

Case Reports

Murcs Association: A most severe form of Mayer-Rokitansky-Küster-Hauser Syndrome, case report and literature review

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BACKGROUND

Mayer-Rokitansky-Küster-Hauser syndrome (MRKH) is a congenital abnormality of sexual development characterized by an aplastic or hypoplastic uterus, as well as the absence of the cervix and the upper third of the vagina. It may be limited to the reproductive tract (MRKH type 1), or in association with abnormalities of the extragenital tract, usually of renal and skeletal origin (MRKH type 2). The presence of a pattern of multiple anomalies has been described, specifically characterized by aplasia of the Müller ducts (MU), renal aplasia (R), and alterations of the cervicothoracic somite (CS), which has been called the MURCS association.

METHODOLOGY

A search was performed in the Medline database via PubMed using the following terms: “Mayer-Rokitansky-Küster-Hauser Syndrome”, “Mullerian anomalies”, “genetics of agenesis/hypoplasia of the uterus and vagina”, “uterine cervical aplasia and agenesis”, from 1979 to 2023, a total of 316 studies were found, 58 studies were selected that included women with a diagnosis of MRKH or MURCS association.

CASE REPORT

A 34-year-old woman attends a gynecologist evaluation presenting primary amenorrhea, with external genitalia with normal development, but has multiple spinal abnormalities. The image reports the absence of the uterus and the superior two-thirds of the vagina, renal aplasia, scoliosis, and cervical, thoracic, and lumbar spinal abnormalities.

CONCLUSIONS

Mullerian abnormalities are a set of abnormalities of sexual development in which the development of the uterus, fallopian tubes, and vagina are mainly affected. Within this group, there is MRKH syndrome. In these variants of GREB1L (estrogen growth regulation gene in breast cancer type 1 gene), variants have been reported in familial cases of bilateral renal agenesis. Establishing the cause of these clinical entities is controversial, making it difficult to deny or affirm whether the atypical forms of the MRKH syndrome and the MURCS association belong to the same phenotypic spectrum originating from common or related causes or simply different entities.

BACKGROUND

MRKH syndrome is a congenital anomaly characterized by an aplastic or hypoplastic uterus, as well as an absence of the cervix and the upper third of the vagina,¹ affecting approximately 1 in 5,000 women.² It is the second most com-

mon cause of primary amenorrhea.³ Consequently, the diagnosis is usually made around puberty.⁴

As part of Müllerian duct agenesis, the phenotypic expression of MRKH syndrome may be limited to the reproductive tract (MRKH type 1), or in association with extragenital tract anomalies, usually of renal and skeletal origin (MRKH type 2). The presence of a pattern of multiple

anomalies has been described, specifically characterized by aplasia of the Müllerian ducts (MU), renal aplasia (R), and alterations of the cervicothoracic somite (CS), which has been called the MURCS association (an acronym for its acronym in English).⁵ It occurs between 10% and 32% of cases and is classified as the most serious form of presentation of MRKH type 2.⁶

Patients with MRKH syndrome develop functional ovaries, complete external genitalia, and regular secondary sexual characteristics.⁷ They have a karyotype of 46,XX, and typical female development of external genitalia and secondary sexual characteristics. Despite the generally normal development and function of the ovaries, women with MRKH syndrome often present with primary amenorrhea.⁸ Clinical examination usually reveals a normal female phenotype with breast development, axillary and pubic hair, and normal external genitalia.⁹

In this article we present the case of a patient who was initially classified as having MRKH syndrome; however, due to the particular findings found within the approach, it was concluded that she presented an extremely rare congenital anomaly. The objective of this review is to evaluate the literature available in electronic databases, including case series, incidence reports and diagnostic approach, with the aim of expanding knowledge regarding this condition.

CLINICAL CASE

A 34-year-old patient, who attended the Gynecology evaluation for the first time, reported primary amenorrhea, as well as the recent onset of active sexual life with limitation in penetration and dyspareunia. Relevant history included a premature, natural birth with low birth weight and low height for the gestational age. Additionally, the patient was breastfed.

She presented slow normal pondo-stature psychomotor development compared to her siblings. She reported apocrine activity at 13 years of age, telarca-adrenarca-pubarch between 13-14 years of age, and very good interpersonal relationships and school achievement. She denied medical, chronic or degenerative diseases. She denied allergies, history of transfusions, chronic consumption of medications, drug addictions as well as surgical interventions. Additionally, she reported first and second-degree relatives without significant medical diagnosis.

The physical examination found that the patient weighed 63 kg, height 1.40 m (father 1.70 m and mother 1.65 m), and vital signs within normal parameters. On general inspection, there were no characteristic facies and no craniofacial alterations. However, the head was not centered to the rest of the body and the left scapula presented lower than the right. She had shoulder asymmetry, a shortened thorax, and an Adams sign with a shortened right hemithorax. She had obvious spine curvature and developed anatomically normal breasts and axillary hair. There were no abnormalities on static and dynamic inspection.

