Euro-Chinese Consensus on Accessory Cavitated Uterine Malformations

PART I. BACKGROUND

Embryology of the Internal Genitalia

The formation of the gonads begins as swellings located on either side of the dorsal mesentery, at the ventromedial surface of the mesonephros or Wolff's body. These protrusions form the gonadal or genital ridge as part of the primitive urogenital ridge.

During the sixth week, in the thickness of the urogenital ridge, the mesonephric excretory tubules converge in a mesonephric or wolffian duct that descends to the cloacae, opening in the urogenital sinus. Meanwhile a longitudinal invagination of the coelomic epithelium is formed on the outer side of the urogenital ridge that originates the paramesonephric or Müllerian duct (Acién et al., 1992).

This duct, at the top, opens into the celomic cavity and descends in parallel and externally to the mesonephric duct. Then, both Müller's ducts cross ventrally the mesonephric ducts, growing in the caudomedial direction until fusing together and forming in the middle line a Y-shaped structure that is the uterine primordium, but without reaching the urogenital sinus (**Figure 1**).

Three portions can now be distinguished in the müllerian ducts: a superior converging, a middle fused and an inferior diverging portion. The tubes come from the uppermost part of the Müllerian ducts, the converging portion, that remain separated and opened into the celomic cavity. The middle-fused parts of the paramesonephric ducts form the uterus and the diverging portion form the cervix up to the external cervical os (Sánchez-Ferrer et al, 2006). And it´s interesting to note that these different areas have also been related to different gene expressions of the HOXA family (Du et al., 2016).

When the ovary is being formed, and therefore testosterone and anti-müllerian hormone (AMH or müllerian inhibitor factor) are absent, the Wolffian ducts become atretic and regress cranially, and the Müllerian ducts develop. However, the adequate development and fusion of the paramesonephric ducts, the reabsorption of the middle septum and the

correct formation of the normal uterus is induced by the laterally located mesonephric ducts. These fusion and reabsorption processes begin at the uterine isthmus (which is the most proximate part between both Müller ducts, right above the internal cervical os) and progress simultaneously, but independently, in both cranial and caudal directions acting the mesonephric ducts as guide elements (Gruenwald et al., 1941; Acién et al., 2009).

The gubernaculum forms from the caudal fold that provokes the mesonephros elevating the covering peritoneum (**Figure 2**). It begins as a muscular cord-like structure that extends from the abdominal wall to the gonadal ridge. But the development of the paramesonephric or Müllerian duct interferes the connection of this tissular column that has arisen between the inguinal cone and the caudal ligament of the gonad. Therefore, the gubernaculum then grows over the paramesonephric ducts, and its muscular fibres incorporate into the wall of the Müllerian ducts, becoming the round ligament. Behind and above, only atretic remnants of the mesonephric duct remain; and, the caudal ligament, uniting the gonad inferior pole to the posterior wall of the Müllerian ducts, constitutes the utero-ovarian ligament (Acién et al., 2011).

The female gubernaculum is likely formed by muscle fibres that are not of a mesonephric or paramesonephric origin and their attachment to the Müllerian ducts allow the adequate development of the uterus. But the gubernaculum might as well be responsible for many other specific human characteristics, including the uterus simplex, the anteflexion and low-intra-abdominal position of the uterus, and the disposition of uterine muscular fibres (Acién et al., 2011).

Key Question: What are the current theories on the etiopathogenesis of ACUM?

The pathogenesis of this entity is controversial. It is possible that the accessory cavitated uterine masses associated with an otherwise normal uterus are considered müllerian choristomas (Batt and Yeh, 2011) as by definition the term refers to the growth of normal tissue at an ectopic location, thus suggesting a developmentally misplaced müllerian tissue. But the main question is where does this ectopic tissue come from? And why?

Much earlier that in the female, during the eighth week of a male embryo, the production of testosterone and AMH begins and the consequence is that the mesonephric or Wolffian ducts develop while the paramesonephric or Müllerian ducts become atretic. Androgens,

together with AMH and INSL-3 (insulin-like hormone), stimulate the growth of the tissular column which from the inguinal cone crosses the mesonephric or Wolffian duct to reach the caudal ligament at the inferior pole of the gonad. Thus, this third element in the crossing area, the gubernaculum, does not attach to the müller duct and becomes the scrotal ligament, responsible for pulling down the gonad to the scrotum. Current thinking favours that the cranial gonadal suspensory ligaments, hormones, genes and other factors might also influence this process (Emmen et al., 2000). And its failure leads to cryptorchidism.

