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Case Report

A Mayer-Rokitansky-Kuster-Hauser Syndrome in a Neonate: A Case Report

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ABSTRACT

Background: Mayer-Rokitansky-Kuster-Hauser (MRKH) syndrome is defined as the congenital incomplete development of Müllerian structures in women who otherwise have the phenotype with a normal karyotype (46, XX), normal external genitalia, and functional ovaries. We present the case of a neonate admitted with features of MRKH syndrome.

Case Report: We present a female neonate with a gestational age of 37 weeks and two days with a birth weight of 2650 grams who was admitted to the hospital. Fistulography radiology was performed for the baby in such a way that water-soluble contrast material was used. The baby was discharged with good general condition, normal tests, and stable hemodynamics vesicostomy.

Conclusion: MRKH syndrome is a very heterogeneous phenotypic and genetic disorder. Although more information is still needed about the etiology and management of MRKH, progress has been made in the past decades regarding efficient diagnostic methods and appropriate medical management.

Keywords: Neonate, Neonatal intensive care unit, Mayer-Rokitansky-Kuster-Hauser, Syndrome

Introduction

Mayer-Rokitansky-Kuster-Hauser (MRKH) syndrome (MRKH; MIM#27700), also referred to as Müllerian agenesis/aplasia, uterovaginal agenesis/aplasia or congenital absence of uterus and vagina (1), is defined as congenital incomplete development of Müllerian structures (uterus, fallopian tubes, proximal vagina) in women who otherwise have the phenotype with a normal karyotype (46, XX), normal external genitalia and functional ovaries, there are however cases of polycystic ovaries and ovarian tumors (2). Also, associated anomalies, usually renal and skeletal, may be observed (3, 4). The incidence of MRKH is about 1:4,500 newborn girls (5).

This anomaly is one of the most severe malformations of the female reproductive system and occurs separately in two-thirds of patients. There appear to be two subtypes of MRKH: the typical (also called type I or isolated) and the atypical form (type II), with the frequency of type II being much greater (6). In patients (type 2), often associated structural anomalies such as unilateral renal agenesis (30%), skeletal defects (10% - 15%), cardiac anomalies (2% - 3%), and deafness (2% - 3%) are manifested. These women have a normal 46, XX karyotype and usually show normal ovarian function with normal development of breasts and external genitalia (7).

The cause of MRKH syndrome is unknown. Years ago, MRKH syndrome was thought to occur

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sporadically due to exposure to pharmacological teratogens such as thalidomide (1). Several genes are involved in the normal development of Müllerian, renal, and skeletal structures, but the HOXA genes and the WNT4 genes appear to be the strongest candidates. Because HOXA10 represents the developing uterine region, HOXA11 the lower uterine segment and cervix, and HOXA13 the vagina, it is biologically plausible that altered expression of these genes leads to the abnormalities found in MRKH. However, HOX genes are also associated with the normal development of kidneys, bones, and vascular structures. This could strengthen the hypothesis of dysregulation of developmental genes involved in the embryonic origin of the female reproductive tract(8, 9).There is a risk of recurrence of this abnormality in relatives, but most cases of MRKH occur sporadically. Familial cases can be explained by autosomal dominant inheritance with reduced penetrance and variable manifestations. However, oligogenic or polygenic inheritance has also been discussed (10).

The first clinical feature is generally primary amenorrhea (5). MRKH syndrome is diagnosed based on physical examination, transabdominal ultrasound, magnetic resonance imaging, laparoscopy, or both. Once the diagnosis of MRKH is suspected, imaging studies have a central role in unveiling the degree and extension of gynecologic and extra-gynecologic abnormalities (6). According to Lermann et al. (2011), laparoscopy can better determine the status of the adnexal (11). Moreover, surgical intervention is mainly performed to repair the vagina. In typical cases, diagnostic procedures show aplasia of the upper two-thirds of the vagina with an absent or rudimentary uterus consisting of two small bilateral fibromuscular remnants, normal fallopian tubes, and ovaries that function normally (12). Vaginoplasty can be achieved either surgically or by progressive dilation of the vaginal dimple. Most surgical or nonsurgical techniques are reported to provide good anatomical and functional results of at least 70% (13). Management of patients with MRKH syndrome includes counseling and psychological support after diagnosis, as well as creating a functional vagina. We present the case of a neonate who was admitted with features of MRKH syndrome.