Exploration of external genitalia, according to age and sex, found pubic hair present and normally distributed, a hyperpigmented labia majora that was anatomically nor-

mal. Vaginal examination found a shortening in length, approximately 3 cm, with no palpable cervix; the bimanual examination without delimiting the uterus or adnexa. Symmetrical extremities were without distal neurovascular compromise. An endocavitary ultrasound was performed in which no uterus was observed; however, we did observe images that suggest ovaries.

According to the protocol, general laboratory studies, thyroid profile and gynecological profile were requested to assess endocrine function. Additionally, we requested office studies based on the pelvic ultrasound, computed tomography (CT) and peripheral blood karyotype. An appointment was made with a report of results for evaluation. She subsequently attended with laboratory studies shown in [TABLE 1](#). Diagnoses were integrated due to findings of hypothyroidism and hyperprolactinemia. In the study, treatment was initiated by the endocrinology service based on Levothyroxine 50 mcg per day, supported by the fact that in hypothyroidism, due to the decrease in thyroid hormones increases the levels of thyrotropin-releasing hormone (TRH), generating an increase in thyroid-stimulating hormone (TSH). Additionally, hyperplasia of lactotroph cells occurs and as a consequence hyperprolactinemia¹⁰; this is due to the stimulatory effect of TRH on lactotroph cells, or due to a reduction in hypothalamic dopamine content secondary to compression of the pituitary stalk.¹¹

After analyzing the tomographic reports, the findings described in each of them were found in the cervical vertebrae ([IMAGE 1](#)), vertebral column ([IMAGE 2](#)), and abdomen ([IMAGES 3](#) and 4). Karyotype report described in [IMAGE 5](#).

With the above, diagnoses of: MURCS association (uterine, tubal, cervical and upper two-thirds of the vagina aplasia, renal aplasia and spinal dysraphism in cervical and lumbar vertebrae, as well as scoliosis), hypothyroidism and hyperprolactinemia were integrated. The patient was questioned about her reproductive desire; however, she did not want it. She was sent to an outpatient spine clinic for evaluation, and to nephrology for close and educational follow-up. She was scheduled for an appointment in three months with a new hormonal profile, for possible modification of the established treatment, and to consider starting a dopamine agonist.

MATERIALS AND METHODS

A search was performed in the Medline database via PubMed using the following terms: "Mayer-Rokitansky-Küster-Hauser Syndrome", "müllerian anomalies", "genetics of agenesis/hypoplasia of the uterus and vagina", "uterine cervical aplasia and agenesis". The search was limited by the following filters: "Case Reports", "Review", "Systematic Reviews", and "Books and Documents", "Spanish and English", from 1979 to 2023, in total 316 studies were found. Editorials, reviews, and duplicate articles were excluded, mainly due to their low level of trust and veracity. 58 studies were selected that included women with a diagnosis of MRKH or MURCS association.

TABLE 1. LABORATORY STUDY REPORT.

BLOOD CHEMISTRY	
GLUCOSE	78 mg/dL
UREA	21.3
BUN	10.0 mg/dL
GFR	117.41 mL/min
SERUM CREATINE	0.63 mg/dL
URIC ACID	3.5 mg/dL
BLOOD BIOMETRY	
TOTAL LEUKOCYTES	4.9 10 ³ /uL
HEMOGLOBIN	15.1 g/dL
HEMATOCRIT	44.3 %
GYNECOLOGICAL HORMONAL PROFILE	
FSH	4.9 mIU/mL
LH	6.5 mIU/mL
PROLACTIN	96.4 ng/mL
ESTRADIOL	144.9 pg/mL
PROGESTERONE	16.5 ng/mL
TUMOR MARKERS	
CEA	1.6 ng/mL
AFP	3.1 ng/mL
CA 19-9	23.7 U/mL
CA 125	19 U/mL
PERFIL TIROIDEO	
T3 L	3.2 pg/mL
T3 T	124.6 ng/dL
T4 L	1.9 ng/dL
T4 T	8.4 ug/dL
TSH	2.91 mIU/L

BUN: Blood Urea Nitrogen, GFR: Glomerular Filtration Rate, FSH: Follicle-Stimulating Hormone, LH: Luteinizing Hormone, CEA: Carcinoembryonic Antigen, AFP: Alpha-feto-protein, T3L: Triyodotironina Free, T3T: Triiodothyronine Total, T4L: Free Thyroxine, T4T: Total Thyroxine, TSH: Thyroid Stimulating Hormone.

