RESEARCH ARTICLE

MAYER-ROKITANSKY-KUSTER-HAUSER SYNDROME II (Rare Case).

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Abstract:
Mayer-Rokitansky-Kuster-Hauser (MRKH) syndrome is a rare disorder that affects one in 4500 females [1,2]. It accounts for approximately 15% patients with primary amenorrhea and is also the second commonest cause. Patients with MRKH syndrome usually express a normal 46,XX karyotype [2]. MRKH syndrome is usually present in the form of primary amenorrhea and abnormalities of internal genitalia, namely the absence of uterus and upper 2/3rd of vagina [1]. MRKH females usually have a small vaginal pouch [3]. These patients usually appear to have normal secondary sexual characteristics. Outer vaginal appearance, breast size and pubic hair growth are normal in most cases [2].

Two types of MRKH syndrome have been described referred to as Type I and Type II. Type I MRKH syndrome occurs in an estimated 44% of MRKH patients and is described as a female presenting with mullerian agenesis and a short vaginal pouch. Patients with Type I donot present congenital complications [1,4]. Type II MRKH syndrome is estimated to present in 56% of cases, with Type I characteristics as well as with congenital abnormalities. These can include renal, skeletal, hearing and cardiac complications [4,5]. All women with MRKH syndrome have increased levels of psychological distress.

The etiology is thought to be polygenic, multifactorial, genes such as the HOXA7, HOXA9-13, HOXD9-13 and WNT4 genes have been considered as possible offenders [1]. The normal external appearance of MRKH syndrome patients makes it difficult to diagnose until puberty, typically diagnosed in mid adolescence. The average age of diagnosis is between 15-20 yrs although occasionally a girl may be diagnosed at birth or during childhood because of other health problems. Diagnosis of this syndrome is usually performed by means of ultrasound and magnetic resonance imaging [6]. MRI is the main stay of imaging evaluation of MRKH syndrome, not only to confirm clinically diagnosed mullerian anomalies of uterus but also to access the degree of vaginal dysgenesis and associated anomalies which have an impact on planning of treatment. An accurate diagnosis of MRKH is important as the patient can actually conceive and have their reproductive functions fulfilled with the help of surrogate uterus.

Key Words:- MRKH, Mullerian agenesis.

Case Report:-
A 22 year old female presented with complaints of primary amenorrhea. No such type of illness was seen in family members. There was no history of cyclical abdominal pain. She was of normal stature (160cms), weight 60kg. Patient had no dysmorphic features, secondary sexual characteristics were well developed. Her other examination was unremarkable.

Routine blood and renal function tests were normal. Hormonal profile included measurement of FSH, LH, prolactin, estradiol, 17(OH) progesterone were all normal indicating normal hypothalamic pituitary ovarian axis.

Ultrasound abdomen and pelvis confirmed small uterus measuring 3.1×1.2 cms including cervix. Endometrium was thin, ovaries normal with follicles. USG also showed hypoplastic left kidney measuring 6.7×3.1cms.
MRI pelvis revealed hypoplastic small sized uterus measuring 3.6×1.2cms in mid-saggital images. Axial images showed intercornual distance of 1.12cm (less than 2cm) with poor zonal differentiation with reduced endometrial and myometrial width. Thin linear endometrial was seen. Axial T2W images showed normal sized ovaries with presence of follicles. No other abnormality was seen. Skeletal survey did not reveal any abnormality. Two dimensional echocardiogram was also normal. Chromosomal study indicated normal (46,XX) female karyotype which differentiates it from other genital defects such as Turner Syndrome (45,OX) and Androgen insensitivity syndrome (46,XY). MRI brain carried out did not reveal any abnormality. Audiogram did not reveal any hearing abnormality.

