Laparoscopic Evaluation of Anatomical Uterovaginal (Müllerian) Duct Anomalies and associated Ovarian Anomalies in Amenorrheic patients

Luma Ibraim Khalel Al-Allaf, * Ahmed Jasim Al-Husaynei,** Elias Ishak Shaaya,*
*Department of Anatomy, Histology, and Embryology, Mosul College of Medicine.
**Depart. of Obstetric and Gynecology , Mosul College of Medicine.

Abstract

Failure or incomplete fusion of the paired uterovaginal (Müllerian) ducts accompanied with a spectrum of uterine, cervical, and vaginal anomalies which are accompanied by obstruction and leading to amenorrhea. The complex anatomy of ovaries and Müllerian ducts require complete evaluation before treatment. This study aims to determine the frequencies of uterovaginal anomalies and that of ovarian anomalies in group of women presented with primary amenorrhea and to determine whether these Müllerian anomalies are associated with the ovarian anomalies in those patients. In addition this study aims to identify the more frequent ovarian anomaly which was associated with uterovaginal anomalies in a group of patients presented with primary amenorrhea. Al-Batool Maternity Teaching hospital in Mosul city in Northern Iraq. This study was conducted over a period of 4 months started from 1st June 2008 to 1st October 2008. The data were collected from the medical reports of 82 women presented with history of primary amenorrhea during the years 2000-2008. Those women who attended to the hospital and in whom a laparoscopy was performed at Al-Batool Maternity Teaching hospital in order to evaluate the morphology of their ovaries and uteruses. Gonadal agenesis/dysgenesis was shown in twenty eight (34.1%) out of 82 women presented with amenorrhea, while forty five (54.8%) women had different uterovaginal anomalies. Four (4.8%) women had no uterus, while rudimentary uterus was shown in the reports of six (7.3%) cases. Ten (12.1%) women had infantile uterus, while absent uterus and upper vagina was shown in eight (9.7%) women, and one case of aplasia in her uterus and cervix was reported. On the other hand, twelve (14.6%) cases had a vaginal transverse vaginal septum and or an imperforated hymen. Eighteen cases (40.0%) out of 45 cases of anatomical uterovaginal anomalies were accompanied with ovarian abnormalities, the laparoscopic reports of five (11.1%) women revealed combined Müllerian agenesis and absent one or both ovaries, while absent uterus and ovaries were shown in one case (2.2%). Nine (20.0%) women had got infantile uterus and bilateral streak ovaries. On the other hand unilateral ovarian and tubal agenesis was shown in one (2.2%) woman. Two (4.4%) cases of polycystic ovaries were accompanied with uterine anomalies one of them was a case of polycystic ovaries and rudimentary uterus while the another case of polycystic ovaries was accompanied with septate uterus. The presence of testis instead of uterus and ovaries was reported in the pelvis of one case (1.2%). Six (13.3%) out of 45 cases of uterovaginal anomalies was associated with ovarian agenesis, while nine (20.0%) out of 45 cases of uterovaginal anomalies was associated with ovarian dysgenesis. The gonadal agenesis was the first cause of the primary amenorrhea, while the transverse vaginal septum was the second cause. The study concluded that the frequency of anatomical uterovaginal anomalies which are not associated with ovarian anomalies was higher than that accompanied with ovarian anomalies. Ovarian dysgenesis was the most frequent ovarian anomaly which was accompanied with uterovaginal anomalies.

Introduction

The identification of congenital anatomical ovarian and uterovaginal anomalies is important in the treatment of symptoms that arise from an obstructed or deformed reproductive tract causing amenorrhea. Correct diagnosis and classification of these anomalies is needed to determine cases requiring interventional therapy (1, 2). The development of the female genital tract is a complex process.
dependent upon a series of intricate events involving cellular differentiation, migration, fusion, and canalization. Failure of any one of these processes results in congenital anomaly (3, 4).