DISCUSSION

Among the most frequent causes of primary amenorrhea are gonadal dysgenesis and Müllerian aplasia, the latter can occur in isolation or be accompanied by abnormalities in various organs and systems.¹² A severe form of MRKH type 2 syndrome is the MURCS association, which It is characterized by abnormalities of Müllerian and renal development and involvement of the cervicothoracic vertebrae.¹³

Most patients diagnosed with MRKH syndrome present with vaginal agenesis with absent or hypoplastic uterus (96%), renal agenesis/ectopia (88%), vertebral anomalies between C5 and T1 (80%), including fused vertebrae and hemivertebrae, and short stature has also been described (60%).⁵ Malformations that include a double kidney have also been described, and within skeletal anomalies, scoliosis and hip dysplasia,¹⁴ characteristics that are present in the case presented. MRKH syndrome may be associated

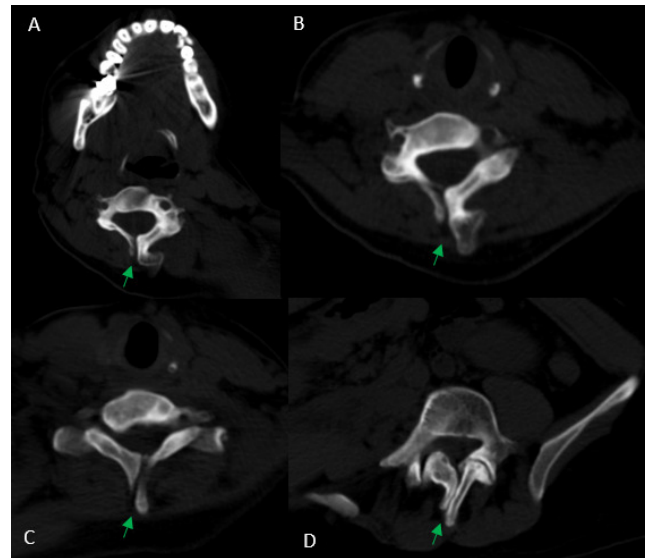


IMAGE 1. COMPUTED TOMOGRAPHY IN AXIAL SECTION OF CERVICAL (A-C) AND LUMBAR (D) VERTEBRAE, THERE ARE CLOSURE DEFECTS (GREEN ARROW) IN THE POSTERIOR ELEMENTS, SUGGESTIVE OF SPINAL DYSRAPHISM.

with hearing defects, and in rare cases, cardiac (atrial septal defect) and digital anomalies such as syndactyly, polydactyly, or ectrodactyly may occur.⁹

Other clinical features of MRKH syndrome include short vagina, which can lead to dyspareunia if penetrative vaginal intercourse is attempted, cyclical abdominal or pelvic pain, and uterine factor infertility. The main challenges in the clinical care of these patients involve addressing reproduction, as well as the ability to have penetrative vaginal intercourse.¹⁵

DEVELOPMENT OF MESODERMAL TISSUES

Tissues affected by MRKH syndrome share a common embryonic origin and genetic programs. Proper mesoderm development is critical, as the reproductive tract, kidneys, skeleton, and heart, the organs most commonly affected by MRKH, originate from this germ layer. It has been suggested that the early differentiation of these organs is regulated mainly by the WNT gene,¹⁶ bone morphogenetic proteins (BMPs),¹⁷ and fibroblast growth factor (FGF).¹⁸ During gastrulation, activation of the Tcf-3 gene by β -catenin signaling is a key event that activates specific pathways that drive mesoderm differentiation into paraxial, intermediate, and lateral mesoderm.¹⁹

The female reproductive system in humans is derived from the Müllerian or paramesonephric (MD) ducts, which give rise to the uterus, cervix, and upper two-thirds of the vagina around the fifth to sixth week of gestation.²⁰ The mesoderm Paraxial (PM) gives rise to muscles and most of the skeleton. The entire urogenital system, including the reproductive tract and kidneys, is derived from the intermediate mesoderm (IM). Finally, the lateral mesoderm (LM) differentiates into the heart, vascular system, smooth mus-

