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Blood Karyotyping, Anti-Müllerian Hormone Level, SRY Gene, and Clinical Evaluation in Patients Reared as Female Presented with Müllerian Duct Agenesis

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ABSTRACT

Background: A range of congenital abnormalities in phenotypic females presenting with primary amenorrhea are represented by Müllerian Duct Agenesis (MDA), which includes Mayer Rokitansky Küster Hauser (MRKH) syndrome. It's crucial to distinguish these illnesses from other Disorders of sex Developments (DSDs) conditions to diagnose, treat, and provide psychosocial care.

Aim: The present study was carried out to investigate the correlation between blood karyotyping, Anti-Müllerian Hormone (AMH) level, Sex-determining Region of Y chromosome (SRY) gene, and clinical evaluation in patients reared as females and presented with MDA to make an accurate diagnosis and direct treatment plans.

Method: This prospective case-control study assessed karyotype, AMH levels, the presence of the SRY gene, and clinical characteristics in 20 females with MDA and 20 age-matched healthy controls (categorized into four groups on age basis). The STROBE guidelines for reporting observations have been adhered to in the study design.

Result: AMH levels showed age-related trends, with elevated values in infants and adults. Two-way ANOVA revealed significant effects of group ($F(1,47) = 42.70$, $p < 0.0001$), age ($F(3,47) = 8.70$, $p < 0.001$), and their interaction ($F(3,47) = 8.89$, $p < 0.001$). Point-biserial correlation revealed a significant positive association with an abnormal karyotype ($r = 0.62$, $p = 0.003$) and a high positive association between AMH and SRY positivity ($r = 0.83$, $p < 0.00001$). These findings indicate that combined genetic and hormonal markers effectively distinguish MDA patients from controls. Moreover, the absence of Müllerian structures despite maintained ovarian function was confirmed in patients with the 46, XX karyotype,

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negative SRY, and normal AMH, which were consistent with MRKH. An androgen receptor deficiency led to the diagnosis of Complete Androgen Insensitivity Syndrome (CAIS) in cases with the following characteristics: female phenotype, high AMH, SRY positive, absence of Müllerian structures, and 46, XY karyotype. Turner syndrome, which manifested as gonadal dysgenesis and low AMH, was confirmed in a subset of individuals with a 45, X karyotype and negative SRY. These differences demonstrated how karyotyping, AMH levels, and SRY tests can work together to provide differential diagnosis.

Conclusion: In patients raised as females with primary amenorrhea, blood karyotyping, AMH level, and SRY gene analysis are trustworthy methods for distinguishing between MDA, MRKH, CAIS, and Turner syndrome. Therefore, correct categorization guarantees the right psychological and social support in addition to directing clinical treatment, such as gonadectomy, hormonal therapy, or fertility counselling. For optimal long-term outcomes, multidisciplinary intervention at an early stage is advised.

Keywords: *Müllerian Duct Agenesis, Case–control study, Karyotype analysis, SRY gene, Anti-Müllerian Hormone, Congenital reproductive anomalies*

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1. INTRODUCTION

Müllerian duct agenesis (MDA), or Mayer–Rokitansky–Küster–Hauser (MRKH) syndrome is one of disorders of sex development (DSDs) characterizes failure of the Müllerian ducts to develop into the uterus and upper two-thirds of the vagina, even in the presence of normal ovarian function and a 46, XX karyotype [1]. Although the patients usually exhibit normal phenotypes, they frequently seek medical attention during adolescence because of primary amenorrhea. While the incidence is thought to be 1 in 4,500–5,000 live births of females, the first reported prevalence was of vaginal agenesis by John Engstad in 1917 [2]. Recently, [3] a study on a Danish cohort was carried out by looking at medical records and searching the National Danish Patient Registry from 1994 to 2015. It was found that the prevalence was 1 MDA patient in 4982 (95% CI: 4216-5887). live female births, with 138 patients born between 1974 and 1996 included in the 168-patient cohort [3]. However, as the two studies were carried out on European populations, it is unclear if the prevalence differs in other populations.

Informatively, it is commonly known that between the fourth and fifth weeks of pregnancy, human gonadal ridges, which are initially comparable in both sexes, start to form. At this point, undifferentiated germ cells move to these ridges, where, in response to particular genetic and hormonal triggers, they will eventually develop into either the testes or the ovaries [4]. So, both the Müllerian (paramesonephric) and Wolffian (mesonephric) ducts are present by the sixth or seventh week of fetal development. At this period of pregnancy, several important genes, such as SRY, SOX9, WT1, SF1, WNT4, RSPO1, and DAX1, which direct gonadal differentiation and control the regression or maintenance of these ducts, are necessary for determining the sexual phenotype [5]. This time, multiple molecular steps regulate germ cell growth, migration to the urogenital ridge, and production of either testes (46, XY) in the presence of a Y chromosome or ovaries (46, XX) in the absence of SRY gene. So in females, the lack of SRY gene enhances other gene pathways such as WNT4, RSPO1, and DAX1, which promote ovarian differentiation, Wolffian duct regression, and Müllerian duct development into the female reproductive canal [6].

Disorders of sex Developments (DSDs), such as MDA/MRKH syndrome, appear in early fetal life, usually between weeks 6 and 12 of gestation, when the Müllerian ducts are developing. In MRKH, these ducts do not develop properly or partially regress, resulting in uterovaginal agenesis or hypoplasia, although ovarian development is normal. This happens due to changes in the molecular pathways governing Müllerian duct differentiation, including mutations in WNT4, RSPO1, and other related genes [7].

In line with the literature, the role of SRY gene testing is essential in differentiating MDA syndrome from other DSDs, particularly in patients reared as female but with atypical presentations. Similarly, Chromosome analysis and karyotyping

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remain a gold-standard diagnostic tool to role out chromosomal abnormalities such as Turner syndrome or 46, XY DSDs variants that can mimic MDA [8]. On the other hand, measurement of AMH levels provides valuable insights into ovarian reserve and gonadal function in these patients [9]. In addition, despite breakthroughs in cytogenetic and molecular techniques, diagnostic uncertainty frequently persists in female patients who present with primary amenorrhea and Müllerian duct agenesis. Studies have emphasized the importance of a multidisciplinary approach that includes clinical examination, imaging, hormonal profiling, and genetic analysis for accurate diagnosis and management [10-12]. However, questions remain about the combined diagnostic value of blood karyotyping, AMH levels, and SRY gene analysis in separating real MDA from other overlapping illnesses on the spectrum of Disorders of sex Developments (DSDs).

Thus, the purpose of the current study is to evaluate clinical examinations and lab investigations such as AMH blood levels, chromosome analysis and the presence of SRY gene in female-raised patients who presented with MDA at Al-Azhar University Hospitals. Aiming to improve diagnostic precision, decrease misclassification, and advance knowledge of the underlying pathophysiology of this complicated illness by combining genetic, hormonal, and clinical markers. In the long term, these understandings could help direct future fertility planning, genetic counselling, patient health and psychotic care.

2. MATERIALS AND METHODS

Study setting and design

The present prospective case-control study was conducted at Al-Azhar University Hospitals from January 2024 to December 2024. The study included 39 individuals; 20 patients selected from pediatric surgery and gynecology clinics presented with disorders of sex development, and 19 presumably normal controls. To reduce selection bias, controls were age-matched to cases, and participants were gathered by a successive sampling technique. The study was designed and reported following the STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) guidelines available at http://www.strobe-statement.org to ensure methodological rigor and transparency.

Study selection criteria

The inclusion criteria were DSDs patients aged between 1 to 30 years with female phenotype, females presenting with primary amenorrhea and confirmed absence of uterus ± upper vagina on imaging

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While inclusion criteria for controls are healthy females aged 1–30 years with regular menstruation and no congenital anomalies. On the other hand, patients with a history of gonadal surgery, known endocrine disorders (thyroid dysfunction, hyperprolactinemia, adrenal abnormalities), or refusal to provide informed consent were excluded.

Data collection

After obtaining complete, well-informed consent, all patients were subjected to a comprehensive clinical workup which was performed in the pediatric surgery or gynecology clinics. Physical, clinical, and laboratory analyses were performed on both sets (patient and control). To make the analysis easier, the data were divided into four groups according to participant age range **(Table 1)**.

Table 1: Grouping of participants according to age group

Age Group (years)	Patients (n)	Control(n)
Infants/Young Children (0–5)	6	6
Children (6–12)	3	3
Adolescents (13–18)	6	3
Adults (19+)	5	7
Total	20	19

History taking and Clinical examination

Detailed demographic data and clinical history were obtained from all participants. Physical examination included assessment of secondary sexual characteristics using Tanner staging, evaluation of external genitalia, and pelvic examination when appropriate. Radiological assessment with pelvic ultrasonography or MRI was performed to confirm the absence of the uterus and upper vagina.

Full clinical examination was done to all participants to assess the presence of dysmorphic features, primary and secondary sexual characters, hoarseness or softness of voice, hair distribution, gynecomastia, presence or absence of palpable gonads, cryptorchidism, urethral opening, or any abnormalities involving urogenital sinuses. In addition to taking care of the patient's medical history regarding any tumors or history of previous operations, either related to gonads, suprarenals, or external genitalia.

Laboratory investigations

Chromosome analysis of patients and controls was done by conventional cytogenetic methods employing trypsin G-banding (GTG) technique. Vacutainer Heparinized tubes were used to collect 3 mL of peripheral blood, and routine procedures were followed to prepare lymphocyte cultures then interpretation of the results was done according to the International System for Human Cytogenomic Nomenclature (ISCN)2020.