Fig 1: - MRI pelvis showing hypoplastic uterus
**Fig 2:** Blood test reports

<table>
<thead>
<tr>
<th>Test</th>
<th>Status</th>
<th>Reference Range</th>
</tr>
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<tbody>
<tr>
<td>Luteinizing Hormone, Serum</td>
<td>3.73</td>
<td>Normal females</td>
</tr>
<tr>
<td></td>
<td></td>
<td>M. Cycle Peak</td>
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<tr>
<td></td>
<td></td>
<td>Luteal Phase</td>
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<td>Follicle Stimulating Hormone, Serum</td>
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<td></td>
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<tr>
<td>Progesterone, Serum</td>
<td>15.36</td>
<td>Females:</td>
</tr>
<tr>
<td>Estradiol, Serum</td>
<td>217.60</td>
<td>(4-32 Days)</td>
</tr>
</tbody>
</table>
**Diagnostic Report**

**Client's Name:** Shreeji Sangat

**Clinic:** Sangat Pathology Lab

**Address:** 52, Mandir Colony, Anand, Gujarat, India

**Test Requested:** Testosterone, Total

**Client's Name:** Swati Mazumdar

**Date of Birth:** 20 Years

**Sex:** Female

**Accession No.:** 0009/A015919

**Date of Test:** 08/20/2012 00:00

**Received:** 08/20/2012 22:55

**Reported:** 08/20/2012 23:51

**Units:** ng/dL

**Range:** 14.00 - 76.30

**Testosterone, Total:** 20.73

**Reference Range:** Females (Untreated) 12.3 - 48.9

**Pathologist:** Dr. Anil Khanna Nagpuri, DNB

**Cert. No.:** M-0137

**Note:** All investigations have their limitations which are imposed by the limits of sensitivity and specificity of individual assay procedures as well as the specimen received by the laboratory. Isolated laboratory investigations cannot confirm the final diagnosis of a disease. They can only help in arriving at a diagnosis in conjunction with clinical presentation and other related investigations. (Also refer to "Conditions of Reporting" on the reverse.)

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Discussion:

This patient presented with Type II MRKH syndrome or mullerian renal cervical somite (MURCS) association. First sign of MRKH syndrome is primary amenorrhea in young women presenting otherwise with normal secondary sexual characteristics and normal external genitalia, with normal and functional ovaries and karyotype (46,XX) without visible chromosomal anomaly. The syndrome was described by Mayer in 1829. Later in
1838, Rokitansky described uterine and vaginal agenesis, Kuster recognized renal and skeletal abnormalities in 1910 and Hauser distinguished MRKH from testicular feminization in 1961. MURCS association is the most severe form of the disorder that may be attributed to an alteration of the blastema of the cervicothoracic somites and the pronephric ducts which by the end of 4th week of fetal life, have an ultimately spatial relationship. These overall features clearly differentiate the MRKH syndrome from other defects of genital tract development such as Androgen insensitivity syndrome and Turner Syndrome. My patient had a blind vagina and a poorly formed uterus, hypoplastic left kidney with a normal female karyotype.

Conclusion:

Incidence of MRKH syndrome/MURCS association has probably been underevaluated mainly because it has until recently seen as female specific and sporadic disorder. Isolated features of the triad of main malformations including kidney and/or skeletal defects were consequently not investigated in all proband relatives. This is understandable given that incomplete degree of penetrance, variable expressivity and similarities of this syndrome with other genetic disorders. Treatment which consists in creating a neovagina is generally offered to patients along with supportive psychological care. Moreover everyday improvement of medical technologies allow in many countries women to appeal for in-vitro fertilization and surrogate pregnancy to bypass the absence of inner genital tract. Number of such women will probably increase with time. This is why characterisation of genetic events responsible for this syndrome is of major importance.

The purpose of this case presentation is:

- because of its rarity
- absence of a large database from India.

We need to have an expert committee recommendations and specialized surgeons who can offer treatment to these patients.

References:

10. Sunil Kumar and Shruti Sharma. MURCS: a rare cause of primary amenorrhoea. Oxford Medical Case Reports, 2016;4, 73-75.