Accessory cavitated uterine masses could be caused by the duplication and persistence of ductal Mullerian tissue in the critical area at the attachment level of the round ligament, possibly related to a gubernaculum dysfunction or abnormal traction and, as such, of congenital origin (Acién et al, 2010). And it can be speculated that an increased tension or traction of the gubernaculum could also favour absence of fusion of the müllerian ducts or traction of an hemiuterus or rudimentary horn towards the inguinal duct and its herniation (Acién et al., 2011). Also, the observation of a tubal rudiment adjacent to the ACUM would speak in favour of detached Müllerian choristoma due to abnormal gubernaculum traction in a female embryo (Acién et al., 2021).

Key Point:

- *Accessory cavitated uterine masses could be caused by the duplication and persistence of ductal Mullerian tissue in the critical area at the attachment level of the round ligament, possibly related to a gubernaculum dysfunction or abnormal traction.*

Key Question: What is the most appropriate terminology for ACUM?

Various terms have been used for ACUM, including adenomyotic cyst, juvenile cystic adenomyosis, myometrial cyst, and uterine-like mass.

It has often been published under the term ‘Juvenile cystic adenomyoma’, but it actually refers to the same pathology as the ACUM.

The Pros and Cons of using the word ‘malformation’ and ‘mass’ are shown in the table 1.

Table 1. Pros and Cons of using the word ‘malformation’ and ‘mass’

	Accessory cavitated uterine mass	**Accessory cavitated uterine malformation**
Pros	It highlights the fact that the anomaly looks like a tumour plus it is often present in a uterus which is otherwise completely normal, making the difference with other uterine malformations like the rudimentary horns or the Robert uterus.	It highlights the fact that the anomaly is a malformation.
Cons	A mass, can be benign or malign	The term anomaly is preferred nowadays to refer to malformations plus, less papers are retrieved in Pubmed using this terminology.

We recommend using the word ‘malformation’ rather than ‘mass’. Not only is it a more accurate reflection of what ACUMs are, but the word ‘mass’ implies uncertainty of the nature of a lesion which can lead to unnecessary concern over possible malignancy.

Key Point:

- *Accessory cavitated uterine malformation is the preferred terminology*

Key Question: How is ACUM classified according to the existing classification systems?

Over the last two centuries, we have gained better knowledge on the embryology and pathogenesis of congenital malformations of the female genital tract. There have been different attempts to classify female reproductive tract anomalies (Kives et al., 2016; Strassmann et al., 1907; Jones et al., 1953; Buttram et al., 1979; AFS classification, 1988; ASRM 2021; Acién et al., 2004; Acién et al., 2011; Oppelt et al., 2005; Grimbizis et al., 2013).

Despite many classifications systems of female genital tract anomalies are available, Acien’s proposal was the first and only one to include ACUM as a gubernaculum anomaly.

It is based on the embryological development and the clinical presentation of the anomaly.

Key Point:

- *Acién's classification is the only system which specifically refers to the ACUM.*
- *Clinicians who care for patients with Müllerian anomalies should be mindful of existence of other rare, unique and potentially very complex variants.*
- *Continued international efforts are needed to conduct high-quality studies that offer evidence-based data to improve the classification systems and their applicability in clinical practice.*

PART II. CLINICAL PRESENTATION, DIAGNOSIS AND DIFFERENTIAL DIAGNOSIS

Key Question: What are the typical and atypical symptoms in patients with ACUM?

ACUMs were associated with substantial pelvic pain symptoms in all published cases. The most frequently reported symptoms are severe menstrual pain that can be central or ipsilateral to the side of the ACUM, and chronic pelvic pain. Other symptoms reported in the literature include dyspareunia and hypogastric pain. The pelvic pain is thought to be caused by accumulation of an increasing volume of menstrual fluid from the functioning endometrium lining the ACUM, within a cavitation that has no outflow. The presumed mechanism for this causing pain is that it leads to increased pressure within the ACUM and subsequent stretching of the cavity.

