

## **Congenital Anomalies of Uterine Development**

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### **Introduction**

Congenital anomalies of the uterus derive from interrupted development of the mullerian duct system. The causes of these anomalies are generally thought to be multifactorial with some genetic and environmental influences (e.g. exposure to diethylstilbestrol). Anomalies may occur either in isolation or be associated with other, sometimes syndromic, abnormalities.

The incidence and prevalence of mullerian anomalies in the general population is not known, but is probably around 1% (1).

### **Presentation**

Uterine anomalies very occasionally present in the neonatal period or early childhood as part of a disorder of sex development (ambiguous genitalia etc.) or as part of a complex anomaly such as a cloacal or anorectal anomaly, extrophy etc. The majority of patients present in adolescence or early adulthood. The mode of presentation is a good clinical indicator of the underlying anomaly.

Primary amenorrhoea is the most common presentation of patients with mullerian anomalies and this may be either painless or painful. Painless amenorrhoea is due to an absent uterus as is found in XX women in Mayer-Rokitansky-Kuester-Hausler syndrome (MRKH) where the gonads are normal, or it can be associated with XX streak gonads where the uterus is unstimulated and therefore very small. Patients with MRKH syndrome go through puberty, but those with streak gonads do not.

In XY women, the uterus is entirely absent in complete androgen insensitivity syndrome and these patients may have ectopic or streak gonads (testes). In Swyers syndrome a very small uterus is present but there are no ovaries, and these patients do not go through puberty.

Painful primary amenorrhoea with or without an abdominal mass is due to obstructed menstruation. These patients are XX and have functioning ovaries, and will have gone through puberty. Obstruction can be at the level of a uterine horn, the cervix or more distally in the vagina. In patients with a double system (uterus didelphys) where only one horn is obstructed, menstruation can occur but be very painful. These patients may present late as they frequently dismissed as having 'painful periods'.

Transverse and longitudinal vaginal septa can present with dyspareunia or difficulty inserting tampons. Infertility and miscarriage are associated with the septate uterus.

### **Embryology**

The mammalian genital tract development is closely related to that of the urinary system. Nephrotomes develop initially consisting of a ciliated funnel communicating with the coelomic cavity and a nephritic tubule connected to a common excretory duct- the Wolffian duct (WD), a pair duct system. In higher vertebrates, the most posterior of the nephrotomes form the ultimate metanephric kidney. As this system develops, a second paired tubular structure, the paramesonephric or Mullerian ducts (MD) appear and grow cranio-caudally (elongating), adjacent to the WD and eventually joining it at the urogenital sinus. The MD develops into the uterus, cervix, fallopian tubes and proximal vagina. To do so it requires the WD as this sends paracrine signals necessary for the maturation of the MDs.

In males, the MDs regress due to the expression of anti-Mullerian hormone (or Mullerian-inhibiting substance). In the absence of testicular hormones, the Mullerian ducts differentiate and the WDs regress. The 2 MDs elongate and the growing tips converge and join at the urogenital sinus. The Mullerian tubules then fuse and form a single lumen tube, the utero-vaginal duct, which gives rise to the proximal vagina, cervix and the uterus. The regression of the septum separating the 2 fusing tubes may be the result of apoptosis, mediated by the Bcl2 gene. The

anterior non-fused region differentiates into the fallopian tubes and the infundibulum. The MDs then mature with 3 processes occurring, region specific differentiation, formation and organization of endometrium and myometrium, and then uterine adenogenesis.

The entire process is controlled by the correct expression of various transcription factors and signaling molecules that are genetically (and also environmentally) dependent (2). Consequently, the development of the reproductive and urogenital systems are intimately linked and disorders of one are likely, through either genetic or environmental factors, to occur in combination with the other.

### **Classification and its problems**

Congenital uterine anomalies are due to

- non-development of a structure (agenesis)
- fusion abnormalities where the 2 paramesonephric ducts fail to fuse normally
- absorption abnormalities where the tissue separating the 2 fused uterine horns persists.

Failure of fusion is the cause of bicornuate uteri and uterus didelphys. Failure of absorption is the cause of the septate uterus. Vaginal abnormalities are either due to an abnormality of the MD development, which affects the proximal vagina, or due to maldevelopment of the urogenital sinus which affects the distal vagina.