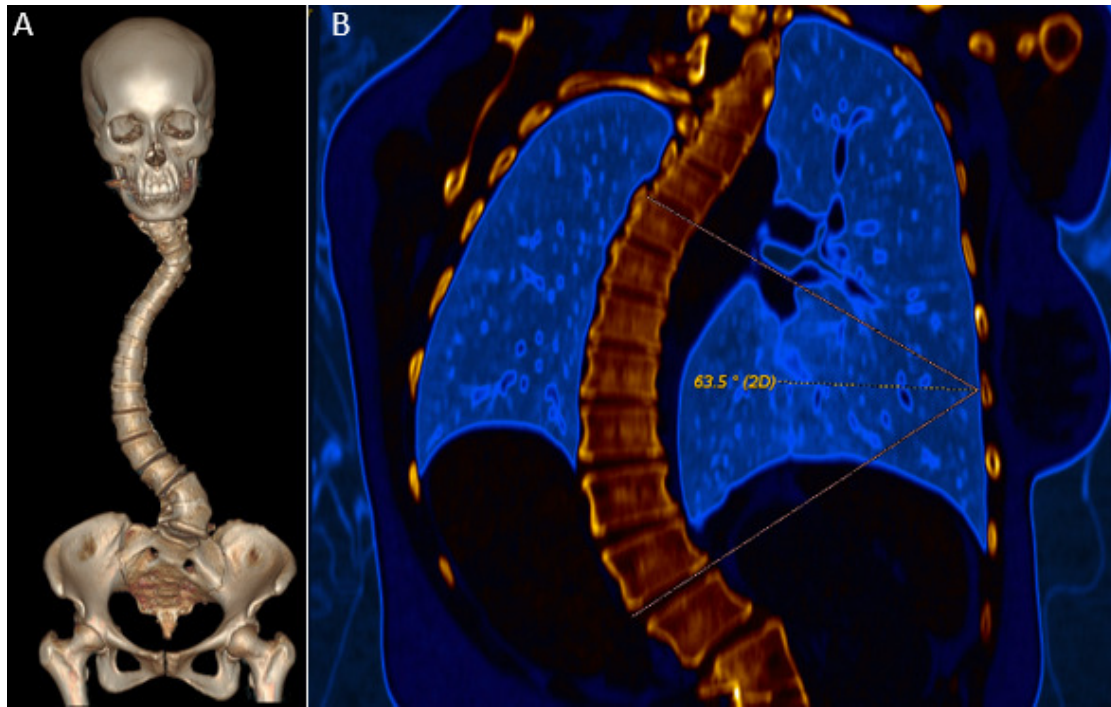


IMAGE 2. A) VOLUMETRIC RECONSTRUCTION OF THE AXIAL SKELETON B) COMPUTED TOMOGRAPHY IN CORONAL SECTION, A COBB ANGLE OF 63.5 DEGREES WAS OBSERVED, SUGGESTIVE OF SCOLIOSIS.

cles, and limb skeleton (FIGURE 1).²¹ Like all other embryonic development processes, the development of the Müllerian ducts is regulated by a coordinated and sequential interaction of molecular pathway networks (MPNs). MPNs consist of transcription factors that regulate the expression of regulatory and effector proteins in carefully directed developmental programming.²²

DEVELOPMENT OF THE NEPHRO-URINARY SYSTEM

The first event during the development of the genitourinary tract is the formation of a ductal system that forms the primordium of the future urinary system. This begins in humans with the appearance of the pronephric duct at the end of the third week of gestation. These ducts migrate caudally to form the Wolffian ducts (WD) in humans around week 4 of gestation.²⁴ The development of the Wolffian ducts is a necessary event for the differentiation of the female reproductive tract. The Wolffian ducts form mesonephric tubules in the adjacent mesonephric mesenchyme. In several species of mammals, these tubules perform the functions of an embryonic kidney. In humans, this occurs for only a few weeks before the caudal part of the Wolffian ducts gives rise to the ureteric bud (UB), which invades the surrounding mesenchyme and forms the metanephros, the future permanent kidneys.²⁵

The WNT/ β -catenin pathway is critical in Wolffian duct development and is required to maintain Wolffian duct epithelium in a precursor state. The WNT4 gene is expressed in the metanephric mesenchyme and acts as an inducer of

mesenchymal to epithelial transmission necessary for kidney development.²⁶

DEVELOPMENT OF THE FEMALE REPRODUCTIVE SYSTEM

After the development of Wolffian ducts, Müllerian ducts (MD) form in a process characterized by three main but poorly understood phases.²⁷ The first begins with the activation of BMP signaling and the induction of the expression of transcription factors. Pax2 and Pax8 in the cranial epithelium adjacent to the Wolffian ducts²⁸ The BMP/PAX2 axis, together with FGF signaling, activates the expression of the transcription factor LHX1 in the coelomic epithelium, stimulating the specification of Müllerian duct epithelial cells²⁹ In the second phase corresponding to invasion, the expression of WNT4 from the mesonephros or coelomic epithelium induces the invagination of these specified cells. Elongation is the third phase regulated by inductive factors from the Wolffian ducts, including WNT4 and WNT9B.³⁰

Tissues affected by MRKH syndrome share common genetic and embryonic programs. Furthermore, early differentiation of these organs is primarily regulated by the same major pathways,¹⁶ bone morphogenetic proteins (BMPs),¹⁷ and fibroblast growth factor (FGF).¹⁸

Both deletion and overexpression of a stabilized form of β -catenin result in urogenital anomalies ranging from renal hypoplasia to agenesis.²² Expression of Pax2 and Pax8 ensures renal lineage specification and survival²⁵; PAX2 induces expression of critical transcription factors, including Lhx1, which is required for Wolffian duct elongation and