Case report

A female neonate with a gestational age of 37 weeks and two days with a birth weight of 2650 grams was admitted to the hospital, where the mother gave birth with symptoms of respiratory distress, tachypnea, low spo2, granting, and cyanosis. Furthermore, on the second day, an abdominal mass and the possibility of MRKH syndrome were diagnosed after ultrasonography. Then, for the treatment of Hydrometrocolpos, she underwent a laparoscopy, a vaginostomy was inserted, and the hemorrhagic cyst was removed and sent to pathology. A drain was installed for the baby. Then, the neonate was transferred to Hazrate Ali-Asghar Children's Hospital, an academic center and a pediatric surgery center, for further examination and was admitted to this hospital's neonatal intensive care unit.

In the initial clinical examination, the neonate was a 2-day-old girl, delivered by cesarean section, the first child, related parents, with a breech presentation, which was diagnosed with an intra-abdominal cyst in the mother obstetric ultrasonography of 32 weeks of gestational age. The neonate has a dysmorphic facial appearance, microcephaly (head circumference 31 cm and z-score -2.5 SD), scaphocephaly head shape, low hairline, short neck, skin protrusion on the back of the neck, low set ear, rotated ear, periorbital, short nose, broad nasal bridge, high arch palate and small month. The baby's chest was mildly scaphoid; the lower extremity was thin and had overlapping fingers. The neonate's sucking was weak, and there were signs of respiratory distress in the baby.

A neonate in the NICU with basic proceedings including NPO and HFNC (flow=2.5, FIo2=50%), start of serum and fluids and electrolyte, daily head circumference measurement of neonates, antibiotic therapy (amikacin and vancomycin) - IL10%, AF 10%, and routine care of newborns, sending biochemical and hematology tests (the process of tests from the admission to discharge is summarized in Table 1) were admitted, as well as surgical heart, surgery, nephrology, neurology, ophthalmology consultation, occupational therapy, and speech therapy. It was requested and done for the baby.

In pelvic and abdominal ultrasonography, the liver had a normal midclavicular span and uniform echogenicity, and no space-occupying lesions were evident in the liver. The vena cava had a normal diameter. The gallbladder has a normal shape and size and contains two echogenic foci with post shadow measuring 5.5 mm and 7 mm, suggesting gallbladder stone. The spleen has normal dimensions and echogenicity. Both kidneys have a length position (right 58mm and left 63mm) and parenchyma thickness (right 9mm

