Case Report

Mayer–Rokintansky–Küster–Hauser syndrome of Müllerian agenesis

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ABSTRACT

Müllerian agenesis, a congenital malformation of the genital tract is the second most common cause of primary amenorrhoea. Its etiology is poorly understood. It may be associated with renal, skeletal or other abnormalities. The diagnosis is often made radiologically or laparoscopically. Three-dimensional ultrasound is a useful diagnostic tool. The hormonal profile and karyotype in these patients are normal. The management varies, but the treatment of choice is non surgical aimed at creating a neovagina. These patients require psychological support due to the implications for reproduction. Here, we present the case of a 24-year-old married woman with primary amenorrhoea with this malformation.

Saudi Med J 2003; Vol. 24 (5): 532-534

Müllerian agenesis is the second most common cause of primary amenorrhea after Turner syndrome. Its incidence is 1:4000 female births. The uterus itself is not developed, and it is associated with congenital absence of the vagina. The vagina is seen in the form of a dimple where the normal vagina ought to be.[1] Normal secondary sex characters are present. The karyotype is 46XX. While at the present time there is no possibility of creating a uterus, a functional vagina can be created in almost all such women.[2]

Case Report. A 24-year-old nullipara was referred to the regional referral hospital with the history of primary amenorrhea. She was married for one year and had no coital problem. There was no similar history in female siblings or in utero exposure to drugs. On physical examination, she was a well-built lady, 160 cm tall and weighed 58 kg. She had normal breast development and hair distribution. External genitalia was normal but a 2 cm dimple was seen in place of the vagina. Neither cervix nor uterus was felt on bimanual examination. Ultrasononographic examination reported normal kidneys but hypoplastic uterus measuring 3.2 x 1.4 x 2.6 cm. Ovaries were not visualized. No endometrial or myometrial differentiation was seen. A complete workup in the form of hormonal profile and karyotype was carried out. The serum hormonal levels were within normal range. (Leutinising hormone 11.84 mIU/ml; Follicle stimulating hormone 5.2 mIU/ml; Prolactin 576mIU/ml; Estradiol 664mIU/ml). Chromosomal analysis was that of a normal female (46XX).

She had examination under anesthesia and diagnostic laparoscopy, which showed no uterus, blind vagina, normal ovaries (with corpus luteum in the right ovary) and fallopian tubes (**Figures 1 & 2**). The uterus was replaced by rudimentary müllerian tissue on both sides of the pelvis at the pelvic brim. These were attached to round ligaments on either side, which were seen passing through the internal inguinal ring. Ovarian biopsy was taken which showed histologically normal ovarian tissue. A diagnosis of müllerian agenesis was made. Postoperatively, the couple were counseled and the poor prognosis for fertility was explained. Since there was no

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Received 4th December 2002. Accepted for publication in final form 18th February 2003.

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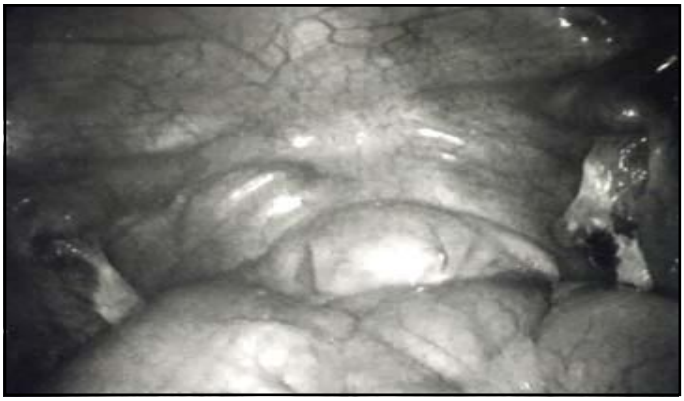

Figure 1 - Rudimentary mullerian tissue on pelvic side wall with normal ovaries, fallopian tubes and round ligaments.

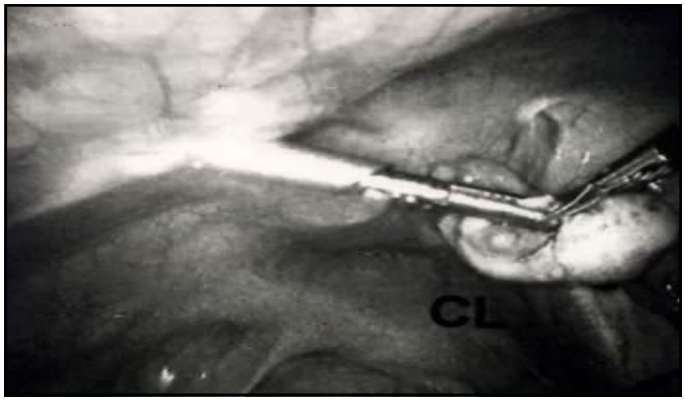

Figure 2 - Right ovary with corpus luteum (CL).

coital problem, there was no need for intervention to create a neovagina.

