Indian Journal of Obstetrics and Gynecology
Volume 3 Number 2, July - December 2015
DOI: https://dx.doi.org/10.21088/ijog.2321.1636.3215.13

A Case of Gonadal Dysgenesis 46 XX Associated with Mayer-Rokitansky-Kuster-Hauser Syndrome: A Rare Co-Existence

Pratibha Singh*, Mathur Neha Satyaprakash, Suyasha Vyas**, Kuldeep Singh*****

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 poorly developed secondary sexual characters with breast development 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: MRKH syndrome and Gonadal dysgenesis both presents as amenorrhea and infertility. The co-existing of these together is a rarity. The treatment options are limited, with hormone replacement to prevent osteoporosis and development of secondary sexual characters, but infertility remains an answered question in these patients.

Keywords: *Gonadal dysgenesis; Mayer-Rokitansky-Kuster-Hauser syndrome; hypogonadism; Primary amenorrhea.*

*Additional Professor, **Senior Resident, Department of Obstetrics and Gynecology, ****Additional Professor, Department of Pediatrics, All India Institute of Medical Sciences, Jodhpur.

Pratibha Singh, Head, Obstetrics & Gynecology, All India Institute of Medical Sciences (AIIMS), Basni Industrial Area, Phase-2, Jodhpur, Rajasthan 342005.
E-mail: drpratibha69@hotmail.com

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 a mullerian agenesis in a 46XX female. This combination of these two syndromes is very rare. This leads to infertility in young couple.

Case Report

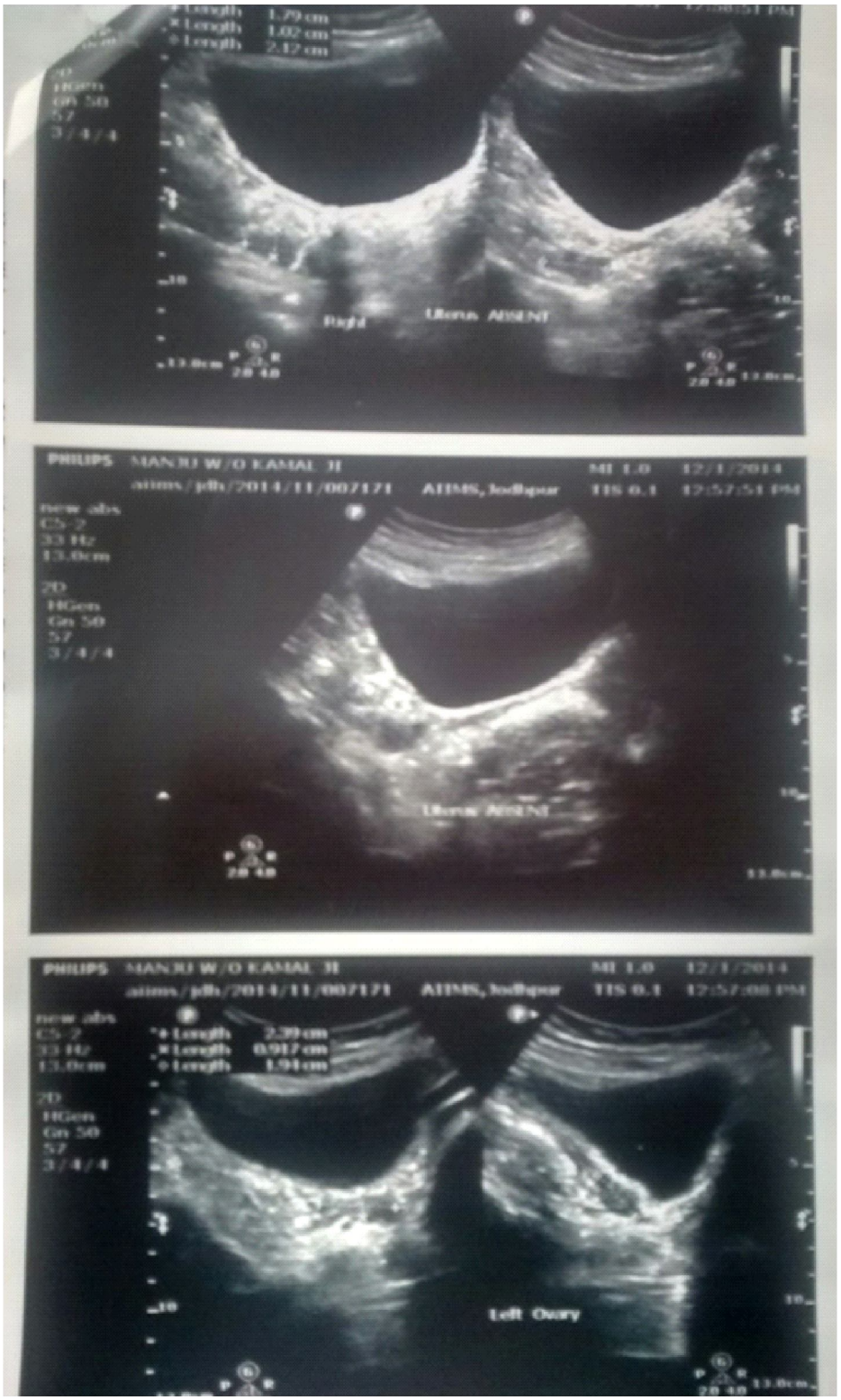
This is a case report of a 30 year old woman who presented with primary amenorrhea. She had been married for 14 years. There was no family history of consanguinity, miscarriage or primary amenorrhea in other female members of her family. She was born of a normal pregnancy with no antepartum or postpartum complaints. There was no other significant medical history. Her mental ability was normal.