Classification of subtypes of congenital abnormalities of the female reproductive system is important in the treatment of amenorrhea and infertility (5). Amenorrhea, either primary or secondary, is a frequently encountered clinical condition in primary care office (6). Amenorrhea is traditionally categorized as primary (menarche has not occurred by age 16) or secondary (menstrual periods have not occurred for >= 3 months in women who previously had menses), although often this distinction is not clinically useful. A functional approach is more helpful (7). Amenorrhea--except that occurring before puberty, during pregnancy or early lactation, and after menopause is pathological. Amenorrhea indicates failure of hypothalamic-pituitary-gonadal-uterine interaction to produce cyclic changes in the endometrium, resulting in menses. Primary amenorrhea is usually the result of a genetic or anatomic abnormality, although amenorrhea may be caused by other reasons like; hypothalamic, pituitary, or other endocrine dysfunction (8). Congenital anatomical abnormalities includes: 1.chromosomal abnormalities causing gonadal dysgenesis (which induces premature ovarian failure due to the premature depletion of all oocytes and follicles) (9). The gonadal dysgenesis represents 50 percent of the causes of primary amenorrhea(10).Gonadal dysgenesis usually presents with an abnormal karyotype, either systemically or as apart of a mosaic within the germ cells themselves (9).

2. Absence of the uterus, cervix and/or vagina, Müllerian agenesis (Mayer-Rokitansky-Kuster-Hauser syndrome i.e MRKS) which represents 15 percent of the causes of primary amenorrhea (11).  
3. transverse vaginal septum or imperforate hymen which cause an obstruction and accumulation of menstrual blood .They represent 5 percent of the causes of primary amenorrhea (10 ). Many classifications of uterine anomalies exist; for instance, the Buttram and Gibbons classification and the American Fertility Society (AFS) classification (12). A modified AFS classification by Rock and Adam (13) because it embraces a broader collection of uterine and vaginal anomalies without the conflicting observations or over simplicity encountered in other classifications. This classification has merit because it correlates anatomic anomalies with embryologic arrests. Accordingly, uterovaginal anomalies are categorized as dysgenesis disorders or vertical or lateral fusion defects. Anomalies are further subcategorized into obstructive or nonobstructive forms, since their treatment differs (14). Obstructive uterovaginal anomalies require immediate attention because of retrograde flow of trapped mucus and menstrual blood and increasing pressure on surrounding organs, while immediate treatment is not warranted for nonobstructive forms. Because genital tract aberrations do not necessarily follow any defined and consistent pattern, class 4 is a useful addition embracing any possible unusual configurations or combination of defects (14).

Class 1.Dysgenesis of Müllerian ducts. This class includes agenesis or hypoplasia of the Müllerian duct derivatives: the uterus and upper two-thirds of the vagina. 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 2.Disorders of vertical fusion. They include cervical dysgenesis and obstructive and nonobstructive transverse vaginal septa.

- Class 3.Disorders of lateral fusion. It includes anomalies due to failure of fusion of the paired Müllerian ducts (as in didelphic and bicornuate uteri) and failure of midline septum resorption after fusion (as in septate uterus).

Disorders due to lateral fusion defects are further subclassified into (a): the symmetric nonobstructive form seen in five types: unicornuate, bicornuate, didelphic, septate, and DES-related uteri and (b): the asymmetric obstructive form seen in three types: unicornuate uterus with obstructed horn, double uterus with unilaterally obstructed horn, and double uterus with unilaterally obstructed vagina. Class 4.Unusual configurations and combinations of defects. Many studies concluded that the
presence of amenorrhea, in combination with anomalies, suggests many possible etiologies whose diagnosis and management is critical especially in the young patient (2). An important step in the management of these cases is to document any associated anomalies. This study aims to identify the frequencies of anatomic uterovaginal defects and that of ovarian malformations in cases presented with primary amenorrhea, in addition to determine the frequencies of the Müllerian anomalies which are associated with ovarian anomalies in those cases.

Subjects and Methods
This study was carried out in Al-Batool Maternity Teaching Hospital and conducted over a period of four months started from 1st June 2008 to 1st October 2008. The data were collected from the medical reports of eighty two (82) women during the years 2000-2008. Those women who attended the hospital were referred either by their consultant or from the out patient clinic or from the consultatory clinic presented with primary amenorrhea and had a previous reports of ultrasonic examination beside hormonal assay and underwent for laparoscopic examination. Laparoscopy was performed in order to ascertain the correct morphology of the uterus and the external uterine contour. Direct visualization of the peritoneal cavity, ovaries, outside of the tubes and uterus by using a laparoscopy was performed. The laparoscopy (which was the gold standard method in this study) is an instrument somewhat like a miniature telescope with a fiber optic system which brings light into the abdomen and enabling the physician to see the reproductive organs (15, 16).

