

A case of gonadal dysgenesis 46,XX associated with Mayer-Rokitansky-Kuster-Hauser Syndrome: a rare co-existence

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Abstract

Introduction: Gonadal dysgenesis 46 XX along with Mayer-Rokitansky-Kuster-Hauser syndrome is a very rare coexistence. Due to the rarity of disease exact genetic cause cannot be hypothesized.

Case report: This is a case of 30 year old lady with primary amenorrhea. She had SSC of Tanner stage II, blind vagina, absent uterus and streak gonads on USG. Her hormone levels were in postmenopausal range. Her karyotype was 46 XX.

Discussion: The coexistence of these two rare syndromes presents as amenorrhea and infertility. The treatment options are limited, with hormone replacement to prevent osteoporosis and development of SSC.

Keywords: Gonadal dysgenesis, Mayer-Rokitansky-Kuster-Hauser syndrome, hypogonadism, primary amenorrhea

Introduction

Gonadal dysgenesis is absent or insufficient development of ovaries, leading to inability of ovaries to produce sex steroids. This presents as primary or secondary amenorrhea. Mayer-Rokitansky-Kuster-Hauser syndrome (MRKHS) is mullerian agenesis in a 46 XX female. This combination of two syndromes is very rare. This leads to infertility in young couple

Case details

This is a case report of a 30 year old woman who presented with primary amenorrhea. She has been married for 14 years with coital difficulty. There was no family history of consanguinity, miscarriage or primary

amenorrhea in other female members of her family. She was born of a normal pregnancy with no antepartum or postpartum complaints. There was no other significant medical history. Her mental ability was normal

On general physical examination; her height was 141cms, weight 41.4 kgs, BP 120/70. Breast, pubic hair and axillary hair were developed to Tanner stage II. There was no gross skeletal abnormality or webbing of neck. Her external genitalia appeared normal, but her vagina was blind about 2-3 cms in length. On per rectal examination, uterus was not palpable.

Investigations were done. On ultrasonography, uterus was absent and

bilateral streak gonads were seen. Bilateral kidneys, ureters and bladder appeared normal. Serum FSH level – 199.73IU/l, LH level – 86.01 IU/L, TSH 3.01 mIU/ml, estradiol -10.2 pg/ml. The karyotype was 46XX.

The patient was diagnosed to have ovarian dysgenesis with Mayer-Rokitansky-Kuster-Hauser syndrome (MRKHS)



Image 1. Ultrasound image of streak left ovary



Image 2. Ultrasound of absent uterus

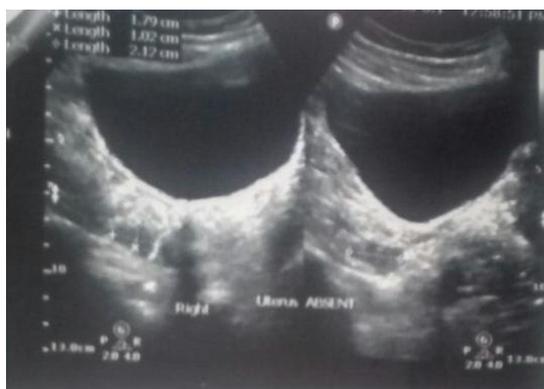


Image 3. Ultrasound of streak right ovary

Discussion

Mayer-Rokitansky-Kuster-Hauser syndrome is characterized by müllerian duct agenesis leading to uterovaginal atresia. The prevalence is about 1 in 4500 female births (1). It is associated with upper urinary tract malformation in 40% cases. Skeletal and cardiac anomalies are also reported. As the mesonephros, müllerian duct and the skeleton; all originate from the mesoderm, deleterious event occurring in embryological phase may give rise to this abnormality (2). It is hypothesized that existence of activating mutation of anti müllerian hormone and antimüllerian hormone receptors may be involved in müllerian agenesis(3). Mutation of WNT4 may also be a factor responsible for MRKH syndrome(4).

46 XX gonadal dysgenesis is a primary ovarian defect leading to premature ovarian failure. It occurs due to defect in primordial follicle formation. Patients may have primary or secondary amenorrhea with normal genitalia. Genetic implications include homozygous or compound heterozygous inactivating mutation of FSH receptor gene, mutation in BMP15 gene and mutation in NR5A1 gene (5, 6, 7, 8, 9)

A review of literature was done by Shah et al. They found 23 reported cases of gonadal dysgenesis with MRKH syndrome. The cases had a wide spectrum of morphologically varied phenotypic presentation. Based on this review it was concluded that there can be three possibilities besides just coincidence; first, there may be mutation or deletion of common genes involved in development and migration of germ cells and müllerian derivatives. Second, micro deletion in part of X-chromosome may result into absent or dysfunctional protein, which may interrupt the development of gonads and müllerian structures; third, possibility of endocrine disruptors cannot be ruled out(10).

The index case reported is such a rare combination of disease. The exact genetic

cause of this association cannot be identified due to rarity of the disease.

Conclusion

Co-existence of ovarian dysgenesis and MRKHS syndrome is very rare. It may be coincidental or may be an independent entity, not yet recognized. Unfortunately this compromises the fertility of a young couple and predisposes the woman to early onset menopause. The treatment is based on replacement of hormones to develop the secondary sexual characteristics and to prevent osteoporosis.

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