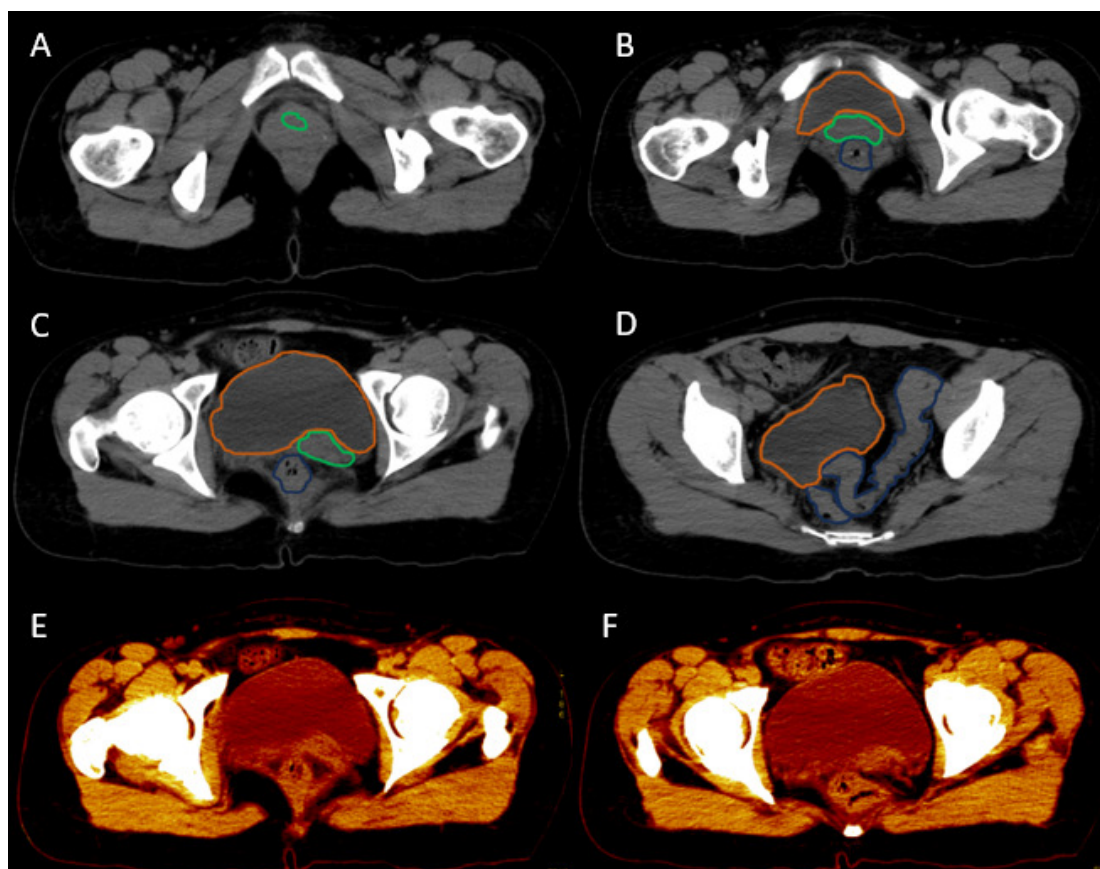


IMAGE 3. SINGLE-PHASE COMPUTED TOMOGRAPHY, AXIAL SECTIONS. A-D: THE LOWER THIRD OF THE VAGINA (GREEN LINE), BLADDER (ORANGE LINE) AND RECTUM/SIGMOID (BLUE LINE) ARE IDENTIFIED; THE CONGENITAL ABSENCE OF THE UTERUS AND THE UPPER TWO-THIRDS OF THE VAGINA IS STRIKING. E-F: THE SAME FINDINGS ARE IDENTIFIED WITH THE CONTRAST PROVIDED BY THE COLOR MAP.

formation of tubular structures in the developing kidney,³⁰ and the *EMX2* gene, which regulates successful renal morphogenesis.³¹

The initiation and invagination of the Müllerian ducts appears to be independent of the Wolffian ducts. However, Wolffian ducts are necessary for Müllerian duct elongation.³² Further differentiation of Wolffian and Müllerian ducts into sex-specific reproductive tracts depends on gonadal development ([FIGURE 2](#)). In the male, the *SRY* gene on the Y chromosome triggers a signaling cascade that leads to the development of testes, which produce testosterone, stimulating the differentiation of Wolffian ducts in the male reproductive tract, and anti-Müllerian hormone (AMH), which causes degeneration of the Müllerian ducts.³³ In females, the absence of *SRY* results in the development of the ovaries through the action of specific genes, including *Foxl2* and *WNT4*. Lack of testosterone and AMH causes regression of the Wolffian ducts and increased differentiation of the Müllerian ducts in the female reproductive tract.³⁴

The anterior regions of the Müllerian ducts develop into the oviducts and uterus. At the same time, the caudal portions fuse in the urogenital sinus to form the uterovaginal duct, giving rise to the cervix and upper vagina.³⁵

GENETIC ETIOLOGY OF MRKH SYNDROME

An alteration of the different pathways involved in the association of developmental abnormalities of the Müllerian ducts with defects in other organs is suggested, not only in sex differentiation but also in the embryonic development of structures derived from the intermediate mesoderm. This syndrome is characterized by a heterogeneous etiology and a pattern of inheritance. Sporadic and familial cases have been reported; studies in familial cases support the existence of hereditary predisposition. The results of the most studied familial cases seem to comprise an autosomal dominant mode of transmission with sex-limited expression (female) and incomplete penetrance; however, no clear pattern of inheritance has been identified, mainly due to heterogeneity of inheritance pattern and incomplete penetrance.³⁶