Samples for serum Anti-Müllerian Hormone (AMH) were taken at random in cases and during the early follicular phase in controls. Using a commercial ELISA kit and the manufacturer's instructions, AMH concentrations were determined. One to four ng/mL was regarded as the reference range for a normal ovarian reserve.

Fluorescence in situ hybridization (FISH) was used to detect the SRY gene. For this purpose, metaphases were analyzed for the presence or absence for expected gene signals verified by applying commercial *CytoCell SRY FISH probe* that was specific for the SRY gene according to manufacturer.

Ethical Considerations

Approval No: [IRB:2527] was granted by local ethical committee, Al-Azhar University Hospitals for the case-control study. To uphold ethical standards, the study prioritized obtaining informed consent from all participants, ensuring their voluntary participation by providing clear information about the research's risks and benefits, and implementing strict data anonymization procedures to safeguard their privacy, All procedures involving human subjects were conducted in accordance with the ethical standards of the responsible ethics committee and in alignment with the principles set forth in the Declaration of Helsinki and its amendments.

Statistical Analysis

The results were presented with the help of Microsoft Office. The mean ± SD and range are used to represent continuous variables like age and AMH levels, whereas counts and percentages are used to represent categorical variables like SRY gene status and chromosomal abnormalities. AMH levels between MDA patients and controls were compared across age groups using a two-way ANOVA, which evaluated the effects of age, group, and interaction. AMH variability and distribution were shown using boxplots. AMH levels and binary variables (abnormal karyotype, SRY positive) were compared using point-biserial correlation. Fisher's exact test or the Chi-square test, when applicable, was used to evaluate the relationships between categorical variables. "Statistically significant" was defined as p-values less than 0.05. Python (SciPy) was used for all statistical analyses, and p-values < 0.05 were considered statistically significant.

3. RESULT

Statistical analyses of diagnostic biomarkers in MDA/MRKH patients

The control group's mean age was 13.10 ± 10.01 years (range: 0-30), whereas the mean age of patients suspected of MDA was 13.45 ± 8.79 years (range: 0-30). The age distribution of the two groups did not differ significantly ($p = 0.91$).

There are clear age-related trends when comparing the measured AMH levels in MDA suspected patients with normal reference values. Since AMH in newborns and young children (0–5 years) is normally below 1 ng/ml, the reported mean of 3.63 ng/ml is quite high, which explains the lack of significance. Outlier values that considerably raise the mean, like 10.98 ng/ml and 8.2 ng/ml, seem to have a major impact on this elevation. The mean result of 0.25 ng/ml in the 6–12 MDA age group suggests diminished ovarian activity and is in line with the expected near-undetectable levels ($p = 0.066$). The average AMH level during adolescence (13–18 years) is 2.14 ng/ml, which is in line with the expected increase that comes with pubertal development. The observed range of 0.55–4.5 ng/ml is in good agreement with the reference values, which are roughly 1.80-2.70 ng/ml. The mean differences between cases and controls were minimal, with considerable overlap, leading to no statistical significance. On the other hand, the mean AMH level of adult patients (19+ years) is 10.28 ng/ml, which is higher than the usual range of 2–6 ng/ml observed in women of reproductive age. The presence of values as high as 15 ng/ml suggests unusually high ovarian reserve or possible abnormal hormonal elevation, greater AMH than controls ($p < 0.01$), indicating a distinct difference in this group. Overall, the dataset indicates the expected developmental trend of low levels in childhood, a rise during adolescence, and higher levels in adulthood; however, both the infant and adult groups show unusually elevated values, likely driven by outliers (**Table 2)**. This is further supported by boxplot analysis, which reveals wide variability in the 0–5 and adult groups compared with the narrower distribution observed in children, highlighting a heterogeneous AMH response within these cohorts **Figure 1**.

Furthermore, Two-way ANOVA revealed a significant group effect, with MDA patients having higher AMH than controls ($F(1,47) = 42.70$, $p < 0.0001$). AMH levels were influenced by age ($F(3,47) = 8.70$, $p < 0.001$), and there was a significant group-age interaction ($F(3,47) = 8.89$, $p < 0.001$), indicating that differences grew more prominent with age, particularly in older adolescents. These findings demonstrate that both numerical and non-numerical criteria effectively differentiate MDA from controls (**Table 3)**.

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Table 2: AMH level in a patient with MDA

*AMH levels (ng/mL)

Age Group	MDA (Mean ± SD)	Range	Control (Mean ± SD)	Range		p-value (t-test)
Infants/Young (0–5)	3.63 ± 4.71 (n=6)	0.01– 10.98	0.79 ± 0.36 (n=7)	0.40-1.30		0.152
Children (6–12)	0.25 ± 0.27 (n=3)	0.09 – 0.56	1.77 ± 0.90 (n=3)	0.80-2.60		0.066
Adolescents (13–18)	2.14 ± 1.74 (n=6)	0.55 – 4.5	3.13 ± 1.59 (n=3)	1.80-2.70		0.324
Adults (19+)	10.28 ± 4.36 (n=5)	4 – 15	2.99 ± 1.30 (n=7)	1.49-4.70		0.004

Table 3: Comparison of AMH levels between MDA patients and controls throughout age groups using two-way ANOVA.

Parameter	Effect	F-value	p-value
Group (MDA vs Control)	Between groups	42.7	<0.0001
Age Group (0–5, 6–12, 13–18, ≥19 years)	Between ages	8.7	<0.001
Group × Age Group	Interaction	8.89	<0.001

* *F*-value = ANOVA test statistic (variance ratio); *p*-value = probability of chance result, with $p < 0.05$ considered significant.

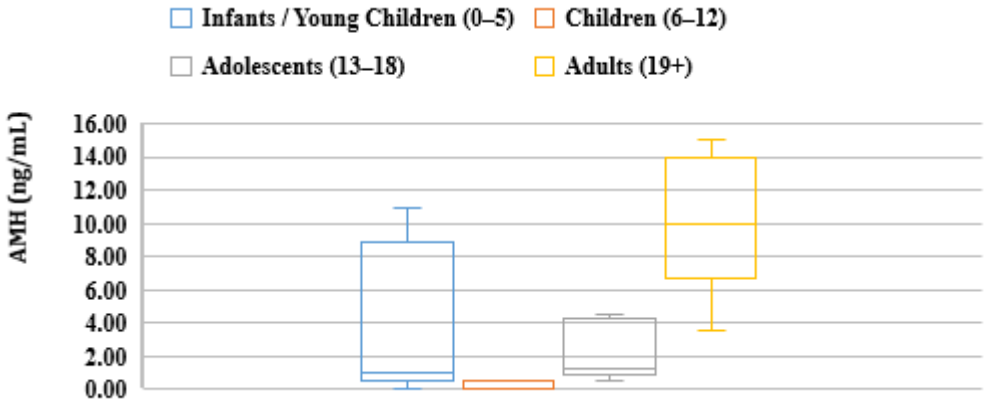

Figure 1: Boxplot analysis of AMH level in a patient with MDA

Karyotype analysis identified an elevated number of chromosomal abnormalities in suspected MDA patients in comparison to controls. A statistically significant difference ($\chi^2(1, N=40) = 10.8$, $p = 0.001$; Fisher's exact $p = 0.00044$) was seen between 50% of MDA patients (10/20) and the controls. When the connection was examined by age group, it was significant in newborns (0-5, $p = 0.021$) and adults (19+, $p = 0.010$) but not in children (6-12) or teenagers (13-18) ($p = 1.0$). These findings show that chromosomal anomalies are substantially linked with MDA, especially in the youngest and oldest patients, although small sample sizes in intermediate age groups may restrict the identification of relevance (**Table 4**). Moreover, a significant positive association between AMH levels and abnormal karyotype was found using a point-biserial correlation test ($r = 0.62$, $p = 0.003$). This suggests that patients with abnormal karyotypes tend to have higher AMH levels compared to those with normal karyotypes.

Table 4: Frequency of chromosomal abnormalities in suspected MDA patients and controls by age group

	MDA		Control		
Age Group	Abnormal karyotype	Normal karyotype	Abnormal karyotype	Normal karyotype	*P*-value
Infants (0–5)	4.0	2.0	0.0	7.0	0.021*
Children (6–12)	1.0	2.0		3.0	1.0
Adolescents (13–18)	1.0	5.0		3.0	1.0
Adults (19+)	4.0	1.0		7.0	0.010*

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***: *p*< 0.05 is considered statistically significant.**

SRY gene study demonstrated that 5 out of 20 suspected MDA patients tested positive, whereas all controls were negative, indicating a statistically significant connection overall (p = 0.047, Fisher's exact test). Adults (19+) had a significant difference (4/5 positive versus 0/7 in controls, p = 0.010); however, newborns, children, and adolescents did not (p ≥ 0.462). These findings indicate that SRY gene positivity is more prevalent in adult MDA patients, although small sample sizes in younger age groups restrict the identification of significance **(Table 5)**. Moreover, a significant positive correlation between SRY positivity and AMH levels was found using a point-biserial correlation test (r = 0.83, p < 0.00001). Patients who tested positive for SRY had significantly higher levels of AMH, highlighting the diagnostic significance of combining genetic and hormonal markers in MDA screening.