The system of classification used most commonly to describe the types of uterine anomalies is the modified American Fertility Society Classification (3). It divides anomalies into Type a- the aplasias, Type b - the unicornuate uterus and its variants and Type c describing fusion/absorption anomalies varying from arcuate deformity, through to septate, bicornuate and didelphic uterus. Alternative systems of classification have also been described including VCUAM (vagina cervix uterus adnex-associated malformation) (4). However anomalies frequently do not fit with any of these classifications and consequently their use is limited.

### **Clinical assessment**

Clinical assessment of the patient includes physical pelvic examination, assessment of body phenotype, breast development and external genitalia. Physical examination is important but vaginal examination can be limited/not possible in very young children, sexually inactive patients and those with no vagina. Consequently much of the structural assessment of the gynaecological tract is dependent on imaging.

In addition to physical assessment patients may undergo other investigations including imaging, genetic and hormonal assessment, and measurement of bone density. Some patients may also require psychosocial assessment and support.

### **Imaging**

MRI is accepted as the most comprehensive and accurate method of assessing the anatomy of the gynaecological tract (5,6). Ultrasound is frequently used in babies and very young children. It is often the first imaging investigation in patients presenting with acute abdominal pain. However its use is limited as the same restrictions apply to transvaginal ultrasound as to clinical vaginal assessment, and the accuracy of morphological assessment is inferior to MRI.

### **Image Assessment- What the specialist needs to know**

In our practise we have found that for clinical purposes, assigning a classification is not a useful part of the report. Instead we concentrate on giving a detailed description of the anatomy, sufficient for the clinician to manage the patient. In patients with no uterus or only non-functional uterus, the management is psychological counselling and fertility advice. In other patients with functioning uteruses the clinician and surgeon require an accurate description of the morphology and an assessment of the functional potential of the uterus in order to decide whether/what surgery is appropriate, what tissue can be sacrificed, what reconstruction is necessary and how the surgery should be approached (laparoscopic v. abdominal v.

transperineal). It is important to know whether the menstrual cycle is being suppressed as this can dramatically alter the appearances of the endometrium and degree of obstruction.

#### **Scheme for systematic reporting of scans:**

- Presence, size, position of ovaries and presence of follicles
- Obstruction and if so, at what level
- Presence or absence of dilated fallopian tubes
- Presence, shape, dimensions and anatomy (eg body, cervix) of any uterine horns
- Extent and site of fusion of uterine horns
- Presence, length and thickness of any septum
- Presence of functioning endometrium
- Presence of vagina, double or septate vagina
- Length of proximal vagina and distal vagina\*
- Length of gap separating distal and proximal vagina, distance from proximal vagina to perineum \*\*
- In patients with DSD, size, site and appearance of any gonads
- Assessment of kidneys \*\*\*
- Assessment of skeletal, bladder and other urological anomalies
- Features of endometriosis and intra-peritoneal blood

\* Vagina measured as described by Humphries et al (7)

\*\* As our urological surgeon says, 4 cm can feel like 10 when being dissected from the perineum.

\*\*\* Unilateral renal agenesis occurs in up to 30% of patients with Mullerian anomalies and is most commonly seen in patients with uterus didelphys (8)

By using this scheme, surgical management can be appropriately planned. For example, the length of available vagina and its distance from the perineum will dictate whether vaginal reconstruction can be made using a perineal or abdominal approach and whether bowel interposition is necessary. Vaginas greater than 1 cm can sometimes be lengthened by the use of dilatation techniques (9). Similarly, resection of a rudimentary unicornuate uterus can be a simple and quick procedure if the uterus has a narrow neck and is superficially related to the dominant unicornuate uterus. However if it is deeply embedded surgery can be difficult and prolonged.

#### **Summary**

Congenital uterine anomalies are uncommon but clinically significant. Imaging and in particular MRI is fundamental to the accurate diagnosis and assessment of these anomalies. Detailed assessment of the reproductive tract is essential for the planning of appropriate therapy and in particular for surgical planning.

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