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MÜLLERIAN DUCT ANOMALIES – A SPECTRUM OF IMAGING ANATOMY

Anil. R. Sherke, Yael Kapoor, M. Krishnaiah and *Dr. Nishat Ahmed Sheikh

Kamineni Institute of Medical Sciences, Narketpally District Nalgonda, State Andhra Pradesh 508254

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ABSTRACT

Background: Müllerian duct anomalies (MDA) are uncommon but can be a treatable form of infertility. Patients with MDA are known to have higher incidences of infertility, repeated first trimester spontaneous abortions, foetal intra-uterine growth retardation, foetal mal-position, pre-term labour and retained placenta.

Aim: The purpose of this study is to identify and categorise Müllerian Duct anomalies using MRI as an imaging modality and to describe the embryological and genetic basis of them.

Materials and Methods: A prospective study was designed to include the patients presenting to the infertility clinic at KIMS, Narketpally for primary amenorrhoea, primary infertility and recurrent pregnancy loss during a period of 3 years i.e from 2011 to2014. 200 such patients reported and the cases of Müllerian Duct anomalies were collected and the radiological, embryological and genetic basis was reviewed.

Observation: Out of 200 selected cases from the Department of OBG of KIMS, Narketpally, 20 cases were found to have Müllerian Duct anomalies by MRI. Such anomalies were studied, compared with the previous similar studies and classified. Most common among the Müllerian Duct anomalies was Mayer-Rokitansky-Kuster-Hauster (MRKH) syndrome (or) agenesis\ hypoplasia of the uterus where there is primary amenorrhoea. Least common was diethylstilbestrol (DES) uterus. Renal anomalies occur in 29% of the MDA and are more commonly associated with uni-cornuate uterus. They are reported in roughly 40% of the patients with uni-cornuate uterus. Among the renal anomalies renal agenesis is most commonly reported occurring in 67% of the cases.

Conclusions: MRI is a gold standard modality of choice used to detect and categorise the cases of MDA.T2WI, fat saturated sagittal sections are best in evaluating the MDA, although coronal and axial sections are also useful. Such study will help in pre conceptional diagnosis and counselling.

INTRODUCTION

Müllerian duct anomalies (MDA) are uncommon but can be a treatable form of infertility. Patients with MDA are known to have higher incidences of infertility, repeated first trimester spontaneous abortions, foetal intra-uterine growth retardation, foetal mal-position, pre-term labour and retained placenta (Fertil Steril, 1998). References regarding the existence of Müllerian defects date back to antiquity, around 300 BC and the first documented case of vaginal agenesis (uterus and vagina) was reported in the 16th century (Steinmetz, 1940). Incidence rates vary widely and depend on the study.

Corresponding author: Dr. Nishat Ahmed Sheikh
Kamineni Institute of Medical Sciences, Narketpally District Nalgonda, State Andhra Pradesh 508254

Most authors report incidences of 0.1-3.5% in general population (Strassmann, 1961; Strassmann, 1966; Golan *et al*., 1989 and Speroff, 2005). The exact distribution depends on the study and on the geographic location (Acién, 1997). Renal anomalies occur in 29% of MDA and are more commonly associated with uni-cornuate uteri than with other MDA. They are reported in roughly 40% of uni-cornuate patients and are ipsilateral to the rudimentary horn. Renal agenesis is the most commonly reported anomaly, occurring in 67% of cases (Li *et al*., 2000). As per the data obtained in various studies on women with recurrent pregnancy loss who are undergoing hysteron-salpingography (Sanders *et al*., 1998) (HSG), the prevalence of Müllerian anomalies was 8-10% (Stray-Pedersen *et al*., 1984 and Stampe Sorensen, 1988). The role of imaging is to detect and classify these MDA so that appropriate treatment is undertaken.