Table 5. SRY Gene positivity in suspected MDA patient's vs controls by age group

	MDA		Controls		
Age Group	**Negative**	**Positive**	**Negative**	**Positive**	***p*-value**
Infants (0–5)	5	1	7	0	0.462
Children (6–12)	3	0	3		1
Adolescents (13–18)	6	0	3		1
Adults (19+)	1	4	7		0.01
Overall	15	5	20		0.047

Clinical valuation for suspected MDA patients

For ease of analysis, four age-based categories have been established using the patient demographics data. Patients suspected of being raised as females and exhibiting MDA, ranging in age from children to adults, were assessed using blood karyotyping, SRY gene analysis, AMH measurement, and clinical examination.

Infant/young children group

The patients in the 0–5-year group ranged in SRY positive and AMH values from abnormally low (0.01 ng/mL) to abnormally raised (10.98 ng/mL), and their chromosome complements included mosaic karyotypes, Turner syndrome (45, XO), and 46, XX, 46, XY. On the other hand, the control group, which consisted of age-matched kids with normal 46, XX karyotype, and negative SRY gene, repeatedly showed low AMH levels within a small range (0.19-1.30 ng/mL), which is indicative of normal ovarian physiology in early infancy. The comparison shows that underlying DSDs such as ovotesticular DSD, androgen insensitivity, congenital adrenal hyperplasia, MRKH syndrome, and Turner syndrome are substantially correlated with departures from the predicted AMH pattern, as well as incorrect karyotyping and SRY results **(Table 6)**.

A thorough examination showed that just one child had classical MRKH syndrome (real MDA), even though these individuals had previously presented clinically as suspected cases of MDA. A wider range of DSDs, such as Turner syndrome, congenital adrenal hyperplasia, androgen insensitivity, and gonadal dysgenesis, were represented by the remaining patients. This emphasizes how crucial an organized diagnosis process is at an early age because several illnesses can present as MDA**.**

Table 6: Clinical summary for infant/young children suspected to have MDA.

Case (Age)	Karyotype/ SRY/AMH (ng/mL)	Clinical Features	Suspected Diagnosis	Reasoning	Treatment & Care Plan
1 yr **Case 1** **Photos 1,2, 3**	46, XX/46, XY mosaic, SRY–, AMH 0.68	No vulva, no labia, no vagina; urethral opening in a reverted appendage; testicular tissue in the inguinal canal	Ovotesticular DSD / Mixed Gonadal Dysgenesis	Mosaic karyotype; dysgenetic gonads; absent Müllerian structures	MDT review; gonadal biopsy ± gonadectomy; delayed genital reconstruction; long-term HRT if gonads removed; psychological support
2 yrs **Case 2**	46, XY, SRY–, AMH 10.98	Bifid scrotum, micropenis, urethral opening on penis, impalpable testes	46, XY DSD – Partial Androgen Insensitivity / Gonadal Dysgenesis	XY with high AMH (functional Sertoli cells) but undervirilization and absent Müllerian structures	Imaging for gonads; hCG test; orchidopexy if testes are viable or gonadectomy if dysgenetic; gender assignment discussion; endocrine follow-up

2 yrs **Case 3**	46, XX, SRY–, AMH 0.9	Absent external genitalia, perineal urethral opening	MDA	Normal female karyotype; absent Müllerian derivatives; low AMH	Confirm ovarian function (FSH/LH/E2); future vaginal reconstruction in adolescence; counselling for fertility (IVF, surrogacy if ovaries present); psychological support.
3 yrs **Case 4** **Photos 4, 5**	46, XY, SRY+, AMH 8.2	Female external genitalia, impalpable testes	CAIS	XY with SRY+, high AMH (no Müllerian structures), but female phenotype, so androgen receptor defect	Leave gonads until puberty (estrogenization), then prophylactic gonadectomy; estrogen replacement after; gender identity support; psychological counselling
2 yrs **Case 5** **Photos 6,7**	46, XX 2q-, SRY–, AMH 1.0	Clitoromegaly with fused labia	46, XX 2q- DSD due to CAH (21-hydroxylase deficiency)	XX with virilized genitalia; low AMH; likely CAH	Biochemical confirmation (17-OHP); start hydrocortisone ± fludrocortisone; electrolyte monitoring; surgical correction of genitalia (deferred in some centers); lifelong endocrine follow-up
5 yrs **Case 6**	45, XO, SRY–, AMH 0.01	Childish genitalia, primary amenorrhea, short stature, webbed neck	Turner Syndrome with Ovarian Dysgenesis	XO karyotype; very low AMH; streak gonads; characteristic phenotype	Growth hormone therapy; estrogen therapy for puberty; cardiac & renal monitoring; fertility counselling; lifelong endocrinology & cardiology follow-up

Hormone replacement therapy (HRT)
Human chorionic gonadotropin test (HCG)
Complete Androgen Insensitivity Syndrome (CAIS)
Congenital Adrenal Hyperplasia (CAH)

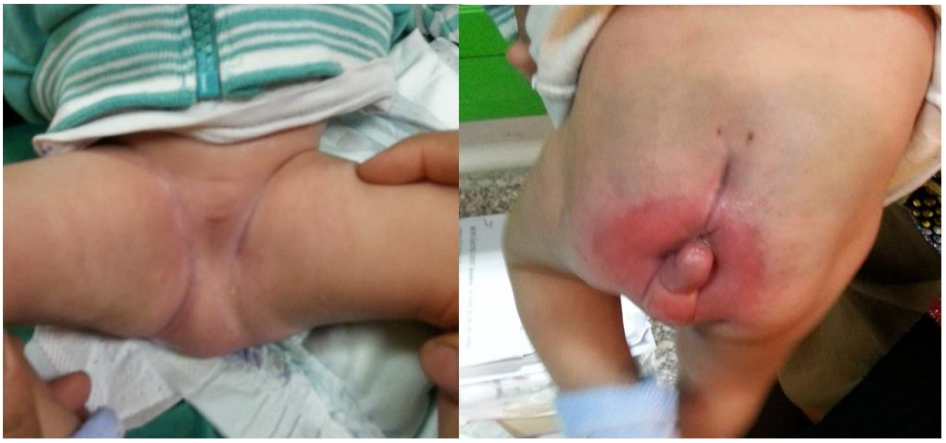

Photo 1: ***Case No.*** **, A 3-month-old reared up as female and presented with no penis, no vulva, testicular tissue in the inguinal canal, and multi-congenital anomalies (renal ectopia and fused ischial bones), Chromosome analysis showed mosacisim 46, XX/46, XY. Case No. 1.**

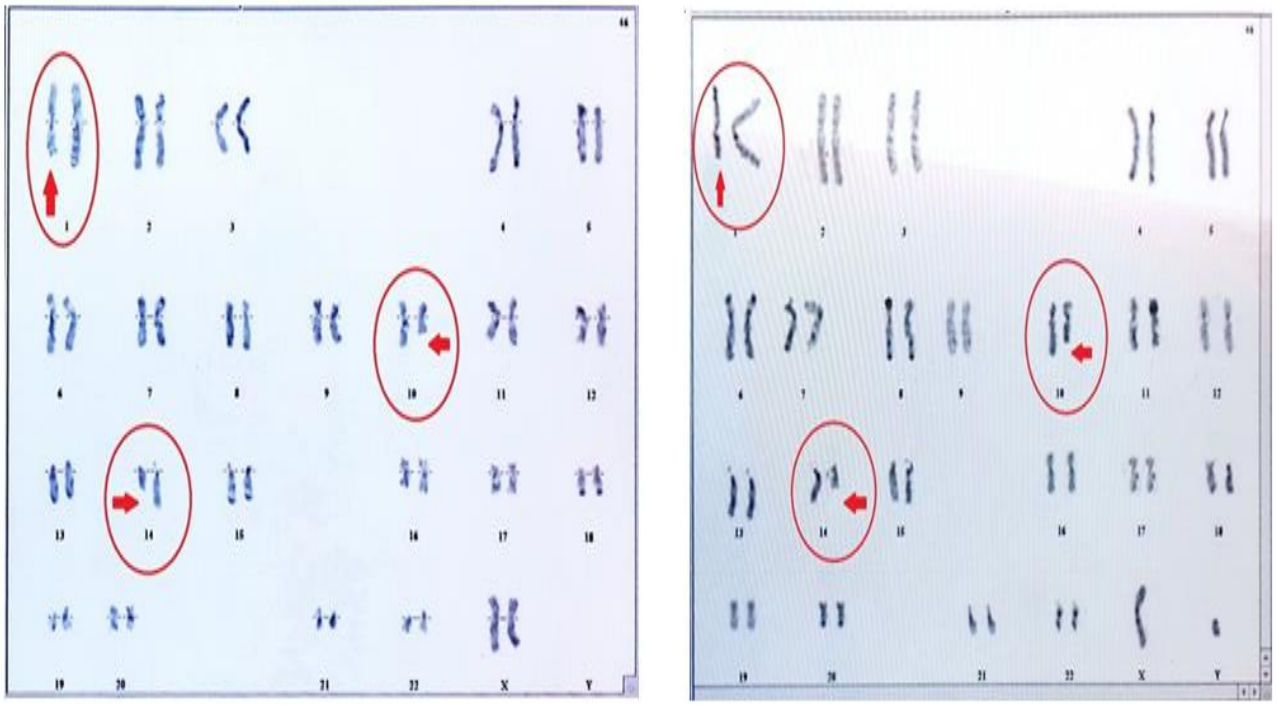

***Photo*. 2: karyogram of *Case No. 1*, showing mosaicism Lt. Kryogram shows 46, XX complement with 1q-, 10q- and 14q- and Rt. Karyogram shows (46,XY) complement with 1q-, 10q- and 14q-**

