6.35 ± 3.86 years (range: 12–43 years), with a range of 0 to 21 years. The mean preoperative vaginal length was 2.2 ± 1.1 cm, with a range of 0 to 3 cm. Surgical vaginoplasty was successfully completed in all cases.

VCUAM Classifications

Vagina (V) and cervix (C). We found that 594 patients (100%) showed stage V5b (complete atresia) development of the vagina and stage C2b (bilateral atresia/aplasia) of the cervix.

Uterus (U). We found that 585 patients (98.5%) showed stage 4b (bilateral rudimentary or aplastic) uterine development, 3 patients (0.5%) showed stage 4a (unilateral rudimentary or aplastic), five patients (0.8%) showed "other," and one patient (0.2%) showed stage 3 (hypoplastic uterus).

Adnexa (A). We found that 571 patients (96.1%) showed stage 0 (normal adnexa) development, six patients (1%) showed other malformations, five patients (0.8%) showed stage 3a (unilateral aplasia), four (0.7%) were not classifiable, three patients (0.5%) showed stage 3b (bilateral aplasia), two (0.3%) showed stage 2a (unilateral hypoplasia), two patients (0.3%) stage 1a (unilateral tubal malformation), and one (0.2%) showed 1b (bilateral tubal malformation). Moreover, ovarian mature cystic teratomas were found in four patients.

Associated malformations (M). In 551 (92.8%) of 594 patients, no associated malformations were diagnosed (stage 0). In 30 patients (5.1%) we found malformations of

TABLE 1

Sociodemographic data of patients with Mayer-Rokitansky-Küster-Hauser syndrome (N = 594).

Characteristic	Patients, n (%)
Marital status	
Married	80 (13.5)
Single	362 (60.9)
Partnership	152 (25.6)
Education level	
Compulsory school[a]	138 (23.3)
High school	267 (44.9)
University	189 (31.8)
Employment status	
Employed	351 (59.1)
Unemployed	87 (14.6)
Student	156 (26.3)

[a] Compulsory school denotes the first 9 y of education.

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