MRI is a gold standard modality of choice used to detect and categorise the cases of MDA (Mueller *et al*., 2007 and Deutch and Abuhamad, 2008). T2WI, fat saturated sagittal sections are best in evaluating the MDA, although coronal and axial sections are also useful. The present study is to different types of Müllerian Duct anomalies which are detected by MRI are categorised into standard groups based on embryology and Genetic basis behind the anomalies is elucidated.

MATERIALS AND METHODS

200 patients reported to the infertility clinic at KIMS, Narketpally for primary amenorrhoea, primary infertility and recurrent pregnancy loss during a period of 3 years i.e from 2011 to 2014. These patients were screened by various methods and the provisionally diagnosed Müllerian Duct anomaly (MDA) patients were subjected to MRI. After diagnosing MDA cases by MRI they were categorised and their embryological and genetic basis were reviewed. It is a record based descriptive study. Sample size was 200 reported cases, 45 had undergone MRI and 20 MDA cases were identified. Females presenting to the infertility clinic with primary amenorrhoea, with primary infertility, recurrent pregnancy loss, were referred to Department of Radiology for evaluation. MRI is a gold standard modality of choice used to detect and categorise the cases of MDA.T2WI, fat saturated sagittal sections are best in evaluating the MDA, although coronal and axial sections are also useful.

Inclusion criteria

Out of 200 cases which came to the infertility clinic, 45 cases provisionally diagnosed as Müllerian duct anomalies were sent for MRI. These females were included in the study.

Exclusion criteria

The infertility cases which are diagnosed as non Müllerian duct anomalies like hypothyroidism, anaemia; heart diseases, etc were excluded from the study.

American Fertility Society (AFS) Classification Scheme (Fertil Steril, 1998**)**

Class I (hypoplasia/agenesis) includes entities such as uterine/cervical agenesis or hypoplasia. The most common form is the Mayer-Rokitansky-Kuster-Hauser syndrome, which is combined agenesis of the uterus, cervix, and upper portion of the vagina.

Class II (uni-cornuate uterus) is the result of complete, or almost complete, arrest of development of 1 Müllerian duct. If the arrest is incomplete, as in 90% of patients, a rudimentary horn with or without functioning endometrium is present.

Class III (didelphys uterus) results from complete non-fusion of both Müllerian ducts. The individual horns are fully developed and almost normal in size. Two cervices are inevitably present.

Class IV (bi-cornuate uterus) results from partial non-fusion of the Müllerian ducts. The central myometrium may extend to the level of the internal cervical is (bi-cornuate unicollis) or external cervical is (bi-cornuate bicollis). The latter is distinguished from didelphys uterus because it demonstrates some degree of fusion between the 2 horns, while in classic didelphys uterus, the 2 horns and cervices are separated completely.

Class V (septate uterus) results from failure of resorption of the septum between the 2 uterine horns. The septum can be partial or complete, in which case it extends to the internal cervical is. The uterine fundus is typically convex but may be flat or slightly concave (<1 cm fundal cleft).

Class VI (arcuate uterus) has a single uterine cavity with a convex or flat uterine fundus, the endometrial cavity, which demonstrates a small fundal cleft or impression (>1.5 cm). Mild thickening of the midline fundal myometrium resulting in fundal cavity indentation but normal outer fundal contour.

Class VII (diethylstilbestrol-related anomaly) has occurred in several million women who were treated with diethylstilbestrol (DES), an estrogen analogue prescribed to prevent miscarriage from 1945-1971. Affected female fetuses have a variety of abnormal findings that include uterine hypoplasia and a T-shaped uterine cavity.

Observations

Out of the 45 provisionally diagnosed cases, 20 females were diagnosed on MRI as having Müllerian duct anomalies. The overall prevalence of MDA was 0.8-4%. The majority had uterine agenesis (n=20), 5 cases, (25%) 3 out of which had renal agenesis of left side approx. (60%). In uni-cornuate uterus, 3 cases, (15%), 2 had infertility 1 had renal agenesis. In bi-cornuate uterus 4 cases, (20%) 3 had spontaneous abortions, 1 had preterm delivery. In uterus didelphys, 2 cases, (10%) 1 had infertility & 1 had preterm delivery. In septate uterus, 3 cases, (15%) all had infertility. In arcuate uterus, 3 cases, (15%) 2 were detected on MRI, & 1 case was incidentally detected in a caesarean section. DES uterus nil reported cases.

