Mullerian Agenesis - Genetic Inheritance: A Case Report

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Abstract

Mayer-Rokitansky-Kuster-Hauser is a malformation complex comprising absent vagina and absent or rudimentary uterus. This is understandable given the incomplete degree of penetrance, variable expressivity, and similarities of this syndrome with other genetic disorders. A 22-year-old unmarried female presented to Santokba Durlabhji Memorial Hospital, Gynaecology Department, with a complaint of primary amenorrhea. Her secondary sexual characters were well developed. Pubic and axillary hairs well-developed Tanner stage 4, breast development is also Tanner stage 4. Her daughters of her 2 uncles were having the same complaint of primary amenorrhea having age 18 and 16 years. A multidisciplinary and comprehensive approach must be sought for mullerian agenesis.

Key words: Autosomal dominant, Genetic transmission, Gonadal dysgenesis, Paramesonephric duct

Introduction

MRKH syndrome was described between 1829 by physiologist Mayer (1829), Rokitansky (1938), Kuester (1910), and gynecologist Hauser (1961).¹ MRKH is the second most common cause of primary amenorrhea, next to gonadal dysgenesis. The incidence of MRKH is 1 per 4000-10000 females, and it results from interrupted embryonic development of the paired mullerian (paramesonephric) ducts between the 4-12th weeks of gestation. The molecular basis for MRKH syndrome has yet to be identified, but multiple genes are being investigated. Genetic transmission is believed to be in an autosomal dominant fashion with incomplete penetrance and variable expressivity.²³

A multidisciplinary and comprehensive approach must be sought for mullerian agenesis. Early involvement with specialty care is necessary to discuss non-surgical and surgical options with psychosocial support.⁴

Case Report

A 22-year-old unmarried female presented to Santokba Durlabhji Memorial Hospital, Gynaecology Department, with a complaint of primary amenorrhea. Her past medical and surgical history was not significant. Her secondary sexual characters were well developed. Pubic and axillary hairs well-developed Tanner stage 4, breast development is also Tanner stage 4.

Ultrasonography examination showed agenesis of the uterus with well-developed ovaries. Her vaginal examination showed blind vagina. Her hormonal profile was normal.

Laparoscopic vaginoplasty by Davydov method was performed (Figures 1 and 2). She had an uneventful recovery and discharged on the 3rd post-operative day with vaginal mold (Figure 3).

On detail family history, we found that she had 2 brothers and 1 sister who were normal. Her father had 7 brothers and 1 sister all of them were normal, but daughters of...
her 2 uncles were having the same complaint of primary amenorrhea having age 18 and 16 years.

**DISCUSSION**

First sign of MRKH syndrome is a primary amenorrhea in young women presenting otherwise with normal development of secondary sexual characteristics and normal external genitalia, with normal and functional ovaries, and karyotype (46, XX) without visible chromosomal anomaly. MRKH may be isolated (Type I); however, it is more frequently associated with renal, vertebral, and to a lesser extent, auditory, and cardiac defects (MRKH Type II or MURCS association).5

Some studies investigated genetic mutations during the earliest phases of the embryonic development. There have been several assumptions about involved genes, such as Wilms tumor 1 (WT1), PAX2 (it is thought that the WT1 oncosuppressor may act as repressor of the transcription of PAX2), HOXA7–HOXA13 (highly important genetic clusters for the correct embryogenesis) 9, and pre-B-cell leukemia homeobox 1 (PBX1), although some researches on direct implications of these genes have not given certain outcomes; the wingless-type MMTV integration site family, member 4 (WNT4) gene seems to be surely involved, since it intervenes on embryonic genital female development with a specific function.6,7

Shokeir investigated 10 families with several members affected by MRKH syndrome. In the majority of them, there were some affected paternal relatives, raising the possibility of an autosomal dominant inheritance with sex-limited (female) expression and incomplete penetrance. It was suggested that female carriers develop mullerian abnormalities, whereas male carriers do not manifest any deleterious effect.

The genetic basis of MRKH syndrome is largely unknown. Array comparative genomic hybridization (CGH) analyses have detected submicroscopic imbalances at 1q21.1, 4q34-qter, 17q12, 22q11.21, and Xq21.31. Recurrent changes have also been identified at 22q11q21.1 and 17q12.1. However, analysis of candidate genes has been inconclusive.

**CONCLUSION**

MRKH is a malformation complex comprising absent vagina and absent or rudimentary uterus. This is understandable given the incomplete degree of penetrance,
variable expressivity, and similarities of this syndrome with other genetic disorders. Treatment which consists in creating a neovagina is generally offered to patients when they are ready to start sexual activity.8

REFERENCES


Source of Support: Nil, Conflict of Interest: None declared.