Like other obstructive uterine anomalies, it tends to present in young women and girls. Nevertheless, while there are case reports describing diagnosis at as young an age as 13 years old (Fisseha et al., 2006), the mean age at diagnosis in the larger case series' varies from 21 years old –29 years old (Acien et al., 2010; Takeuchi et al., 2011; Acien et al., 2012; Peyron et al., 2019; Naftalin et al., 2021). This most likely reflects the commonly experienced delays in reaching a diagnosis of ACUM, rather than being an accurate description of the onset of symptoms, which is classically described as starting with menarche or soon afterwards.

Key Points:

- *Typical symptoms: dysmenorrhea, dyspareunia and recurrent pelvic pain*

- *Atypical symptoms: gastrointestinal pain and generalised pelvic pain as can be seen in any chronic/recurrent pain problem*
- ACUMs should be considered in all young women presenting with severe menstrual pain symptoms after menarche

Key Question: What are the diagnostic criteria for an ACUM?

ACUMs are almost certainly under-diagnosed, due to a lack of awareness by patients and clinicians, as well as the absence of widely agreed diagnostic criteria. Failure to diagnose ACUMs will often condemn women to years of debilitating pain while trialling empirical, often ineffective, treatments. Many will undergo unnecessary investigations, procedures and operations in an attempt to diagnose the cause of their pain or to treat the pain. There is also an additional psychological impact to experiencing debilitating symptoms with no clear explanation for them. Most importantly, failure to diagnose ACUMs denies women the opportunity for surgical excision, which in most cases substantially reduces or even completely cures the symptoms. Various diagnostic criteria have been proposed for the diagnosis of ACUMs, as detailed below.

Acien et al 2010

1) an isolated accessory cavitated mass
2) normal uterus (endometrial cavity), tubes, and ovaries
3) surgical case with excised mass and with pathological examination
4) accessory cavity lined by endometrial epithelium with glands and stroma
5) chocolate-brown– colored fluid content
6) no adenomyosis (if uterus removed), but there could be small foci of adenomyosis in the myometrium adjacent to the accessory cavity.

Takeuchi et al 2010

1) solitary myometrial cyst measuring >1 cm surrounded by hypertrophic endometrium, independent of the uterine lumen
2) found in women $\leq$30 years of age
3) associated with severe dysmenorrhea

Chun et al 2011

1) the age of onset of severe dysmenorrhea is within 5 years after menarche or ≤18 years of age
2) no history of suspected endometrial or uterine injuries (delivery, myomectomy or dilatation and curettage)
3) the presence of a cystic lesion ⩾0.5 mm indicated by imaging studies or observed during surgery.

Naftalin et al 2021

1) Solitary cavitated lesion with a
2) myometrial mantle and
3) echogenic contents in the anterolateral wall of the myometrium beneath the insertion of the round ligament
4) Ruling out obstructive congenital anomalies, such as a communicating and noncommunicating horns is crucial to diagnosis

Timmerman et al 2024

1) A uterine abnormality, presenting as a cavitated lesion surrounded by a myometrial mantle, in continuity with the anterolateral uterine wall, and located beneath the insertion of the round ligament and the interstitial portion of the fallopian tubes.
2) The appearance on imaging reflects the surrounding rim of functional endometrium and the haemorrhagic content of the cyst.
3) to distinguish ACUMs from other uterine abnormalities, a normal uterine cavity should be visualized.

There is unsurprisingly substantial overlap between these diagnostic criteria but there are specific criteria that apply to most cases but are not ubiquitous. Acien et al's criteria describe a normal uterus (endometrial cavity) tubes and ovaries as a criterion although not indispensable (Acién et al., 2012). More specifically they state that the patient must not have adenomyosis apart from small foci of adenomyosis surrounding the ACUM. Women may often however have coincidental uterine or ovarian pathology such as

fibroids, a dermoid cyst or even adenomyosis elsewhere in the uterus that would not need to influence the diagnosis of an ACUM. Further, their criteria include surgical excision of the ACUM for a definitive diagnosis, but there are increasing numbers of case descriptions of women with ACUMs not undergoing surgical excision. Increasing imaging quality means that the diagnosis can be confidently reached without requirement of surgical excision. Nevertheless, as the original description of ACUMs, Acien et al's criteria have formed the basis of all the subsequent descriptions.