DISCUSSION

The WNT4 gene encodes glycoproteins that serve as signalling molecules during early development. Normally the absence of Anti Müllerian Hormone (AMH), gene is SOX9 will trigger stabilization of the Müllerian system and regression of the Wolffian system leading to development of the female reproductive tract. WNT4 gene is the ovary determining gene (Sadler, 2010). This gene up-regulates DAX1that inhibits the function of SOX9 which is an autosomal gene. It is a transcriptional regulator and induces the testes differentiation also called AMH (anti-Müllerian hormone). Exposure of the mother to DES (diethylstilbestrol) which was used to prevent miscarriages till 1971, female foetuses developed a “T” shaped uterus. Random mutation; WNT4 gene mutations were evaluated as a potential cause of MDA in human females. An association with deletion mutation in chromosome 17 (17 q 12) has been reported. The gene LHX1 is located in this region and may be the cause (Dutta, 2011). Erica L. Smith (ETSU) Obstetrics and Gynaecology, in her study on Müllerian duct anomalies—A clinical review published in 2011 (Erica *et al*., 2011) reported that Class1-agenesis is 5-10% Class2-unicornuate uterus is

Table 1. Showing the proportionate percentage of Müllerian duct anomalies in the present study n=20

S. No.	Type of MDS	No. of cases	Proportionate %	Associated anomaly	Other features
1	Agenesis	5	25%	3 had renal agenesis of (L) side	-
2	Unicornuate uterus	3	15%	1 had renal agenesis of (L) side	2 had infertility
3	Bicornuate uterus	4	20%	-	3 had spontaneous abortion 1 had preterm/ delivery
4	Didelphs uterus	2	10%	-	1 had infertility 1 had preterm delivery
5	Septate uterus	3	15%	-	All had infertility
6	Arcuate uterus	3	15%	-	2 cases detected on MRI 1 case was incidentally detected on a caesarean section
7	DES uterus	-	-	-	Last detected in 1995 net figure

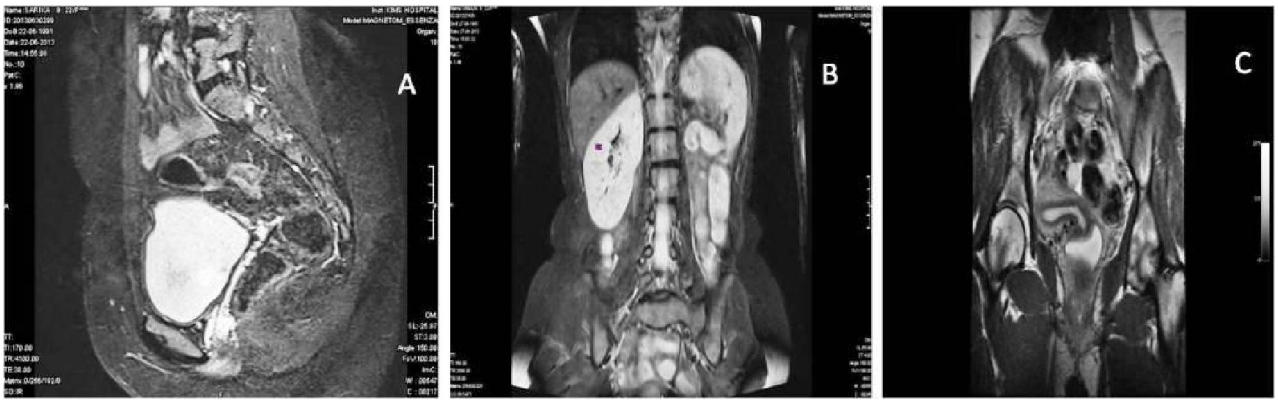

Fig. 1. MRI image of uterine agenesis A: Uterine agenesis B: Left kidney not visualised C: MRI shows development of right cornua, of the uterus, left cornua absent, left kidney not visualized