The identification of germline genetic alterations in a few patients, as described regarding discordant twins for the MRKH phenotype, supports the sporadic nature of the disorder and the lack of heritability. In fact, epigenetic or environmental factors could be the basis for the spontaneous appearance of congenital uterine malformations.³⁷

This etiological diversity of MRKH is also evidenced by the occurrence of multiple genetic and genomic lesions in affected patients. The genes that cause MRKH syndrome

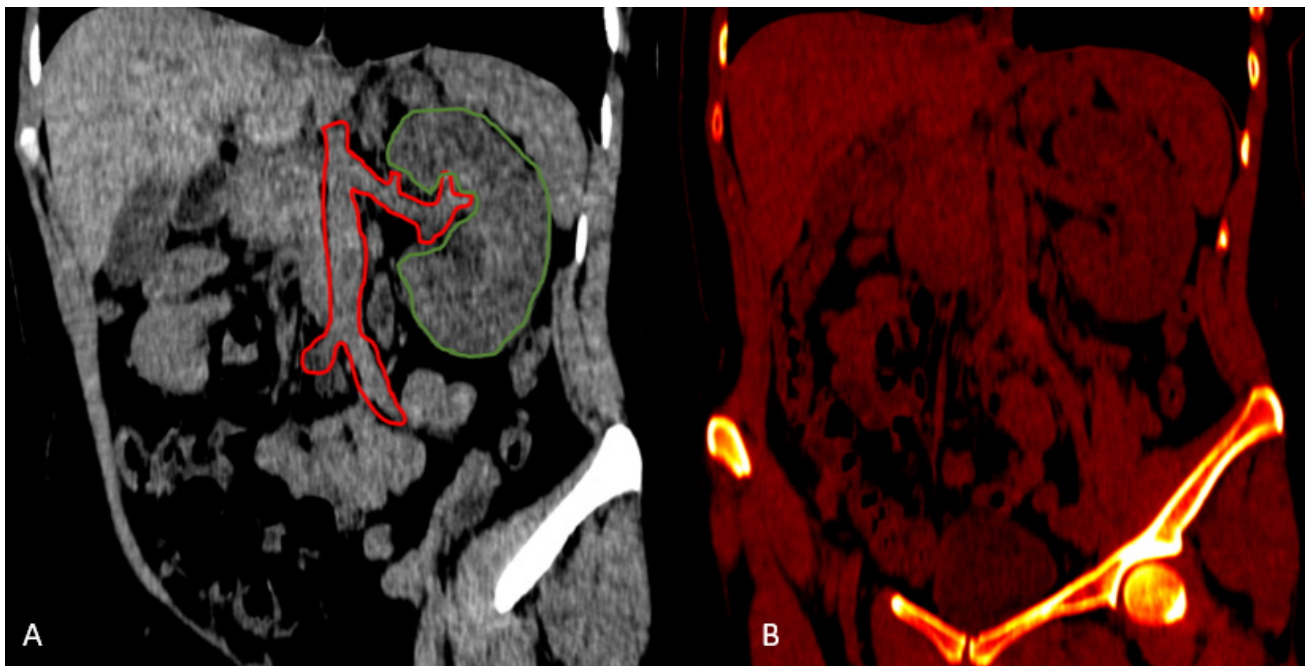


IMAGE 4. SINGLE-PHASE COMPUTED TOMOGRAPHY, CORONAL SECTION; (A) THERE IS RIGHT RENAL AGENESIS, THE RED LINE SHOWS THE AORTA WITH THE LEFT RENAL ARTERY, AS WELL AS THE LEFT KIDNEY (GREEN LINE) WITH COMPENSATORY HYPERTROPHY. B) THE SAME FINDINGS ARE SEEN WITH THE COLOR MAP.



IMAGE 5. KYOTYPE 46,XX. PERIPHERAL BLOOD.

Method: cell culture with mitotic stimulant. Standard chromosome analysis with GTG bands. ISCN Nomenclature 2020.

Female karyotype with no numerical alterations observed. An increase in the satellite of the short arm of chromosome number 13 is observed, considered as a structural variant which has no clinical correlation (marked with a blue arrow).

have been identified according to their location within the genomic rearrangements observed in patients. Many other candidates belong to genetic pathways that drive embryonic development or have emerged from studies of animal

models or syndromic conditions in which uterine malformations are a frequent clinical manifestation. A genotype-phenotype correlation for WNT4 mutations has been reported in MRKH patients with hyperandrogenism,