Both Takeuchi and Chun's diagnostic criteria include stipulations about age (Takeuchi et al., 2010; Chun et al., 2011). While these criteria help focus on the younger age group in which women with ACUMs frequently present, there are many case reports that describe women with ACUMs presenting outside of these age-related criteria. Chun et al go onto state that no history of suspected endometrial or uterine trauma should have occurred including delivery (Chun et al., 2011). Again, however, there are multiple case reports of women with ACUMs being diagnosed despite having had children or having previously undergone uterine surgery. More recent diagnostic criteria by Naftalin et al & Timmerman et al have focused more on the imaging appearance of ACUMs while still maintaining Acien et al's original focus on the importance of ensuring that other uterine anomalies with similar appearances to ACUMs are excluded (Naftalin et al., 2021; Timmerman et al., 2024; Acién et al., 2012). These criteria have evolved over time as more has been learnt about ACUMs. Mindful that there remains a great deal about ACUMs that we do not yet know, it is important that diagnostic criteria account for this uncertainty and do not become overly proscriptive.

Key Points:

In order to diagnose ACUM, the following criteria should be fulfilled:

- *Isolated cavitated lesion located in the anterolateral myometrium, in the proximity of the round ligament*
- *The cavity is lined by endometrial tissue and typically filled with haemorrhagic/menstrual fluid.*
- *The cavity is surrounded by a myometrial mantle with concentric orientation of myometrial fibres.*
- *They are typically associated with a normal uterine cavity*

Additional notes

- While large ACUMs may enlarge to *involve* the posterolateral myometrium, because they are thought to originate from the gubernaculum, they should predominantly be within the anterolateral myometrium.

- ACUMs are found within the myometrium but the extent of their involvement with the myometrium can vary. They can be completely embedded within the myometrium or substantially outside the myometrium with minimal myometrial involvement. A grading system could be used to describe this based on the FIGO classification of type 4, type 5 and type 6 fibroids as this will inform the extent of surgical dissection necessary as well the risk of uterine cavity breach (Munro et al., 2011).

Key Question: What are the diagnostic tools for diagnosing ACUM?

Transvaginal ultrasound is the primary diagnostic tool in gynaecology and in expert hands, is sufficient to diagnose ACUMs with confidence. Nevertheless, not all gynaecologists or sonographers will have the experience or confidence to diagnose ACUMs on ultrasound alone. MRI is important in these circumstances and with expert radiologists, the diagnosis can be made with confidence. Furthermore, given that the population in which ACUMs will be suspected often includes young women and girls in whom transvaginal ultrasound might not be appropriate, MRI should be considered in preference to transvaginal ultrasound. Consideration can also be given to transrectal ultrasound, which gives equivalent views to transvaginal ultrasound, although it may also not be appropriate or considered acceptable by the patient.

Ultrasonography

On ultrasound, ACUMs are visualised as cavitated lesion with a myometrial mantle and echogenic contents seen in the antero-lateral wall of the myometrium or within the broad ligament (**Figure 3**). While the myometrial mantle will likely be of similar echotexture to the surrounding myometrium, the concentric orientation of its muscle fibres means that it can be clearly distinguished from it. The endometrial lining will often be visible. The fluid within the cavity should be echogenic and is most often seen as being of

'groundglass' echogenicity, being equivalent to the altered blood content seen in endometriomas. The contents have, also been reported as hyperechogenic.

3D ultrasound can also be useful in confirming the diagnosis, although it can be difficult to get a single clear image both the uterine cavity and the ACUM within it, because they are rarely in the same plane. Coronal 3D ultrasound image should reveal a circular cavity adjacent to the otherwise normal uterine cavity with no communication between the two cavities (**Figure 4**). 3D ultrasound is also crucial to excluding other uterine anomalies and so in women with ACUMs, the main uterine cavity will be visible with both uterine horns.