Discussion. The syndrome of müllerian agenesis was first characterized by Hauser and Schreiner.[3] It is a developmental defect characterized by agenesis of the uterus and vagina but normal gonads. The syndrome can be regarded as resulting from cessation of development of müllerian duct, which in this condition extends only as far as its attachment to the round ligament.[4] The incidence varies from 1:4000 to 1:5000 female births. In females presenting with primary amenorrhea the disorder is fairly common, second only to gonadal dysgenesis as the cause.[5] Although the etiology is unknown several, hypotheses have been postulated for the underlying mechanism. The foremost is an activating mutation of either the gene for the anti-müllerian hormone or its receptor, resulting in inappropriate production of anti-müllerian hormone or the receptor, which then acts as if bound to the hormone. A genetic female fetus exposed to anti-müllerian hormone in utero during embryogenesis at a time when müllerian structures are sensitive may develop müllerian duct regression.[6] It is a polygenic problem with genes almost certainly located on chromosome 16[1]. A strong familial element has been recorded.[7] The principal clinical features are:[8] Primary amenorrhea with normal ovarian function and normal ovulation. There is congenital absence of vagina and variable uterine involvement. Female breast development, body proportion and body hair distribution are normal. There is frequent association of renal (30%-40%), skeletal and other congenital anomalies. These women have normal external genitalia and 46XX karyotype.

Müllerian agenesis is usually diagnosed at puberty due to primary amenorrhea. If endometrial tissue is present in the rudimentary uterine horns, the patient may present with cyclical lower abdominal pain. In this case, the ultrasound did not show any endometrial and myometrial differentiation which would account for the absence of cyclical abdominal pain. Ovarian function as assessed by hormonal assay and basal body temperature fluctuation is also normal. The diagnosis can be made by radiological [ultrasound or magnetic resonance imaging (MRI)] or endoscopic examination. Two-dimensional ultrasound is not a reliable method of diagnosis, as exemplified by this case. Three-dimensional ultrasound provides accurate diagnosis of congenital uterine anomalies.[9] Therefore, while evaluating these patients the first investigation should be pelvic and renal tract ultrasonography. Until recently, laparoscopy was considered necessary for definitive diagnosis. MRI, which has the advantage of being noninvasive, although costly and not universally available, has superseded laparoscopy. Laparoscopy, on the other hand, will define the precise anatomical location and abnormalities of the uterus and ovaries. The main differential diagnosis is testicular feminization syndrome where the karyotype is 46XY. Failure to obtain a karyotype, therefore, may miss the diagnosis altogether. The treatment is usually delayed till the patient is ready to start sexual activity. Successful management of the congenital anomalies of genital tract demands both intense psychological support and high degree of surgical skill. In depth consultation should be obtained or patients should be referred to centers where such expertise exists and where long-term follow up can be provided. Each case has to be dealt with individually, depending on the patient's anatomy, desires and age.[10] Laparoscopy is useful for diagnosis and for any treatment required, for example, for the resection of rudimentary horn where indicated.[11]

The creation of vagina is by non-surgical and surgical approaches. The non-surgical procedure may be in the form of Frank's dilator method or Ingram's variation utilizing a specially designed bicycle stool. Both use graduated dilators to stretch the short vagina and are successful in 85% of the cases and should therefore be the treatment of choice.[1] The most commonly used surgical method is Abbe McIndoe technique, which utilizes skin graft from the gluteal region to epithelilize the neovagina. Modification of the McIndoe procedure

use different materials such as human amnion, peritoneum, segments of colon, gracilis or rectus abdominis muscle. The Vecchietti operation is a mixture of surgical and non-surgical methods and has been frequently performed in Europe.[12]

All the techniques at the present time have a success rate of around 80% and failure is usually the result of contracture of the neovagina due to the failure of the use of either a mould or dilators in the postoperative period. Surrogacy, where legally and ethically accepted is a feasible option and has made it possible for these patients to have their own genetic children.[13] Patients who make such options should be well informed and supported. Success with surrogacy is high as suggested by recent reports from North America. The ultrasound assessment of the pelvis of the female children born to these women so far has revealed the presence of a uterus. The inheritance of these disorders is therefore, not a dominant one. A recurrence rate of 2-5% is expected in polygenic abnormalities. Since so far less than 50 female infants have been born it is more than possible that this phenomenon of Rokitansky syndrome will occur in the offspring of one of these women.[1]

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