Table 1. The process of clinical laboratory results

Variable	Reference range	Hospital day 1	Hospital day 5	Hospital day 10	Hospital day 17	Hospital day 22	Hospital day 28	Hospital day 32
White blood cell count (×103/mm3)	4.0-10	9.7	3.6	6.28	6.4	9.1	14.2	5.9
Red blood cell count (mill/ mm3)	4.2-5.4	3.84	3.37	3.3	3.94	3.24	2.97	3.48
Hemoglobin (g/dl)	12-16	13.9	11.7	11.1	12.5	9.8	8.9	10.2
Hematocrit (%)	37–47	37.6	32.7	31.6	34.8	28	24.3	29.5
M.C.V(fL)	77-97	97.9	97.6	95.8	88.3	86.4	81.8	84.4
M.c.H(Pgm)	26-32	36.2	34.9	33.6	31.7	30.2	30	29.3
M.C.H.C(g/dl)	32-36	37	35.8	35.1	35.9	35	36.6	3406
Platelet count (x×1000mm3)	140-440	245	340	600	265	305	382	292
Lymph%	4.0-10	35.2	37	76.7	65.1	55.4	-	73.2
PDW(FL)	10-17	12.1	11.5	11	13.6	12.2	-	10.7
MPV(FL)	8.5-12.5	9.7	9.3	9.4	10.7	9.7	-	9.2
Retic Count%	3-7	9	-	-	-	-	-	-
Blood sugar (mg/dl)	<140	127	-	85	87	-	-	-
B.U.N (mg/dl)	3-25	23	18		9	12	11	12
Creatinine (mg/dl)	0.6-1.2	1.5	1.26	1.25	0.86	0.9	0.87	0.8
Serum Na(mEq/L)	130-145	132	138	144	139	136	139	134
Serum K(mEq/L)	3.0-6.0	5.8	6.5	4.7	5	5.3	4.5	4.5
Serum Ca(mg/dl)	6.2-11	10	9.5	10.4	10.5	10		10
Inorganic P(mg/dl)	4.5-9.0	7.7	4.7	4.3	5.1	5.1		6.5
Serum Mg(mg/dl)	1.6-2.4		1.6	1.9	1.3	1.5	1.6	1.6
SGOT(AST)(U/L)	47-150	33	-	-	-	-	-	-
SGPT(ALT)(U/L)	13-45	11	-	-	-	-	-	-
Prothrombin time (sec)	28-34	38	-	-	-	-	35	-
CRP(mg/L)	<10	38.2	4.4	21.4	13.2	29.7	11.1	9.9

and left 9mm), and echogenicity is normal. Mild hydronephrosis was observed in the left kidney with an AP pelvis diameter of 5 mm. The bladder had a normal wall thickness and no stones or space-occupying masses. The endometrial cavity of the uterus as well as the cervix was found to expand and contain fluid debris level with an approximate volume of 60 cc, which completely expanded the endometrial cavity and the above findings are in favor hydrometrocolpus, matching with the patient's previous records and the description of the surgery and a supplementary examination of It is recommended to follow up Müllerian's anomaly. Free fluid is not observed in the abdomen and pelvis.

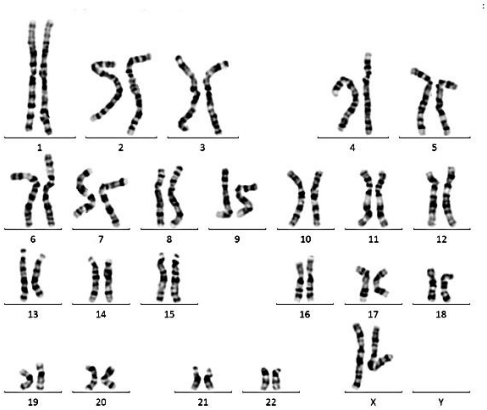

Figure 1. Karyotype report

Then, fistulography radiology was performed for the baby in such a way that water-soluble contrast material was introduced through the catheter embedded in the LLQ area. The contrast material entered the cavity with approximate dimensions of 45 x 26 mm (anterior-posterior, craniocaudal diameter) in the middle part of the pelvis, in front of the rectum, which is related to the uterine cavity. There was no evidence of the exit of the contrast material from the uterine cavity and its entry into the vagina and perineum. The above finding suggested congenital obstruction in the vaginal area (atresia/septum) (Figure 2 and Figure 3).