Key Point

- *In expert hands, the diagnosis of ACUM can confidently be made on transvaginal or transrectal ultrasound.*

Magnetic Resonance Imaging

Similarly on MRI, ACUMs will be seen to have a central cavity, surrounded by a well-defined ring with low T1 and T2 signal enhancements, which is similar to that of the junctional zone (**Figure 5**, **Figure 6**). The surrounding myometrial mantle has been described as thickened and hypointense on T2-weighted images, which demonstrates myometrial hypertrophy. In addition, the cavities had a thin inner lining that moderately enhanced after gadolinium contrast and appeared hyperintense on T2-weighted images, indistinct from endometrium. The internal content of the cavities displays high T1 signal intensity, which persists after fat saturation and is indicative of haemorrhagic content. Some lesions will demonstrate T2 shading, which is seen in ovarian endometriomas.

Key Point

- *If there is diagnostic uncertainty after ultrasound examination, consideration should be given to using MRI.*

Histology (Microscopy)

Microscopically, the cavity of the lesion is lined with functional endometrium consisting of glands and stroma and blood is seen within the cavitation (**Figure 7**). Studies report that the endometrial tissue within ACUMs positively stains for CD10, estrogen receptors (ER) and progesterone receptors (PR), which are markers of normal endometrium. They also reported that the myometrial mantle of the ACUMs contained smooth muscle cells that stained positive for desmin, ER, and PR. The myometrium surrounding the cavitated lesion may be hypertrophic and will often contain foci of adenomyosis.

Key Point

- *Not all histopathologists are familiar with ACUMs so it is important to let them know what that you suspect an ACUM and ensure they are aware of their histoapthological features*

Differential diagnoses

Obstructive congenital uterine anomalies are key differentials of ACUM and therefore excluding them is crucial to the diagnosis of ACUMs. It is therefore important, that whichever imaging modality is used, it can be demonstrated that there is no connection to either the uterine cavity or to the Fallopian tubes and that there are two normal interstitial portions of the Fallopian tubes. Those without sufficient expertise in ultrasound and MRI may consider other more invasive investigations such as hysterosalpingography (HSG), HyFoSy/HyCoSy or hysteroscopy to exclude other congenital anomalies, but these should only be required in rare circumstances.

Other important differentials of ACUMs are cystic adenomyomas, unicornuate uteri with functioning rudimentary horns, Complete septate uterus with unilateral cervical aplasia (Robert uterus) and degenerating fibroids. It is particularly important to differentiate these entities because the management options and strategies vary greatly. Knowledge of their different features can help distinguish them (Table 2). Other potential differentials that could be confused with ACUMs are endometriomas that are adherent to the lateral aspect of the uterus and rarer ectopic pregnancies including interstitial, intramural and rudimentary horn pregnancies.

Table 2. Key differential diagnoses

	Accessory Cavitated Uterine Malformations	**Cystic adenomyomas**	**Rudimentary horn with functioning endometrial cavity**	**Complete septate uterus with unilateral cervical aplasia (Robert uterus)**	**Degenerated fibroids**
Location	Located in the anterolateral myometrium, in proximity to the round ligament	Located in the myometrium	Located at the lateral cornual aspect or lateral and distinct to the myometrium	Located in the lateral aspect of the uterus with a thin septum between cavities that can be bulging	Can be located anywhere in the myometrium
Pathophysiology	Have a myometrial mantle and endometrial lining	Absence of myometrial mantle and endometrial lining	No myometrial mantle	Will not have a myometrial mantle that is distinct from surrounding myometrium	Fibroid pseudocapsule and heterogeneous aspect
Relation to the uterine corpus	Typically bulge outside the uterine corpus	Typically entirely within the uterine corpus, close to the endometrial-myometrial junction	Can be separate from the main uterine body or not, but the uterine cavity will be unicornuate.	Typically within the uterine corpus	Could be within the body of the uterus or pedunculated
Content	Typically echogenic cavity content	Often anechoic cavity content	There´s ususally not hematometra found as the content refluxes to the abdomen	Typically echogenic content	Can be echogenic or anechoic content
Age	Commonly found in young women or teenagers	Commonly found in older parous women	Can be found in any age group	Commonly found in young women or teenagers	Can be found in any age group

Key Point:

- *As exclusion of other uterine anomalies is crucial to the diagnosis, in the rare circumstances where ultrasound and MRI have failed to clarify the morphology of the uterine cavity, consideration could be given to more invasive tests such as saline infusion sonohysterography, HyCoSy/HyFoSy or hysteroscopy.*

PART III. TREATMENT AND COUNSELLING

Key Question: What are the clinical indications and available treatment options for ACUM?