SRY FISH probe positive signal

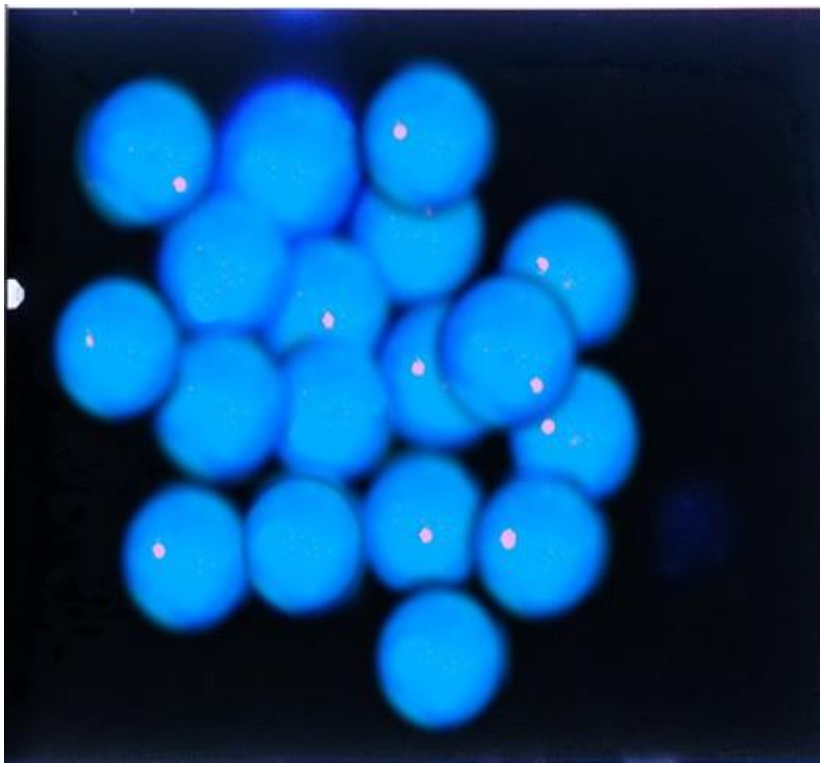

Photo 3: A clone of cells of *Case No. 1* whose karyotype result showed mosaicism (46, XX/46, XY) by examination under fluorescent microscope using *CytoCell* : positive signal for SRY gene had been detected in some nuclei while others were negative.

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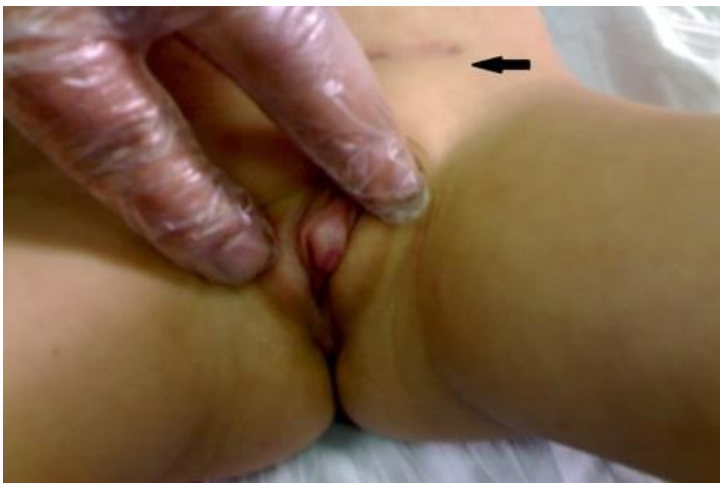

Photo 4: Case No 4, **A 3-year-old reared up as female presented with female-like external genitalia and accidentally discovered testes in inguinal canal.**

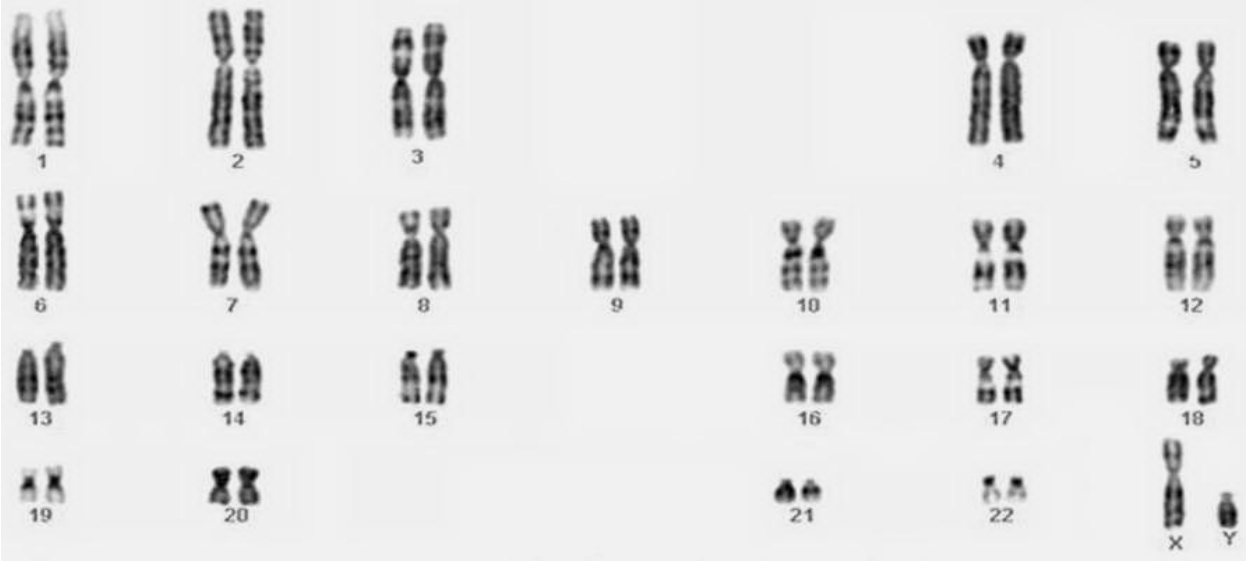

Photo 5: **A karyogram of *Case (No .4)* reared up as female showing 46, XY chromosome complement in all cell examined.**

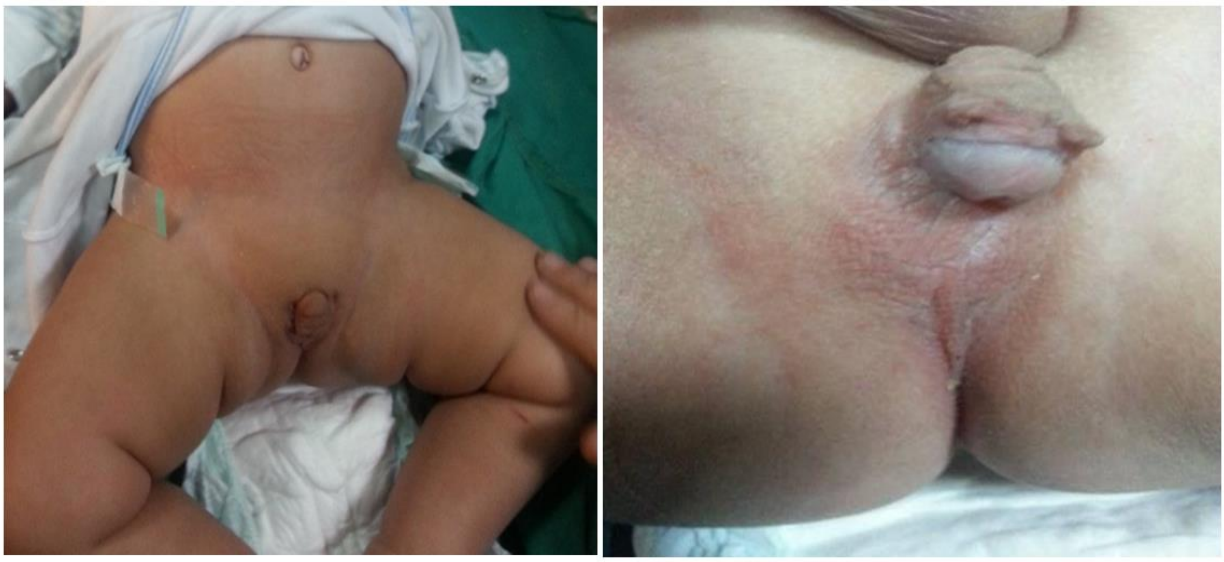

Photo 6: Case No. 5, **A 9-month-old patient reared up as Male and presented with micro-penis, no scrotum and no testes.**