On general physical examination; her height was 141cms, weight 41.4kgs, BP 120/70 mmHg. Breast, pubic hair and axillary hair were developed to Tanner stage II. Her sense of smell and hearing ability was normal. She seemed to have normal intellect. There was no gross skeletal abnormality, cardiac or renal abnormality, and no webbing of neck. Her external genitalia appeared normal, but her vagina was blind about 3-4 centimeters in length. On per vaginal as well as per rectal examination, uterus was not palpable.

Investigations were done to further work up the case. On ultrasonography, uterus was absent and bilateral streak gonads were visible. Serum FSH level – 199.73IU/l, serum LH level – 86.01 IU/L, TSH 3.01 mIU/ml, estradiol -10.2 pg/ml. Her karyotype was 46XX.

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

Fig.1 : USG showing absent uterus and streak ovaries



Discussion

Mayer-Rokitansky-Kuster-Hauser syndrome is characterized by mullerian 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, mullerian 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 mullerian hormone and antimullerian hormone receptors may be involved in mullerian 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 is the most common cause of amenorrhoea with poor development of secondary sexual characters. 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 [10]. 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 mullerian derivatives. Second, micro deletion in part of X-chromosome may result into absent or dysfunctional protein, which may interrupt the development of gonads and mullerian 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 the rarity of the disease.

MRKH syndrome usually presents with amenorrhoea and infertility, they have a well functioning ovaries and biological pregnancy can be possible with the help of newer treatment options and surrogacy. Ovarian dysgenesis requires long term treatment with hormonal replacement therapy to prevent osteoporosis and for the full development of secondary sexual characters if started in time. Combination of these two rare disorders presents a challenge to the gynecologist; though they can be treated with HRT but options for infertility remains largely remains unavailable to these patients.

It is important for the gynecologist and physician to be aware about this condition, and to start treatment at an early time for proper sexual development and to prevent long term complications for these patients. These patients require not only medical treatment but also psychological support as long term medical therapy is planned.

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 prevent long term problems of osteoporosis, though treatment for infertility remains bleak as no treatment is available for these women as yet.

References

1. Rampone B, Filippeschi M, Di Martino M, Marrelli D, Pedrazzani C, Grimaldi L, et al. Mayer-Rokitansky-Küster-Hauser syndrome presenting as vaginal atresia: Report of two cases. G Chir. 2008; 29: 165–7.
2. Sharma S, Aggarwal N, Kumar S, Negi A, Azad JR, Sood S. Atypical Mayer-Rokitansky-Kuster-Hauser syndrome with scoliosis, renal and anorectal malformation-case report. Indian J Radiol Imaging. 2006;16: 809–12.
3. Gorgojo JJ, Almodóvar F, López E, Donnay S. Gonadal agenesis 46, XX associated with the atypical form of Rokitansky syndrome. FertilSteril. 2002; 77: 185–7.
4. Philibert P, Biason-Lauber A, Rouzier R, Pienkowski C, Paris F, Konrad D, et al. Identification and functional analysis of a new WNT4 gene mutation among 28 adolescent girls with primary amenorrhea and müllerian duct abnormalities: A French collaborative study. J ClinEndocrinolMetab. 2008; 93: 895–900.
5. Heufelder AE. Gonads in trouble: Follicle-stimulating hormone receptor gene mutation as a cause of inherited streak ovaries. Eur J Endocrinol. 1996;134: 296–7.
6. Aittomäki K, Lucena JL, Pakarinen P, Sistonen P, Tapanainen J, Gromoll J, et al. Mutation in the follicle-stimulating hormone receptor gene causes

hereditary hyper gonado-tropic ovarian failure. Cell. 1995; 82: 959–68.

7. Lourenço D, Brauner R, Lin L, De Perdigo A, Weryha G, Muresan M, et al. Mutations in NR5A1 associated with ovarian insufficiency. N Engl J Med. 2009; 360:1200–10.
8. Ferraz-de-Souza B, Lin L, Achermann JC. Steroidogenic factor-1 (SF-1, NR5A1) and human disease. Mol Cell Endocrinol. 2011; 336: 198–205.
9. Ledig S, Röpke A, Haeusler G, Hinney B, Wieacker P. BMP15 mutations in XX gonadal dysgenesis and premature ovarian failure. (e1-5). Am J Obstet Gynecol. 2008;198: 84.
10. Shah VN, Ganatra PJ, Parikh R, Kamdar P, Baxi S, Shah N. Coexistence of gonadal dysgenesis and Mayer-Rokitansky-Kuster-Hauser syndrome in 46, XX female: A case report and review of literature. Indian J Endocrinol Metab. 2013 Oct; 17(Suppl1): S274–S277.