Treatment aims to restore normal anatomy and to alleviate pain. Reported ACUM management options range from medical treatment to surgery. Factors that influence decision-making include the severity of symptoms, age, and patient preferences (Naftalin et al., 2021; Azuma et al., 2021; Deblaere et al., 2019).

Surgical Treatment

Surgery is considered the definitive treatment for ACUM and has shown excellent results in symptom relief, pregnancy prognosis and long-term management (Naftalin et al., 2021;

Takeuchi et al., 2010; Acién et al., 2010; Acién et al., 2012; Peyron et al., 2019; Kriplani et al., 2011; Paul et al., 2015). There is no direct evidence to guide the timing of ACUM surgery or on the role of preoperative GnRHa therapy.

Surgical approaches include laparoscopy, robot-assisted laparoscopy, and laparotomy (Akar et al., 2010; Acién et al., 2010; Acién et al., 2012) and they involve the excision of the ACUM.

Irrespective of the approach, surgical treatment involves various steps. After injection of dilute vasopressin along the uterine-ACUM interface for hemostasis, incision and circumferential enucleation of the ACUM is performed. Finding the cleavage plane can be challenging as the typical pseudocapsule present in fibroids will not be found in ACUM. Assisted by instruments such as a tenaculum or suction device, the procedure is completed by transecting the ACUM from its attachment and closing the uterine defect with sutures.

Considering that ACUM is a benign condition, its contents are not thought to pose any threat if they leak. Thus, various techniques, such as morcellation and specimen retrieval in endo bags have been described for removing specimens of ACUM (Timmerman et al., 2024).

Adhesion barrier agents can be used during surgery to prevent postoperative adhesions (Kriplani et al., 2011).

The boundaries of an ACUM can sometimes be imprecise and so some authors have described using intraoperative ultrasound to help with lesion localisation and excision (Timmerman et al., 2024), also using intraoperative 3-dimensional ultrasonography, which not only clearly can locate the nodule but also show the thickness of the myometrium overlying the cystic cavity (Takeda et al., 2007).

For older patients who do not desire future pregnancies, hysterectomy may be recommended as it offers permanent relief from dysmenorrhea. Total laparoscopic hysterectomy (TLH) is a common, safe, and minimally invasive option for women with benign gynecological conditions like ACUM (Azuma et al., 2021).

Medical Treatment

Medical treatments for ACUM generally focus on pain relief and symptom management and are based on non-steroidal anti-inflammatory drugs (NSAIDs) and analgesics or on hormonal treatments (include continuous oral contraceptive pills (OCPs) (Branquinho et al., 2012; Deblaere et al., 2019; Steinkampf et al., 2004; Potter et al., 1998; Brosens et al., 2015), the levonorgestrel intrauterine system (LNG-IUS, e.g., Mirena), and gonadotropin-releasing hormone (GnRH) agonists (Takeuchi et al., 2010; Akar et al., 2010).

These therapies may temporarily reduce symptoms allowing patients to defer or avoid surgery or to help them manage their symptoms while awaiting surgery (Mondal et al., 2023). It is unclear whether factors such as age at the start of treatment, the size of the ACUM, or other morphological characteristics influence the success of medical treatment (Timmerman et al., 2024). However, if medical treatment is not effective, conservative minimally invasive surgery should be considered, always considering fertility preservation in young patients (Branquinho et al., 2012).

Sclerotherapy

An alternative treatment is sclerotherapy with ethanol, as described by Merviel et al (2021).

The procedure typically involves general anesthesia and ultrasound guidance to insert a needle through the vaginal wall and into the ACUM. After aspirating the cyst's contents, 96% ethanol is injected to fill the cavity for about 15 minutes, then drained.

This method can offer temporary relief from symptoms, it is rarely a permanent solution. Risks include leakage of the sclerosing agent into the peritoneal cavity.