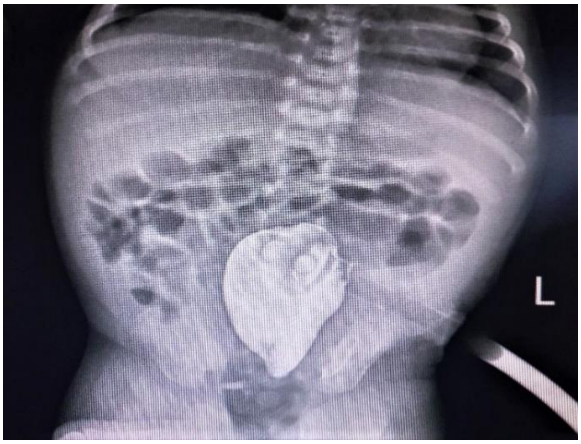

Figure 2. Fistulography radiology in anterior posterior view

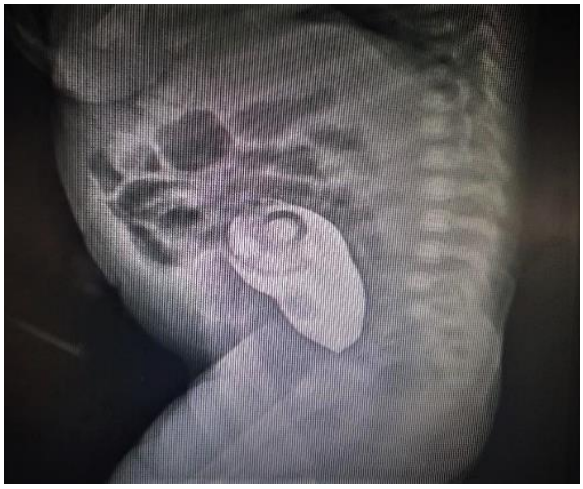

Figure 3. Fistulography radiology in lateral view

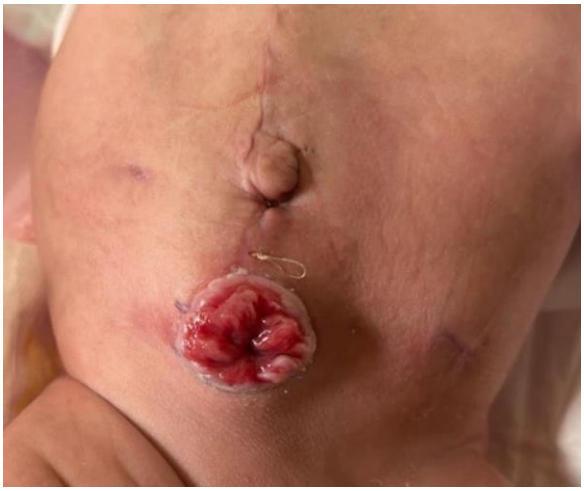

Figure 4. Vesicostomy for neonate

Two days after admission to the NICU, breast milk was started for the baby at five cc every three hours, and the baby was monitored regarding feeding tolerance. The amount of milk increased over time. The neonatal Sucking was weak and hypotonic. Sucking practice was done for the neonate. Also, body positioning and massage are done to increase muscle tone. Occupational therapy is performed once a day for the baby. Two weeks after hospitalization, the baby had secretions from the drain area, and thus, the drain was removed, and culture, smear, and analysis of the fluid from the drain and other parts of the baby's body were sent, shown in Table 2. Lumbar puncture was also performed and in CSF fluid, RBC=2880mm^3/dl, glucose=45mg/dl, protein <1mg/dl, and WBC=0mm^3/dl were reported. After removing the drain, appropriate antibiotics and amphotericin B were started for the baby. This treatment continued for two weeks until the results were negative. After removing the drain, the baby had hydrometrocolpus again.

Moreover, finally, at the age of 34 days, a reconstructive surgery was performed for the baby. The description of the operation was as follows: first, after prep and drape, the baby was put under general anesthesia, then cystoscopy was performed in the lithotomy position, and no orifice was observed in the urethra. Furthermore, there were no traces of vagina and hymen in Nod. A suspicious orifice appeared near the bladder neck and attempted cannulation without success. The bladder was completely deviated to the right side. Then, a midline abdominal incision was performed, an enterovision was performed, and the uterus and ovaries were observed. The vagina was opened, and a Petzer's tube drainage 14 was placed inside the vagina for the baby. A vesicostomy (Figure 4) with Vicryl was installed for the baby, and the abdominal wall was repaired. After the operation, the condition of the baby was stable, the drain did not secrete, and urination continued through the vesicostomy. The abdomen was not distended, and the patient's secretions from the drain were clear.