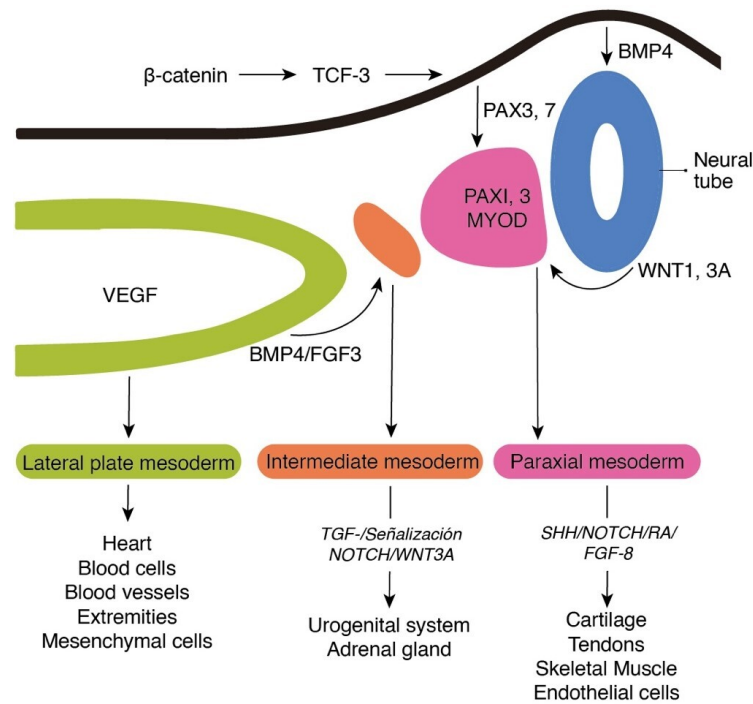


FIGURE 1. MOLECULAR REGULATION OF THE MESODERMAL PATTERN

β -catenin induces TCF-3, which regulates the expression of transcription factors and regulatory proteins, including Pax3,7, Bmp4, and Wnt1,3a. These signals lead to the differentiation of the three main components, the lateral mesoderm, the intermediate mesoderm, and the paraxial mesoderm. VEGF expression in the lateral mesoderm (LM) initiates the specification of progenitor cells for the development of the heart, blood vessels, extremities, and mesenchymal cells. LM BMP4/FGF3 signaling stimulates TGF- β /Notch signaling, which activates WNT3a expression in the intermediate mesoderm that drives the urogenital system and adrenal gland development. Neural tube WNT1,3a expression regulates Pax1,3 and MyoD in the paraxial mesoderm. Pax1,3 and MyoD stimulate SHH/NOTCH and RA/FGF-8 signaling to differentiate the paraxial mesoderm into cartilage, tendons, skeletal muscles, and endothelial cells.²³

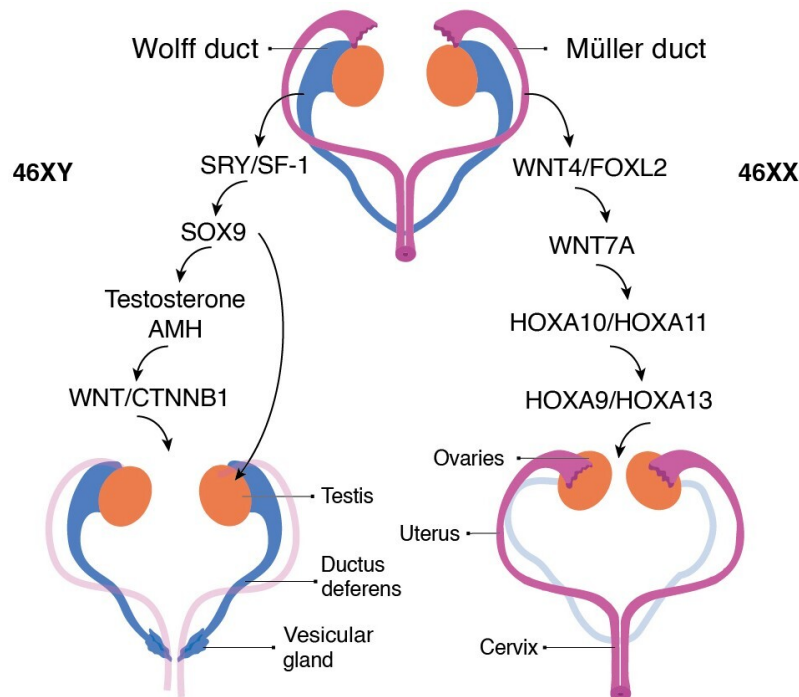


FIGURE 2. MOLECULAR MECHANISM OF SEXUAL DIFFERENTIATION.

Prior to sex determination, each embryo has undifferentiated or bipotential gonads. In men, the Y-bound SRY protein interacts with steroidogenic factor-1 (SF-1) to increase Sox9 expression levels. This drives the differentiation of Sertoli cells and Leydig cells within the testes. Sertoli cells produce anti-Müllerian hormone (AMH) to stimulate MD regression, while Leydig cells produce testosterone that stabilizes WD development through signaling, including WNT/ β -catenin. In women, the expression of Foxl2 inhibits the expression of Sox9. As the gonads develop in the ovaries and male factors do not occur, WDs degenerate and MDs develop in the female reproductive tract under the action of several factors, including WNT7A and members of the HOX family.²³

TABLE 2. GENES INVOLVED IN THE DEVELOPMENT OF THE FEMALE REPRODUCTIVE TRACT (FRT) FROM STUDIES IN MOUSE MODELS AND CANDIDATE GENETIC VARIATIONS FOUND IN MRKH SYNDROME.