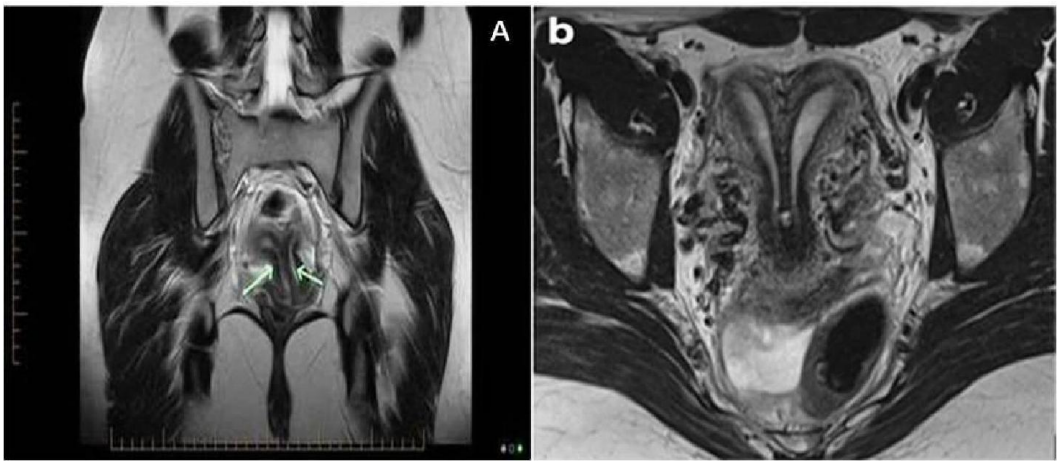

Fig. 2. A: MRI showing didelphys uterus, B: MRI showing bi-cornuate uterus

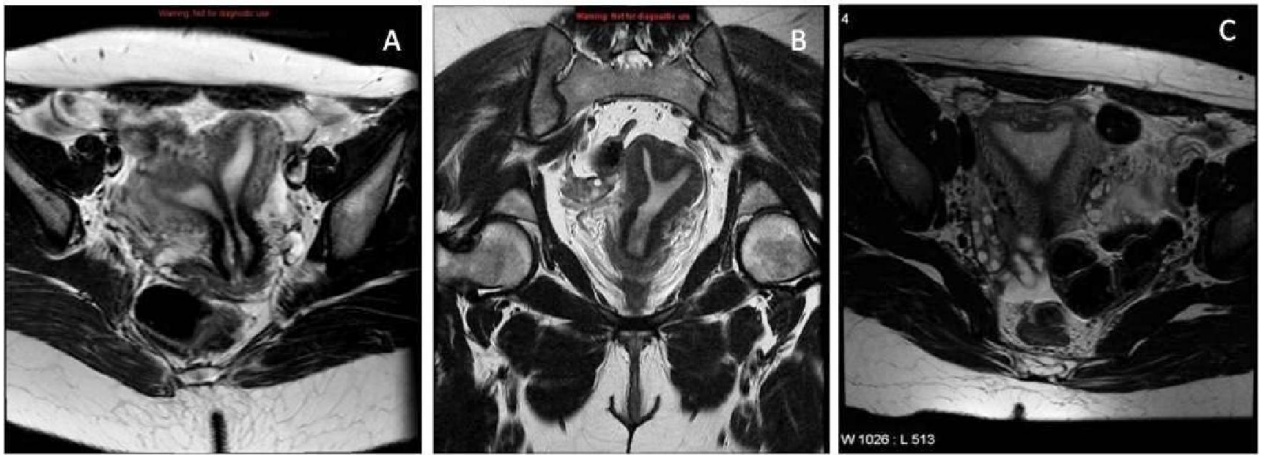

Fig. 3. A: MRI image of complete septate uterus B: MRI image of incomplete septate uterus C: MRI image of the arcuate uterus