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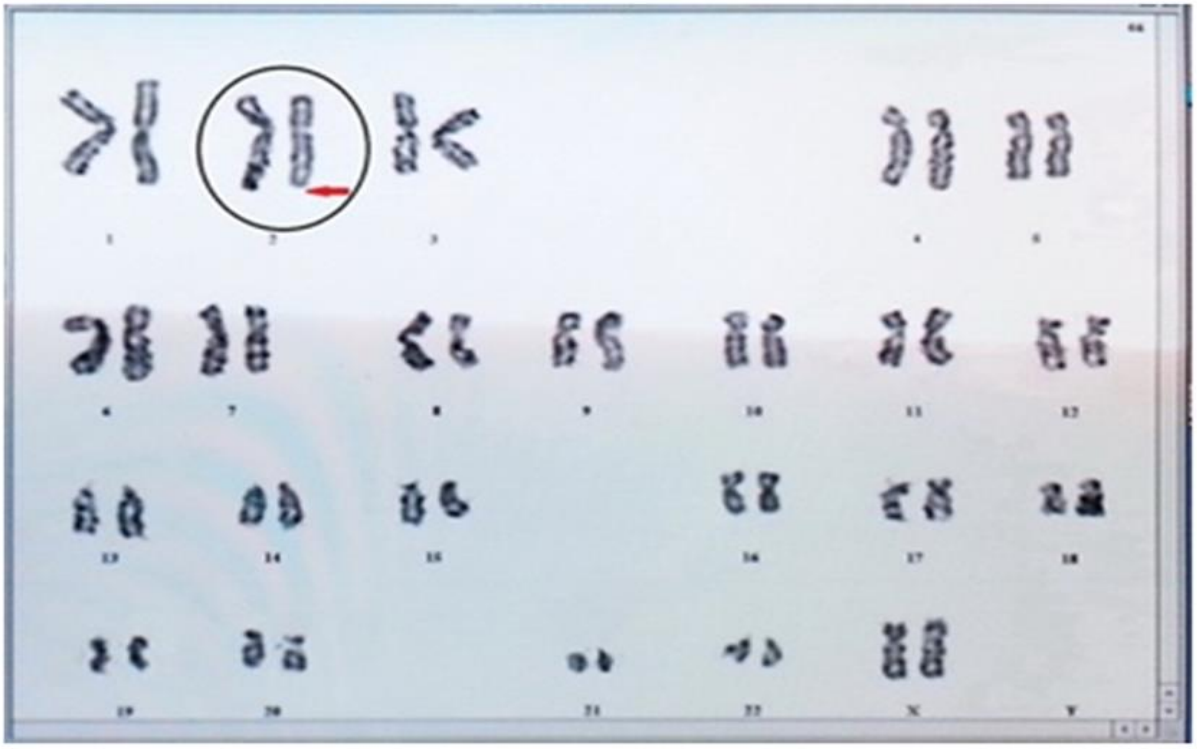

***Photo 7*: A karyogram of *Case No .5* showing abnormal chromosome complement as all cells examined showed 46, XX with deletion of the long arm of chromosome 2.**

Young children group

All patient cases showed significantly lower AMH levels, indicating decreased ovarian function, when compared to age-matched controls of the children's group (6–12) having AMH in between **0.80-2.60 ng/ml**. Absence of pubertal characteristics and decreased AMH are consistent with MDA linked to ovarian insufficiency in patients with a 46, XX karyotype and a negative SRY gene. A diagnosis of Turner syndrome with streak gonads is supported in the 45, XO instance by the distinctive phenotypic and extremely low AMH, **Table 7**. These findings highlight the spectrum of gonadal dysfunction underlying abnormal sexual development and underscore the importance of early endocrine assessment to guide pubertal induction, growth, systemic monitoring, and psychosocial and fertility counselling. Collectively, the interpretation suggests that early endocrine intervention, hormone replacement for pubertal induction, growth, and systemic monitoring in Turner syndrome, and long-term psychosocial and fertility support are essential elements of care.

Table 7: Clinical summary for children suspected to have MDA.

Case (Age)	Karyotype / SRY / AMH	Clinical Features	Suspected Diagnosis	Reasoning	Treatment & Care Plan
12 yrs **Case 7**	46, XX, SRY–, AMH 0.56 (low)	Childish external genitalia, no maturity features	MDA (MRKH type-I)	Female karyotype (46, XX), absent SRY, very low AMH → ovarian dysfunction / underdeveloped gonads. Lack of pubertal features suggests MRKH with hypogonadism.	Multidisciplinary evaluation (pediatric endocrinology gynaecology, psychology) HRT to induce puberty; Long term: psychological support counselling for infertility Future surgical options i vaginal agenesis is confirme (vaginoplasty if symptomatic).
12 yrs **Case 8**	46, XX, SRY–, AMH 0.1 (very low)	Childish genitalia, absent secondary sexual characters	MRKH with Primary Ovarian Insufficiency (severe gonadal dysgenesis)	AMH extremely low → poor ovarian reserve. 46, XX with negative SRY excludes androgen insensitivity. Absence of puberty + low AMH suggests ovarian failure with Müllerian	- HRT for pubertal induction and bone health; Monitoring for associated renal/skeletal anomalies; Psychosocial support for body image and infertility; Long-term follow-up in adolescent gynaecology.

				agenesis.	
12 yrs **Case 9** **Photo 8**	45, X, SRY–, AMH 0.09 (very low)	Normal female genitalia, short stature, webbed neck	Turner Syndrome (Gonadal Dysgenesis)	Classic phenotype (short stature, webbed neck) + karyotype 45, XO. Very low AMH = streak gonads (ovarian failure). Distinguished from MRKH (here uterus may be hypoplastic but not typically absent).	Growth hormone therapy (if still in growth period); Estrogen replacement for puberty induction; Monitor cardiac, renal, thyroid function (common Turner comorbidities); Fertility counselling (oocyte/embryo donation if future pregnancy desired); Lifelong surveillance for complications.

Hormone replacement therapy (HRT)
Human chorionic gonadotropin test (HCG)
Complete Androgen Insensitivity Syndrome (CAIS)
Mayer-Rokitansky-Küster-Hauser (MRKH)

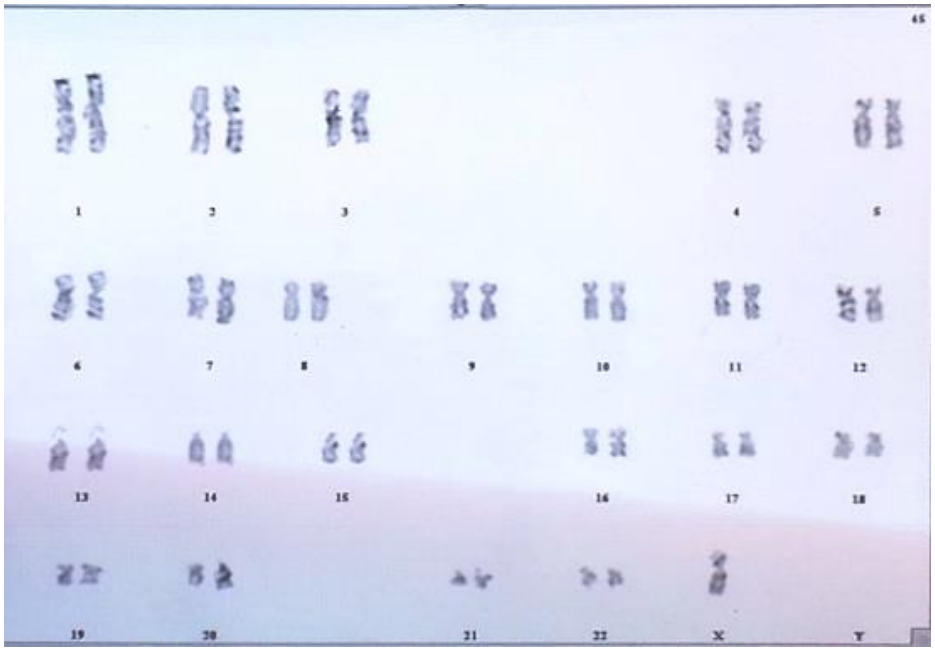

Photo 08 : A karyogram of *Case No.09:* A 12 years old patient reared up as female and presented with short stature, webbed neck, wide inter nipple space and lumbar lordosis, showing abnormal chromosome complement (45,X) in all cells examined which is consistent with the clinical diagnosis of Turner syndrome.

Adolescents group

In the case of adolescent selected patients, the study assessed six female patients who were at least 18 years old and had primary amenorrhea along with various degrees of secondary sexual features that were underdeveloped. Except for one patient who had a chromosomal rearrangement and a 45, XO variation, which is compatible with Turner syndrome, all of the patients were 46, XX. AMH levels varied from 0.55 to 4.5 ng/mL, while control females aged 18+ years had normal menstruation, fully developed secondary sexual characteristics, with AMH levels ranging from 1.8 to 4.9 ng/mL. One patient demonstrated low AMH (0.55 ng/mL) and chromosomal abnormalities, consistent with Turner syndrome, contributing to gonadal dysgenesis and primary amenorrhea. The findings indicate that MDA patients may have variable ovarian functions, some exhibit severely reduced AMH and delayed sexual development, while others maintain ovarian activity despite absent uterine structures (**Table 8)**. Primary amenorrhea and underdeveloped genitalia in all patients confirm MDA as the primary aetiology of delayed sexual maturation. **Management and care plans** involve hormone replacement therapy to induce secondary sexual characteristics, psychosocial support, fertility counselling, including donor egg or surrogacy options, and routine monitoring for associated comorbidities in chromosomally abnormal patients.

Table 8: Clinical summary for adolescents suspected to have MDA.