The baby was discharged with good general condition, normal tests, and stable hemodynamics without bleeding or purulent discharge around the vasicostomy. The parents of the baby were advised to visit the nephrology, infectious, and neonatal clinic on an outpatient basis 48 hours after discharge in connection with the continuation of drug recommendations, emergency symptoms, and advice on their occurrence.

Table 2. Discharge cultures in neonate

Culture site	Discharge type	Sensitive	Resistance
Vaginal	klebsiella Pneumoniae	Colistin	Amikacin, Ampcilin, Cefepim, Ciprofeloxacin, Ceftazidime, Cefotaxime, Co-trimoxazole, Gentamycin, Imipnem
Urine	Mixed gram positive cocci & gram negative bacilli		
Iv line	klebsiella Pneumoniae	Colistin	Amikacin, Ampicillin, Cefepime, Cefazolin, Ciprofloxacin, Ceftazidime, Cefotaxime, Co-trimoxazole, Gentamycin, Imipenem, Piperacillin
Eye	No growth	-	-
pharynx	No growth	-	-

Ethical Approval

This study was conducted under the ethical principles of the World Medical Association (WMA) declaration of Helsinki (DoH-Oct2013). Necessary information was provided and Informed written and verbal consent was obtained from parents.

Discussion

MRKH syndrome is a very heterogeneous phenotypic and genetic disorder with a prevalence of 1:4500 female infants. Congenital abnormalities of the genital tract are rare. Most cases are sporadic, but analysis of the few reported familial cases suggests autosomal dominant inheritance with reduced penetrance (5). Various reports in the literature regarding the relationship between MRKH sequence and different abnormalities and age groups (14, 15). However, to the best of our knowledge, only one article presents a case of an infant with MRKH (4).

All patients with MRKH syndrome should undergo (ultrasonography, magnetic resonance, and urography) to identify possible abnormalities related to MRKH syndrome. In our neonate, related renal was detected by pelvic and abdominal ultrasound. Fistulography radiology was determined, and the necessary measures were taken for the patient. The cause of MRKH syndrome is unknown, but it is believed that fetal growth stops in the sixth or seventh week of pregnancy. Because the mesonephros (which give rise to the kidneys), the Müllerian ducts, and the skeleton all originate in the mesoderm, it is believed that a deleterious event occurs at this stage of pregnancy that leads to the abnormalities seen in MRKH syndrome (16).

Deciding which surgical procedure to perform for patients is often based on the surgeon's experience and personal preference. It is better to advise the patient to refer to specialized centers because the initial surgery has the highest probability of success (17). Numerous studies have shown that subsequent surgeries increase the possibility of complications caused by surgery, including damage to the surrounding organs (18).

Although more information is still needed about the etiology and management of MRKH, progress has been made in the past decades regarding efficient diagnostic methods and appropriate medical management. More non-surgical and surgical methods should be evaluated to manage this disease. Treatment in childhood or early adolescence is not recommended due to the unacceptable rate of complications and the need for full understanding and participation of the patient for optimal results. Continuous monitoring of the mental health of these patients should be considered (19). There is consensus among pediatric surgeons, pediatric urologists, and gynecologists regarding the avoidance of vaginoplasty for girls with MRKH in childhood. Furthermore, long-term follow-up has shown that vaginas created in childhood may be associated with a high error rate, and additional procedures are needed to create a functional vagina in later years. It is recommended that any procedure to create a functional vagina be postponed until mid-to-late adolescence when the patient can easily make decisions for herself (17).

The increase in the number of cases in familial aggregates suggests the existence of a genetic cause for this disease. The transmission mode is most likely an autosomal dominant trait with incomplete penetrance and variable expression (16).

Conclusion

In this case report, we present a rare cooccurrence of congenital incomplete development of Müllerian structures (uterus, fallopian tubes, proximal vagina) in a neonate. Early recognition of these conditions, followed by timely intervention, can significantly improve clinical outcomes. The multidisciplinary approach and long-term follow-up can improve the situation.

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Conflicts of interest

The authors declare no conflicts of interest.

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