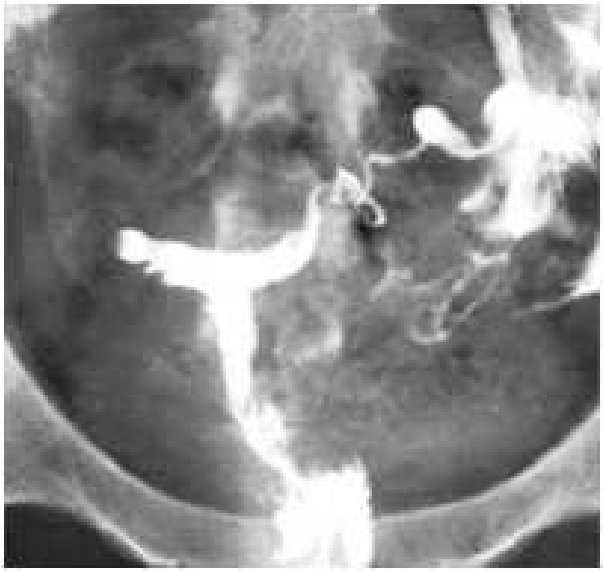

Fig. 4. HSG showing "T" shaped uterus

10-20% Class3-uterus didelphys is 5-20% Class4-bicornuate uterus is 10% Class 5-septate uterus is 55% Class 6-arcuate uterus –? In the present study, agenesis was most common 25%, least common was uterus didelphys 10%. Lawrence S. Amesse *et al* in their study on Müllerian duct anomalies (Lawernce *et al*., 2012) reported incidence of uterine /cervical agenesis (class 1) occurred 1 in 5000 females i.e. 7-10%. Complete Müllerian aplasia (MRKH syndrome) is the most common variant characterised by complete absence of uterus, cervix and upper vagina occurred in 90-95% cases. Fallopian tubes, ovaries, endocrine functions were normal. Urologic abnormalities range between 15-40%. Uni-cornuate uterus (class 2) accounts for approximately 2.4-13% of all Müllerian anomalies renal abnormalities range from 15-67%. Uterus didelphys (class 3) accounts for approximately 11% of the Müllerian anomalies. Renal anomalies occur around 20%. Bi-cornuate uterus (class 4) accounts for approximately 8-10% of the MDA, in which preterm delivery incidence was 28% and spontaneous abortions was 66%, Septate uterus (class 5) ranged from 1.1-3.9%, Arcuate uterus (class 6) incidence was 1-20%. In the present study, agenesis was most common 25%. Least common was uterus didelphs10%.

Conclusion

Most common among the Müllerian Duct anomalies was Mayer-Rokitansky-Kuster-Hauster (MRKH) syndrome (or) agenesis/hypoplasia of the uterus where there is primary amenorrhoea. Least common was uterus didelphys. Diethylstilbestrol (DES) uterus was not reported. Among the renal anomalies renal agenesis is most commonly reported occurring in 60% of the cases with uterine agenesis. MRI is a gold standard modality of choice used to detect and categorise the cases of MDA.T2WI, fat saturated sagital sections are best in evaluating the MDA, although coronal and axial sections are also useful. There is a wide variation in clinical presentations, Müllerian duct anomalies is difficult to diagnose but once an accurate diagnosis is rendered, many treatment options exist, and they are usually tailored to the specific Müllerian anomaly. Such study will help in pre conceptional diagnosis and counselling.

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Author Disclosures

Authors have no conflict of interest. This study was a part of departmental research activities in Anatomy department in collaboration with Radiology department at Kamineni Institute of Medical Sciences, Narketpally.

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