Case (Age)	Karyotype/ SRY/AMH (ng/mL)	Clinical Features	Suspected Diagnosis	Reasoning	Treatment & Care Plan
18 yr **Case 10** **Photo 10**	46, XX, SRY–, AMH 1.3	Childish external genitalia, no maturity features, primary amenorrhea, short stature, underdeveloped breasts, widely spaced nipples	MDA	AMH slightly below control mean (~2.5); primary amenorrhea, absence of secondary sexual characteristics, short stature suggests ovarian insufficiency/MDA	HRT (estrogen/progesterone) to induce secondary sexual characteristics; psychological support; fertility counselling and possible reproductive options (surrogacy, IVF with donor eggs)
17 yr **Case 11**	46, XX, SRY–, AMH 1.27	Childish external genitalia, no maturity features, primary amenorrhea	MDA	AMH below the lower range of control; primary amenorrhea and absent secondary sexual development consistent with MDA	Hormone replacement therapy; monitoring bone health; counselling on fertility and psychosocial support
16 yr **Case 12** **Photo 09**	46, XX, SRY–, AMH 1.0	Childish external genitalia, no maturity features, primary amenorrhea	MDA	Very low AMH compared to control; absence of secondary sexual characteristics and amenorrhea indicates gonadal dysfunction.	Estrogen therapy for sexual development; psychological support; family counselling, and discussion of future fertility options
14 yr **Case 13**	46, XX, SRY–, AMH 4.5	Childish external genitalia, well-developed breasts, primary amenorrhea	MDA	AMH within control range; breast development present, but genitalia remain immature; primary amenorrhea suggests MDA with functional ovaries	Conservative management with gynecological follow-up; hormone therapy if needed; counselling about reproductive options and sexual health
15 yr **Case 14**	46, XX, SRY–, AMH 4.2	Childish external genitalia, well-developed breasts, primary amenorrhea	MDA	AMH near upper control range; breast development present; primary amenorrhea indicates absence of uterus/vagina development	Gynecological follow-up; discussion of fertility options; hormone therapy only if secondary sexual development is incomplete
15 yr **Case 15** **Photo 11**	45,X,t(X;8;12),del(14) SRY–, AMH 0.55	Narrow blind vagina, well-developed breasts, primary amenorrhea	Turner Syndrome variant with Müllerian anomalies	Low AMH, chromosomal abnormality (45, X variant); primary amenorrhea and gonadal dysgenesis consistent with Turner syndrome	Estrogen replacement therapy; regular cardiac and renal screening (Turner-associated comorbidities); counselling for fertility and psychosocial support

Hormone replacement therapy (HRT)
Müllerian Duct Agenesis (MDA)
Anti-Müllerian Hormone (AMH)

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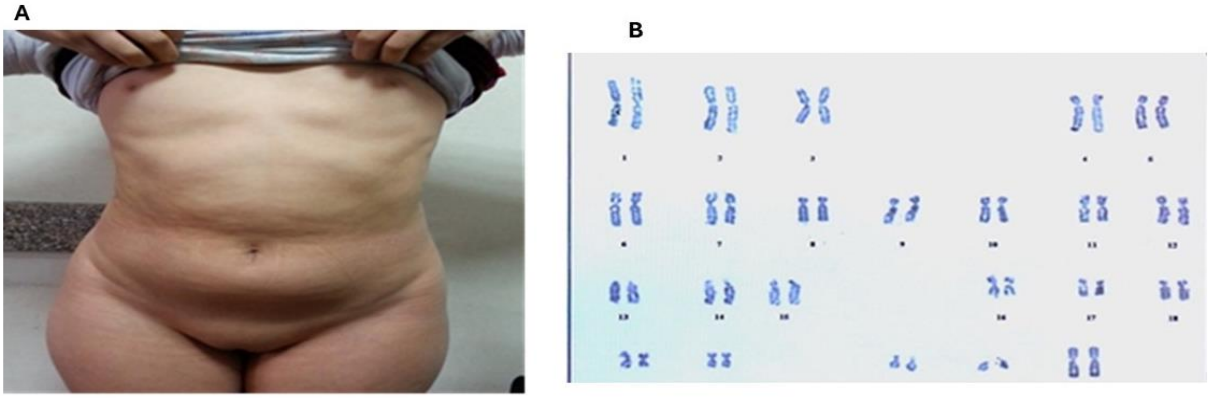

Photo 09: Case No.12: A: 16 years old patient reared up as female presented with 1ry amenorrhea, no 2ry sexual characters, no uterus and no ovaries seen by MRI. B: A karyogram of Case No .12 showing 46, XX karyotype.

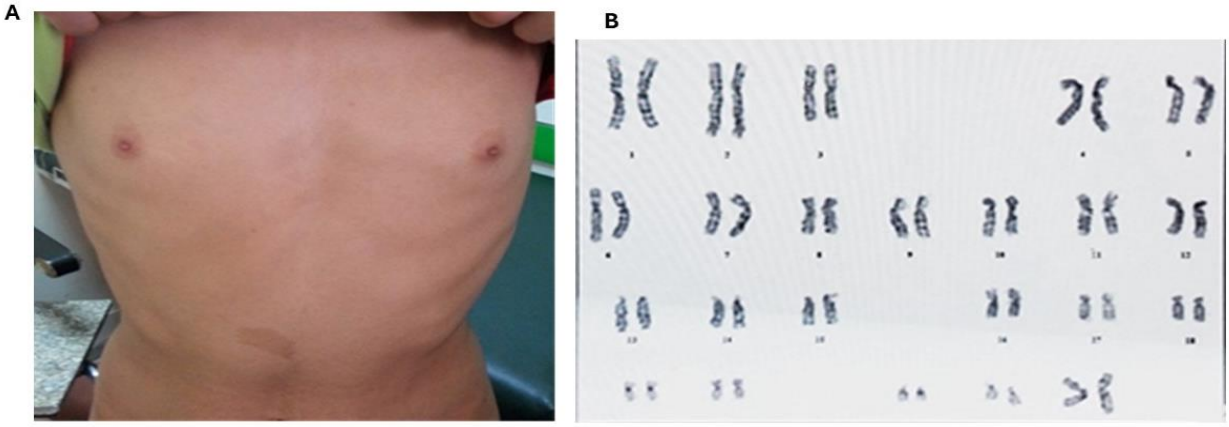

Photo 10: *Case No.10*: A 18 years old patient reared up as female presented with 1ry amenorrhea, widely spaced nipples, no 2ry sexual characters, no uterus and streak ovaries seen by MRI. B: A karyogram of case No .10 showing 46, XX karyotype.

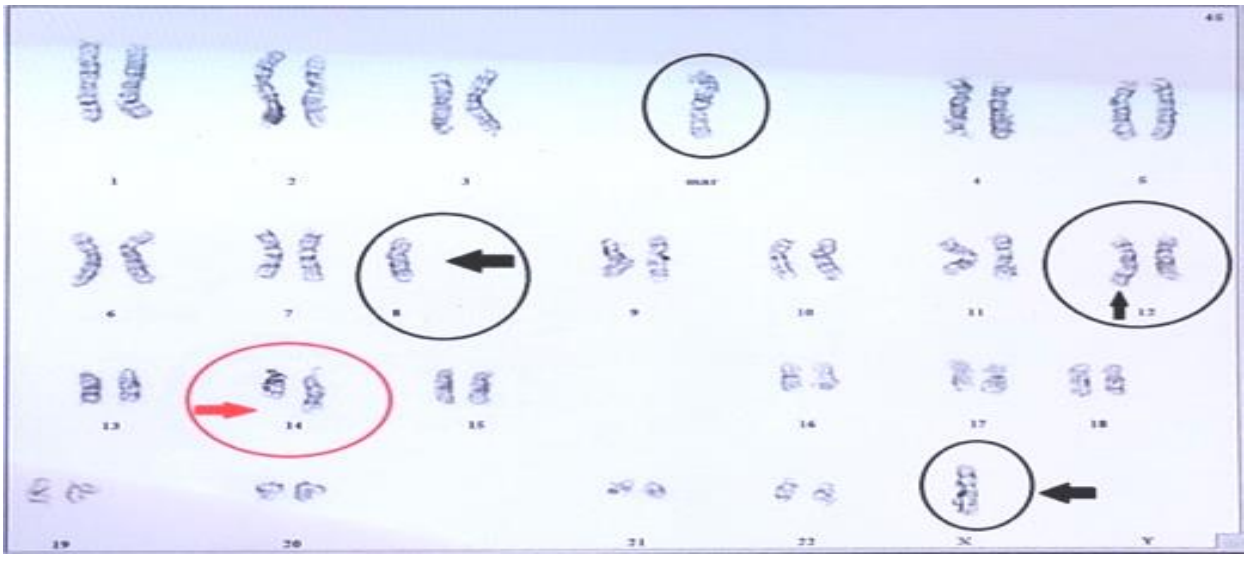

Photo 11: A karyogram of *case No .15*: A 15-year-old patient reared up as female and presented with primary amenorrhea, and short, narrow, blind vagina and histological study of ovarian sample revealed presence of suspicious Leydig cells in the ovary. Karyotyping result shows a three break rearrangement in which chromosome complement was 45,X,t(X;8;12),del(14) in all cells examined with a segment of one 8 chromosome has been translocated onto chromosome X, and a segment of the distal part of the long arm of chromosome 8 has been translocated onto chromosome 12. In addition to deletion in the long arm of chromosome 14.

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Adult group

Out of all the adult patients, five patients with primary amenorrhoea and underdeveloped or absent internal reproductive tissues were assessed for karyotype, SRY gene status, AMH levels, and clinical characteristics. A 46, XY karyotype and a positive SRY gene were found in patients who were close 19 years old or more,, suggesting a genetically male profile. All four had clinically developed breasts, primary amenorrhoea, and a narrow, blind vagina. Inguinal or labial folds were the locations of the testes, or in certain situations, they were not palpable. Functional Sertoli cells that produce AMH were evident in the AMH levels, which ranged from 9.9 to 15 ng/ml, which were noticeably greater than those of the adult female control group (1.40–4.70 ng/ml). These features are consistent with **Complete Androgen Insensitivity Syndrome (CAIS)**, where genetically male individuals develop a female phenotype due to androgen receptor defects, resulting in absent Müllerian structures despite functional testes. **Only one patient** had a 46, XX karyotype with a negative SRY gene and an AMH level of 4 ng/ml, within the normal adult female range. Clinically, this patient exhibited a narrow blind vagina, well-developed breasts, and primary amenorrhea. These findings are consistent with **MDA (MRKH Syndrome)**, characterised by an absent or underdeveloped uterus and vagina in phenotypic females with normal ovarian function **(Table 9)**.