GEN	TRF PHENOTYPE	VARIANTS	REFERENCES
WNT4	Renal dysgenesis, agenesis of TRF	p.L12P;p.R83C	39
WNT5A	Vaginal agenesis, uterine agenesis	-	40
WNT7A	Homeotic transformation from the oviduct to the uterus and from the uterus to the vagina	-	41
WNT9B	TRF dysgenesis	p.Q326Ter	42
CTNNB1	Uterine hypoplasia	-	43
LRP10	-	dup 14q11.2;p.D419N	44
LHX1	Uterine hypoplasia	del 17q12	45
HNF1B	-	del 17q12;p.C1027T	46
HOXA10	Homeotic transformation of the uterus into an oviduct	p.Y57C	47
HOXA11	Partial homeotic transformation from uterus to oviduct	-	48
EMX2	Renal and TRF agenesis	p.E142X	49
TBX6	-	del 16p11.2, c.621+1G>A	42
SHOX	-	-	50
PRKX	-	dup Xp22.33	51
PAX8	TRF dysgenesis	del 2q12.1q14.1, p.V53AfsTer24, c.25+1G>T, p.Y66TfsTer10, p.R108Ter, p.S181F, p.V89A, p.Ser79Cys	42
GREB1L	Renal and TRF agenesis	p.Q743Rfs*10], p.C646R, p.V1324Lfs*34, p.E93K, p.W235C	52
DACH1/2	Agenesis of TRF	-	53
DOCK4	-	p.V770M; dup 7q31.1	44

suggesting a clinically and genetically distinct MRKH sub-type associated with this gene, likely involved in androgen regulation.³⁸

Several candidate genes have been proposed for genetic analyses of women affected by MRKH syndrome. A few are mentioned in [TABLE 2](#), whose fundamental role in the development of the urogenital tract has been established.

Among the genes associated with the development of MRKH syndrome is the estrogen growth regulation gene in the androgen-regulated breast cancer type 1 gene (GREB1L), which is a coactivator of the retinoic acid receptor (RAR) gene, whose activation regulates the retinoic acid pathway,⁵⁴ and which has been shown to trigger the differentiation of Müllerian epithelial cells and establish the boundary between the uterus and vagina⁵⁵; therefore, GREB1L plays an indispensable role in the development of embryonic metanephrosis and the genital tract.⁵⁶

Many patients diagnosed with Rokitansky syndrome manifest the MURCS association because the pattern of pathophysiological development is similar in both conditions; therefore, patients with Rokitansky syndrome should be studied to detect the characteristic alterations of the MURCS association and avoid underdiagnosis.⁵⁷

MANAGEMENT OF PATIENTS WITH DIFFERENT MÜLLERIAN ANOMALIES

Müllerian anomalies are associated with high rates of preterm delivery, premature rupture of membranes, fetal malpresentation, and perinatal mortality.⁵⁸ There is insufficient evidence to suggest that Müllerian anomalies are associated with infertility, as similar rates have been reported compared to the general population.⁵⁹ However, in patients diagnosed with MRKH syndrome, specifically MURCS association, uterine surrogacy, and more recently the implementation of uterine transplantation, seem to be the only feasible options for patients with this pathology. However, the latter practice is widely debated.

Depending on the type of presentation diagnosed and the severity of the findings, part of the treatment of patients with Mayer-Rokitansky-Küster-Hauser syndrome includes psychological counseling for them and their families since this diagnosis has repercussions on future reproduction.⁶⁰ The treatment is mainly aimed at creating a neovagina that allows sexual intercourse. Surgical and non-surgical treatments are available. Surgical options include graft placement using the McIndoe⁶¹ or Vecchiotti⁶² procedure. The mechanical approach includes the application of dilators, as described in Frank's procedure.⁶³

Differential diagnoses include androgen insensitivity, the presence of a transverse vaginal septum, isolated distal vaginal agenesis, and imperforate hymen.⁶⁴

CONCLUSIONS

Müllerian anomalies are a set of abnormalities of sexual development during the embryonic period. Within this group of abnormalities is MRKH syndrome, in which it is suggested that it is a defect of mesodermal origin. The genetic etiology of MRKH syndrome is not clear, nor is it one hundred percent established.

Some authors agree on separating the MRKH syndrome from the MURCS association, and others consider the MURCS association as a phenotypic variant of the MRKH syndrome when abnormalities in other organs accompany it. The first clinical feature is usually primary amenorrhea. The main challenges in the clinical care of these patients involve addressing reproduction as well as the ability to have penetrative vaginal intercourse. As for the fertility of people with MRKH, surrogacy is an option.

Although this syndrome is not uncommon, subtype 2 of MRKH syndrome is, so the disclosure of a complete clinical case is important when trying to understand and address it. However, until the cause of these clinical entities is established, it will be difficult to deny or affirm whether the

atypical forms of MRKH syndrome and the MURCS association belong to the same phenotypic spectrum originating from common or related causes or are simply different entities.

AUTHORS' CONTRIBUTION - [CREDIT](#)

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