Results
A retrospective study of 82 women attended the hospital due to primary amenorrhea and in whom a laparoscopy was performed at Al-Batool Maternity Teaching hospital during the years 2000-2008 in order to ascertain the correct morphology of their uteruses and ovaries. Their data were collected over a period of two months from June 1st to October 1st 2008. Mean age was 19.5 years ±2.8 (range 15-25). The mean of the duration of primary amenorrhea was 2.20 years ±1.5. Their durations range from 1 to 6 years. Thirty four (41.4%) out of 82 women had got normal ovaries, while positive laparoscopic findings of ovarian abnormalities were shown in 48 (58.5%) out of 82 women, including Absent ovary/ovaries in 7 (8.5%) out of 82 patients, while ovarian dysgenesis was shown in 21 (25.6%) out of 82 patients as revealed in Figure (1). On the other hand other ovarian lesion as polycystic ovaries, ovarian cysts were found in 20 (24.3%) patients. Gonadal agenesis/dysgenesis was shown in 28 (34.1%) out of 82 women presented with amenorrhea.

Thirty seven (45.1%) out of 82 women had got normal uterus, while the laparoscopic reports of the remaining 45 (54.8%) out of 82 patients revealed different abnormalities including: combined Müllerian agenesis in 8 (9.7%) out of 82 women, while 4 (4.8%) had got no uterus, one of them accompanied with vaginal atrasia, and another one accompanied by cervical agenesis. On the other hand, one (1.2%) case of vaginal agenesis was reported among 82 patients with amenorrhea. Rudimentary uterus was shown in 6 (7.3%) cases, ten (12.1%) women had got infantile uterus, while infantile uterus with absent part of the vagina was shown in three (3.6%) cases. Three (3.6%) cases of transverse vaginal septum was reported, one (1.2%) of them accompanied with septate uterus. Examination under anesthesia revealed the presence of 9 (10.9%) cases had got an imperforated hymen, one (1.2%) case of them was accompanied by vaginal atrasia. A case (1.2%) of double uterus, vaginal dysgenesis and imperforated hymen was shown. (Table 2).

Eighteen cases (40.0%) out of 45 cases had got different anatomical uterovaginal anomalies, were accompanied with ovarian abnormalities. (Table 1). The laparoscopic reports of five (11.1%) out of 45 women revealed combined Müllerian agenesis and absent one or both ovaries as shown in Figure (2), while absent uterus and ovaries were shown in one case (2.2%). Nine (20.0%) women had got infanteile uterus and bilateral streak ovaries. On the other hand unilateral ovarian and tubal agenesis was
shown in one (2.2%) woman. Two (4.4%) cases of polycystic ovaries were accompanied with uterine anomalies one of them was a case of polycystic ovaries and rudimentary uterus while the another case of polycystic ovaries was accompanied with septate uterus. The laparoscopic report of one case (1.2%) revealed the presence of testis instead of uterus and ovaries in the pelvis. Six (13.3%) out of 45 cases of uterovaginal anomalies was associated with ovarian agenesis, while 9 (20.0%) out of 45 cases of uterovaginal anomalies was associated with ovarian dysgenesis.

**Discussion**

Amenorrhea is one of the important symptoms that generally present to the gynecologist for evaluation and therapy (2). Many factors affect the development of the female reproductive tract (17). Obstructive anomalies prevent normal menstruation, allow collection of blood in the uterus and vagina, and may increase the incidence of retrograde menstruation and may increase the incidence of endometrioses. A high index of suspicion is necessary to diagnose these disorders, and an adequate workup is essential (17). Anatomic examination is however necessary to evaluate cases presented with amenorrhea (11).

Müllerian and Wolffian ducts are the primordia for the internal reproductive systems of females and males respectively and co-exist in the undifferentiated embryo until genetic sex triggers differentiation of either ovaries or testes. Müllerian ducts differentiate into Fallopian tubes, uterus, cervix and upper part of the vagina while the Wolffian ducts degenerate in the females (18).