Table 9: Clinical summary for an adult suspect to have MDA

Age (yrs)	Karyotype/ SRY/AMH (ng/mL)	Clinical Features	Suspected Diagnosis	Reasoning	Treatment & Care Plan
19 yr **Case 16**	46, XY, SRY +, AMH 9.9,	Narrow blind vagina, Testis in labial folds, Well-developed breasts, 1° amenorrhea	CAIS	Phenotypic female, 46, XY karyotype, functional testes, elevated AMH, absence of uterus	Gonadectomy (to prevent malignancy), HRT, psychological support, vaginal dilation if needed
25 yr **Case 17**	46, XY, SRY +, AMH 10,	Narrow blind vagina, Testis inguinalis, Well-developed breasts, 1° amenorrhea	CAIS	Phenotypic female, XY karyotype, functional testes, elevated AMH, absence of uterus	Gonadectomy, HRT, counselling, and sexual health support
23 yr **Case 18**	46, XY, SRY +, AMH 13,	Narrow blind vagina, Inpalpable testis, Well-developed breasts, 1° amenorrhea	CAIS	High AMH suggests functioning Sertoli cells, no uterus	Gonadectomy, HRT, psychological support, vaginal reconstruction if needed
26 yr **Case 19**	46, XY, SRY +, AMH 15,	Narrow blind vagina, Inpalpable testis, Well-developed breasts, 1° amenorrhea	CAIS	High AMH confirms testicular function	Gonadectomy, HRT, counselling, and sexual health support
30 yr **Case 20**	46, XX, SRY -, AMH 4,	Narrow blind vagina, Well-developed breasts, 1° amenorrhea	MRKH	Female karyotype, absent uterus, normal ovaries, primary amenorrhea	Vaginal dilation or neovagina creation, psychological support, fertility counselling (IVF with surrogacy if desired)

Hormone replacement therapy (HRT)
Complete Androgen Insensitivity Syndrome (CAIS)

4. DISCUSSION

In early life, ambiguous or malformed genitalia are often the first sign of the complex clinical diseases known as MDA and related DSDs. Early detection is essential for accurate diagnosis and gender assignment, as well as for the planning of appropriate hormonal, psychological, and surgical interventions. Because depending on the time at which Müllerian development stops in utero, a variety of abnormalities can arise, from moderate (such as a partial uterine septum) to severe (such as Müllerian agenesis), which involves the complete absence of the cervix, uterus, and fallopian tubes. The time of presentation, the constellation of related symptoms, and the need for either medicinal or surgical care are all correlated with the reproductive tract components involved and, crucially, whether an obstruction of the tract is involved [11]. Therefore, in this clinical presentation, we analysed patients reared as females who presented with MDA with the help of analysing blood karyotyping, AMH level assay, the existence of the SRY gene, and clinical evaluation to refine diagnostic categorisation and guide management.

In line with typical MRKH/MDA phenotypes, our results show a preponderance of a normal female karyotype (46, XX)

with no SRY gene. While some of the individuals in our sample met the criteria for MRKH syndrome, a particular subgroup of MDA, others were diagnosed with MDA [7]. Although MDA is a more general category that may include partial absence of Müllerian derivatives, aberrant genitalia, or related defects, MRKH is characterised by a 46, XX karyotype, absence of SRY, normal ovarian function, and full agenesis of the uterus and upper vagina [13]. Therefore, blood karyotyping, SRY testing, and AMH measurement are necessary to distinguish these conditions from other DSDs. Moreover, proper classification is essential since MRKH treatment emphasises neovagina formation, psychological support, and reproductive counselling, whereas broader MDA may call for customised endocrine and surgical therapy.

In contrast, in this study, cases of phenotypic females with a 46, XY karyotype and positive SRY, alongside elevated AMH levels without Müllerian structures, were also found after a multimodal diagnostic approach, which indicates CAIS. Then again, these differential findings are critical because CAIS is indicated by phenotypic female patients with a 46, XY karyotype, positive SRY, and increased AMH levels devoid of Müllerian structures, but is fundamentally unique in its genesis and therapy. Basically, CAIS originates owing to androgen receptor mutations, failing to respond to androgens despite testicular function, leading to regression of Müllerian structures and feminised external genitalia [14]. As we know, Sertoli cells release AMH, which is lacking in normal female development and plays a crucial role in Müllerian duct regression in genetic males. The usefulness of AMH as a diagnostic and monitoring biomarker is confirmed by the fact that its levels in CAIS patients are often high before gonadectomy and drastically decrease following gonadectomy [15]. AMH levels, on the other hand, indicate ovarian reserve rather than Müllerian regression in MRKH/MDA with 46, XX karyotype, highlighting the hormone's context-specific interpretive relevance.

Another distinct mechanism is Persistent Müllerian Duct Syndrome (PMDS), which occurs in 46, XY individuals where Müllerian structures remain despite normal androgen receptor activity because of abnormalities in AMH or AMH receptor signalling. In contrast, in 46, XY CAIS, external masculinisation fails because of androgen insensitivity, although Müllerian regression happens normally because of functional AMH [16]. Consequently, developmental differences between these syndromes can be further clarified by molecular pathways controlling Müllerian duct regression, such as the SOX9-AMH axis and upstream regulation by SRY, SF1, and GATA factors [17].

In this regard, our diagnostic approach is in line with earlier case studies that highlight the difficulty of diagnosing DSDs. For instance, whole genome sequencing identified a novel SRY mutation, leading to the reclassification of a case that was originally diagnosed as CAIS as gonadal dysgenesis [18].

Moreover, several of the studied participants had a 45, XO karyotype and were SRY negative, which is more in line with Turner syndrome than MDA. In contrast to CAIS or MRKH/MDA, where the absence of the uterus is explained by Müllerian regression or agenesis, Turner syndrome is characterised by ovarian dysgenesis (streak gonads), which results in infertility, poor pubertal development, and oestrogen insufficiency. Additionally, short stature, gonadal dysgenesis, and primary amenorrhoea are common clinical presentations for these patients; ambiguous genitalia are not, as seen in some patients of our study. They differ from XY DSD cases like CAIS in that their external genitalia are often normal for females [19]. Furthermore, AMH helps distinguish ovarian dysgenesis (Turner) from Müllerian agenesis or androgen insensitivity because it is usually very low or undetectable in 45, XO patients, indicating absent functional ovarian tissue, in contrast to normal-range AMH in MRKH/MDA (where ovaries are intact) and high AMH in CAIS (functional Sertoli cells but androgen receptor defect) [20].

In addition, the absence of Y-chromosome material is confirmed by SRY negativity, which is significant because the presence of Y pieces in some Turner variations (45, X/46, XY mosaics) increases the risk of gonadoblastoma. Unlike Y-positive mosaics, identifying SRY-negative 45, XO guarantees that prophylactic gonadectomy is not necessary. Yet still chromosome analysis and karyotyping from blood lymphocytes remains the gold standard for Turner diagnosis, allowing early differentiation from MRKH, which shares the phenotype of primary amenorrhea but with a 46, XX karyotype and functional ovaries [21].

In conclusion, diagnostic uncertainty still exists, though, because these patients exhibit a variety of hereditary and hormonal traits. But still, this case-control study assessed the combined diagnostic utility of blood karyotyping, SRY gene identification, AMH levels, and a comprehensive clinical examination in different age groups raised as females who presented with MDA. By comparing these findings with age-matched controls, the study hopes to provide a more unified diagnostic paradigm that can guide physicians in early identification, risk stratification, and multidisciplinary treatment planning for affected individuals. Accordingly, a multimodal diagnostic approach guarantees each patient a precise diagnosis and suitable treatment planning.

Parallel to our findings, we cannot ignore the fact that apart from clinical treatment, most of the DSD patients do need psychological attention. It is reported that, in contrast to their peers, patients with MRKH/MDA syndrome or other DSDs often experience severe psychological distress, including higher levels of anxiety and depression, particularly in late

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adolescence and early adulthood when identity, sexuality, and future family planning become major concerns. In literature, it is shown that nearly 25% of 141 MRKH patients in a research study had moderate to severe anxiety, and they showed noticeably more depressive symptoms than matched controls [22]. Neurotic personality traits and dental difficulties, especially the perception of being "less than" or "not fully functioning as a woman," were found to be important risk factors for these patients' anxiety [23]. Nevertheless, when given early treatment, focused psychological interventions like cognitive-behavioural therapy or systematic post-operative counselling can be successful in lowering anxiety and sadness. Therefore, the findings of this analysis also emphasise that, in addition to the physical components of treatment, psychological assessment and management must be essential and continuous parts of any study which is trying to present a diagnosistic methodology for care of MDA/MRKH patients.