The mean age of the cases involved in this study was 19.5 years ±2.8, which is higher than assumed mean age of the group of women suffering from problem like primary amenorrhea and that may be due to the approach of the thinking in people of eastern society and low education. The gonadal dysgenesis was reported in the laparoscopic reports of 28 (34.1%) women which represents the highest frequency, this finding is similar to that of Garson et al in 1983 and that of Timmreck et al in 2003 which revealed that the gonadal dysgenesis was the first cause of primary amenorrhea (19,20), while this study showed that 9 (10.9%) had got congenital absence of the uterus and vagina or congenital absence of the uterus and cervix, this finding is being consistent to that of another study done by Michael et al in 2004 who concluded that the complete Müllerian agenesis (Mayer–Rokitansky–Kuster–Hauser syndrome) was the etiology of 15% of causes during the work-up for primary amenorrhea (21), however Reinhold et al (22) reported that the Mayer–Rokitansky–Kuster–Hauser syndrome was revealed in 9 (31.0%) out of 29 women with amenorrhea, this finding is being inconsistent with that of this study, may be due to the difference in the method of the diagnosis which was the magnetic resonance imaging (MRI) or due to the small study sample used or in the method of the selection of his cases.

In spite of the fact that MRI has high accuracy rate and detailed description of uterovaginal anomalies (23) but the accurate evaluation of the ovarian and uterovaginal anomalies must based on the estimation of serosal surface so the laparoscope seems to be used for precise classification of these anomalies in order to reserve the correct intervention (24, 25). Twelve (14.6%) out of 82 women presented with primary amenorrhea, had got different vaginal anomalies and or an imperforated hymen, this finding is inconsistent with that of other study of Reindollar et al in 1986 which showed that the transverse vaginal septum or imperforate hymen represent 5 percent of the causes of primary amenorrhea among 262 women, may be due the difference in the size of study sample or due to the effects of environmental or difference in race and war condition in Iraq (10), however, a study done by Reinhold et al in 1997, revealed that transverse vaginal septum and imperforated hymen was shown in 13.7% women with amenorrhea (22).

Eighteen (40.0%) out of 45 cases had gone abnormal uterus accompanied with abnormal ovaries while the remaining 27 (60.0%) out of 45 cases had got uterovaginal anomalies had normal ovaries. On the other hand thirty (36.5%) out of 48 cases of ovarian anomalies was accompanied with normal uterus while...
Laparoscopic Evaluation of Anatomical Uterovaginal (Müllerian) Duct Anomalies and associated Ovarian Anomalies in Amenorrheic patients

the remaining 18(21.9%) out of 48 cases of ovarian anomalies was accompanied with uterovaginal anomalies, these findings are similar to that of Atkinson et al in 2003 (26), who reported that most of the uterovaginal anomalies are not accompanied with ovarian anomalies.

The laparoscopic reports of 5(11.1%) out of 45 cases of amenorrhea revealed combined Müllerian agenesis with unilateral or bilateral gonadal agenesis this finding is similar to that of Marrakchi et al in 2004 who reported that aplasia or absence of Müllerian derivatives suggestive of MRKH syndrome have been described in cases of gonadal dysgenesis or agenesis (27). At present, these types of ovarian pathologies are not considered to be part of the MRKH type I or MURCS clinical spectrum(type II which is associated with renal , skeletal, hearing and cardiac defects) since no single group of patients showing a random association between any of these pathologies and utero-vaginal aplasia has been reported so far(28,29,30). However, such studies should be undertaken on large cohorts of women with MRKH, to confirm this assumption (11).

Other studies which were done by Phansey et al in 1981, Aydos et al in 2003,Lichiardoplo and Coculescu in 2005, and Pittock et al reported that the Müllerian aplasia is often associated with gonadal dysgenesis (31,32,33,34), they concluded that however the pathogenesis of Müllerian aplasia with or without associated malformation is now well described, its etiology remains unknown (35) and therefore, the study of genetic factors is of considerable interest.

It is important to diagnose the exact cause of amenorrhea in order to manage the cause correctly and to perform the medical and psychological adjustment (36). Many studies concluded that it is necessary to perform careful examination to detect testes in patients instead of normal female genital system, as these testes are more likely to undergo malignant neoplasia (37,38). In addition, Nine (10.9%) out of 82 women had got infantile uterus and bilateral streak ovaries, Krasna et al discussed the risk of malignancy in bilateral streak gonads (39).

This study revealed that only two (4.4%) out of 45 cases presented with amenorrhea had got Müllerian anomalies with polycystic ovaries, this is inconsistent with that of Appelman et al in 2003, and that of Uqur et al in 1995, who reported that there is an association between polycystic ovaries and high rate of uterine Müllerian anomalies and suggested that the embryogenetic defect may also be involved in the etiopathogenesis of the polycystic ovary syndrome, whose etiopathogenesis is not clearly understood, has a wide spectrum of clinical presentations, and may co-exist with other pathologic conditions (40,41). Both studies have been used an ultrasound alone as a diagnostic method of their cases while this study used both of ultrasound and laparoscope for diagnosis of the cases presented with primary amenorrhea and that may explain the difference between the findings between this study and that of their studies.

References

Laparoscopic Evaluation of Anatomical Uterovaginal (Müllerian) Duct Anomalies and associated Ovarian Anomalies in Amenorrheic patients


Laparoscopic Evaluation of Anatomical Uterovaginal (Müllerian) Duct Anomalies and associated Ovarian Anomalies in Amenorrheic patients

Table 1. Frequencies of different anatomical uterovaginal anomalies associated with ovarian abnormalities in comparison with these associated with normal ovaries.

<table>
<thead>
<tr>
<th>Uterus/Ovaries</th>
<th>Normal Uterus</th>
<th>Anatomical Uterovaginal Anomalies</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ovarian Anomalies</td>
<td>30 (36.5%)</td>
<td>18 (21.9%)</td>
<td>48 (58.5%)</td>
</tr>
<tr>
<td>Normal Ovaries</td>
<td>7 (8.5%)</td>
<td>27 (32.9%)</td>
<td>34 (41.4%)</td>
</tr>
<tr>
<td>Total</td>
<td>37 (45.1%)</td>
<td>45 (54.8%)</td>
<td>82 (100.0%)</td>
</tr>
</tbody>
</table>

Table 2. Frequencies of different anatomical uterovaginal anomalies in amenorrheic patients.

<table>
<thead>
<tr>
<th>Uterus/ovaries</th>
<th>Absent Uterus And upper vagina</th>
<th>Absent Uterus</th>
<th>Vaginal Agenesis</th>
<th>Tubal Agenesis</th>
<th>Septate Uterus</th>
<th>Infantile Uterus</th>
<th>Transverse Vaginal septum/Imperforated Hymen</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>With ovarian Anomalies</td>
<td>5 (11.1%)</td>
<td>2 (4.4%)</td>
<td>0 (0.0%)</td>
<td>1 (2.2%)</td>
<td>1 (2.2%)</td>
<td>9 (20.0%)</td>
<td>0 (0.0%)</td>
<td>18 (40%)</td>
</tr>
<tr>
<td>Without ovarian Anomalies</td>
<td>3 (6.6%)</td>
<td>2 (4.4%)</td>
<td>1 (2.2%)</td>
<td>0 (0.0%)</td>
<td>0 (0.0%)</td>
<td>10 (22.2%)</td>
<td>11 (24.4%)</td>
<td>27 (60%)</td>
</tr>
<tr>
<td>Total</td>
<td>8 (17.7%)</td>
<td>4 (8.8%)</td>
<td>1 (2.2%)</td>
<td>1 (2.2%)</td>
<td>1 (2.2%)</td>
<td>19 (42.2%)</td>
<td>11 (24.4%)</td>
<td>45 (100.0%)</td>
</tr>
</tbody>
</table>
Laparoscopic Evaluation of Anatomical Uterovaginal (Müllerian) Duct Anomalies and associated Ovarian Anomalies in Amenorrheic patients

Figure (1). A case of ovarian dysgenesis in 18 year old female presented with primary amenorrhea.

Figure (2). A case of combined Mullerian agenesis in a 17 year old female presented with primary amenorrhea.