5. LIMITATION

There are multiple limitations to this study. In addition to introducing heterogeneity in AMH levels and sexual development, the small sample size and the age range of only 30 years limit the findings' generalisability and could skew comparisons. Because it is a cross-sectional study carried out at a single clinical site, it can't represent a variety of geographic or ethnic groups or evaluate longitudinal changes in AMH, puberty, or clinical outcomes; instead, it simply offers a snapshot of hormonal, genetic, and clinical aspects. While the status of the SRY gene and karyotype were examined, other genetic alterations linked to AIS or MRKH, such as those involving the AR gene or WNT4, were not. The precise anatomical assessment of Müllerian structures may have been impacted by the fact that not all patients had sophisticated imaging. Knowledge of ovarian or testicular function was limited by the functional evaluation of gonadal hormone activity being restricted to AMH and the incomplete analysis of other reproductive hormones (FSH, LH, oestradiol, and testosterone). Instead of using contemporaneously matched controls, control AMH values were obtained from a different group, which could introduce bias. The quality of life and psychosocial factors, which are crucial for patients with MDA/MRKH syndrome, were also not thoroughly assessed.

6. RECOMMENDATIONS

Our results suggest that in order to ensure accurate diagnosis and differentiation between MRKH, MDA, CAIS, and Turner syndrome, all patients presenting with a female phenotype and absent or hypoplastic Müllerian structures should undergo a thorough evaluation with blood karyotyping, SRY gene analysis, AMH measurement, and detailed clinical assessment. To address issues with anxiety, depression, body image, and gender identity, psychological support ought to be a crucial component of care. Treatment must be tailored to the individual diagnosis, such as gonadectomy and endocrine follow-up for CAIS, hormone therapy with systemic monitoring for Turner syndrome, individualised surgical and endocrine care for atypical MDA, and vaginal reconstruction and fertility counselling for MRKH. To enhance long-term quality of life, early intervention, patient counselling, and physician training in sensitive communication are crucial. Additionally, future research involving genetic and molecular analyses may help improve diagnostic accuracy and direct focused treatments.

7. CONCLUSION

In order to diagnose individuals who were raised as females and present with MDA and related illnesses, this study emphasises the significance of integrating blood karyotyping, SRY gene analysis, AMH measurement, and clinical evaluation. The statistical analyses of the AMH levels, SRY gene status, and chromosomal aberrations were evaluated between 20 suspected MDA patients and 19 controls. In 10/20 MDA patients, chromosomal abnormalities were seen, but not in controls. All controls lacked SRY positivity, but five MDA patients (mostly adults) had it. There were age-related changes in AMH levels, with lower levels in children and adolescents and higher levels in adults and babies. A two-way ANOVA showed a significant age effect ($F(3,47) = 8.70$, $p<0.001$), group effect ($F(1,47) = 42.70$, $p<0.0001$), and group × age interaction ($F(3,47) = 8.89$, $p<0.001$). Point-biserial correlation revealed a **significant positive association** with an abnormal karyotype ($r = 0.62$, $p = 0.003$) and a high positive association between AMH and SRY positivity ($r = 0.83$, $p < 0.00001$). Significant differences between groups were confirmed using Chi-square and Fisher's exact tests for categorical variables. These findings suggest that MDA patients can be successfully distinguished from controls using both genetic and hormonal indicators.

While the comprehensive clinical examination results show that although MRKH syndrome's 46, XX karyotype, lack of SRY, and normal AMH make it a well-defined subset of MDA, other cases like CAIS (46, XY, SRY+, high AMH) and Turner syndrome (45, X, SRY–, low AMH) can have similar clinical features but need quite different treatment strategies. Therefore, precise differentiation is necessary to direct hormonal, psychiatric, and surgical treatment as well as to maximize long-term results, such as fertility counselling.

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Author Contributions
Concept and design.
Acquisition, analysis, and interpretation of data.
Drafting of the manuscript, Critical review of the manuscript for important intellectual content,
Supervision, and approval of publication.

Conflicts of Interest
The authors declare that they have no conflicts of interest to disclose related to this work.

Confidentiality of Data
The authors affirm that all data collected were handled in accordance with confidentiality protocols approved by their institution. No identifying patient data has been published.

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REFERENCES
[1] 1. Morcel K, Camborieux L, fr PdRslAMp-ncu-r, Guerrier D: Mayer-Rokitansky-Küster-Hauser (MRKH) syndrome. Orphanet journal of rare diseases. 2007, 2:13. 10.1186/1750-1172-2-13
[2] 2. Engstad J: Artificial vagina. J Lancet. 1917, 37:329-331.
[3] 3. Herlin M, Bjørn A-MB, Rasmussen M, Trolle B, Petersen MB: Prevalence and patient characteristics of Mayer–Rokitansky–Küster–Hauser syndrome: a nationwide registry-based study. Human reproduction. 2016, 31:2384-2390. 10.1093/humrep/dew220
[4] 4. Satoh M: Histogenesis and organogenesis of the gonad in human embryos. Journal of anatomy. 1991, 177:85.
[5] 5. Polipalli SK, Kapoor S: Molecular Regulation of Gonadal Development. Children with Differences in Sex Development: Taking a Multidisciplinary Management Approach. Springer; 2024. 11-20. 10.1007/978-981-97-1639-5_2
[6] 6. Koopman P, Wilhelm D: SRY, sex determination and gonadal differentiation. eLS. 2011. 10.1002/9780470015902.a0001144.pub3
[7] 7. Herlin MK, Petersen MB, Brännström M: Mayer-Rokitansky-Küster-Hauser (MRKH) syndrome: a comprehensive update. Orphanet journal of rare diseases. 2020, 15:214. 10.1186/s13023-020-01491-9
[8] 8. Chandler T, Machan L, Cooperberg P, Harris A, Chang S: Müllerian duct anomalies: from diagnosis to intervention. The British journal of radiology. 2009, 82:1034-1042. 10.1259/bjr/99354802
[9] 9. Peluso C, Fonseca F, Rodart I, et al.: AMH: An ovarian reserve biomarker in assisted reproduction. Clinica Chimica Acta. 2014, 437:175-182. 10.1016/j.cca.2014.07.029
[10] 10. Troiano RN, McCarthy SM: Mullerian duct anomalies: imaging and clinical issues. Radiology. 2004, 233:19-34. 10.1148/radiol.2331020777
[11] 11. Bortoletto P, Romanski PA, Pfeifer SM: Müllerian anomalies: presentation, diagnosis, and counseling. Obstetrics & Gynecology. 2024, 143:369-377. 10.1097/AOG.0000000000005469
[12] 12. Al Najar MS, Al Ryalat NT, Sadaqah JS, Husami RY, Alzoubi KH: MRI evaluation of mullerian duct anomalies: practical classification by the new ASRM system. Journal of multidisciplinary healthcare. 2022:2579-2589. 10.2147/JMDH.S386936
[13] 13. Yoo R-E, Cho JY, Kim SY, Kim SH: A systematic approach to the magnetic resonance imaging-based differential diagnosis of congenital Müllerian duct anomalies and their mimics. Abdominal imaging. 2015, 40:192-206. 10.1007/s00261-014-0195-9
[14] 14. Verim L: Complete androgen insensitivity syndrome in three sisters. International Journal of Fertility & Sterility. 2013, 7:353.
[15] 15. Kusumi M, Mitsunami M, Onoue H, et al.: Complete androgen insensitivity syndrome and anti-Müllerian hormone levels before and after laparoscopic gonadectomy. Gynecology and Minimally Invasive Therapy. 2017, 6:126-128. 10.1016/j.gmit.2016.11.001
[16] 16. Liu Y, Wang S, Lan R, Yang J: Identification of AMH and AMHR2 variants led to the diagnosis of persistent Müllerian duct syndrome in three cases. Genes. 2022, 13:159. 10.3390/genes13010159
[17] 17. Moses MM, Behringer RR: A gene regulatory network for Müllerian duct regression. Environmental Epigenetics. 2019, 5:dvz017.

[18] 18. De Sousa SM, Kassahn KS, McIntyre LC, Chong C-E, Scott HS, Torpy DJ: Case report of whole genome sequencing in the XY female: identification of a novel SRY mutation and revision of a misdiagnosis of androgen insensitivity syndrome. BMC Endocrine Disorders. 2016, 16:58. 10.1186/s12902-016-0141-7

[19] 19. Obara-Moszynska M, Dzialach L, Rabska-Pietrzak B, Niedziela M, Kapczuk K: Uterine development during induced puberty in girls with Turner syndrome. Frontiers in endocrinology. 2021, 12:707031. 10.3389/fendo.2021.707031

[20] 20. Lunding SA, Aksglaede L, Anderson RA, et al.: AMH as predictor of premature ovarian insufficiency: a longitudinal study of 120 Turner syndrome patients. The Journal of Clinical Endocrinology & Metabolism. 2015, 100:E1030-E1038. 10.1210/jc.2015-1621

[21] 21. Frelich J, Irzyniec T, Lepska K, Jeż W: New insights into clinical features, karyotypes, and age at diagnosis in women with Turner syndrome. Endokrynologia Polska. 2019, 70:342-349. 10.5603/EP.a2019.0016

[22] 22. Chen N, Song S, Duan Y, et al.: Study on depressive symptoms in patients with Mayer-Rokitansky-Küster-Hauser syndrome: an analysis of 141 cases. Orphanet journal of rare diseases. 2020, 15:121. 10.1186/s13023-020-01405-9

[23] 23. Song S, Chen N, Duan Y-P, et al.: Anxiety symptoms in patients with Mayer-Rokitansky-Küster-Hauser syndrome: a cross-sectional study. Chinese Medical Journal. 2020, 133:388-394.

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