Recently, lauromacrogol has also been introduced as a sclerosing agent for ACUM (Zhao et al., 2022). This compound offers the dual benefits of sclerotherapy and local anesthesia, although its long-term efficacy and safety remain under investigation.

Radiofrequency ablation has also been used with similar results as ethanol sclerotherapy in terms of symptoms relief (Zhou et al., 2020; Liu et al. 2023)

Key Points

- *Treatment aims to restore uterine anatomy through excision of the ACUM and to alleviate symptoms*
- *ACUM typically requires treatment in case of severe dysmenorrhea or chronic/ recurrent pelvic pain.*
- *Surgical Management, consisting of ACUM removal from the myometrium and suturing of the uterine defect, is the definitive treatment and it has shown nearly complete remission of symptoms. Options include laparotomy, laparoscopy, and robot-assisted laparoscopy. Minimally invasive approach should be preferred when possible.*
- *Medical Management including administration of NSAIDs, oral contraceptive pills (OCP), levonorgestrel-releasing intrauterine system (LNG-IUS), and GnRH agonists. Medical management provides temporary relief but is often not a definitive solution.*
- *Sclerotherapy is an alternative for those who wish to avoid surgery, though it may lead to recurrence.*

Key Question: What are the optimal skills and facilities to remove the ACUM while protecting the uterine myometrium wall?

Key Points:

- *Ability to accurately estimate the penetration depth in the myometrium to remove the lesion while minimizing risks.*
- *Use of intraoperative ultrasound, including 3D ultrasonography, for precise localization and excision of the ACUM.*
- *Surgical skills and experience to apply proper surgical techniques including careful enucleation of the ACUM using mechanical, monopolar or bipolar energy, with various tools assisting in the dissection and suturing (especially for laparoscopy / robotics)*

Key Question: What is the best timing of surgery for ACUM?

Key Point:

- *There is no direct evidence to guide the timing of ACUM surgery.*

Key Question: What is the recommended interval before attempting pregnancy after surgery?

There is no direct evidence to guide decision making on the interval before embarking on pregnancy.

Key Point:

- *After surgery for ACUM, a recommended waiting period of 4-6 months is advised before attempting pregnancy; this allows the proper healing of the myometrium.*

Key Question: What is the recommended mode of delivery for future pregnancy?

Key Point:

- *There is no data to determine the optimal mode of delivery after ACUM excision. Cesarean sections and vaginal deliveries are described in literature. In determining the mode of delivery after ACUM excision, consideration should be given to the depth of myometrial involvement/ FIGO type of ACUM.*

Conclusion

There remains a great deal that is unknown about ACUMs, which provides challenges for clinicians managing patients with ACUMs. The embryological origin is still unclear although it´s possibly related to a gubernaculum dysfunction or abnormal traction. Existing classification systems except for Acién´s, while widely utilized, do not adequately incorporate ACUM. The diagnostic criteria that ACUM should fulfill are: to be isolated cavitated lesions located in the anterolateral myometrium, in the proximity of the round ligament with a cavity lined by endometrial tissue and typically filled with haemorrhagic/menstrual fluid. They are surrounded by a myometrial mantle with

concentric orientation of myometrial fibres are typically present with a normal uterine cavity. There is a paucity of high-quality evidence to guide clinical decision-making regarding certain aspects of the optimal surgical interventions and more specifically regarding management of future pregnancies.

Bibliography

Acién P. Review: Embryological observations on the female genital tract. Vol. 7, Human Reproduction. 1992.

Acién P, Acién M, Sanchez-Ferrer M. Complex malformations of the female genital tract. New types and revision of classification. Hum Reprod Update. 2004; 19: 2377-84.

Acién P, Acién M, Sánchez-Ferrer ML. Müllerian anomalies “without a classification”: from the didelphys-unicollis uterus to the bicervical uterus with or without septate vagina. Fertil Steril. 2009 Jun;91(6):2369–75.

Acién P, Acién M, Fernández F, José Mayol M, Aranda I. The cavitated accessory uterine mass: A müllerian anomaly in women with an otherwise normal uterus. Obstetrics and Gynecology. 2010;116(5).

Acién P, Acién MI. The history of female genital tract malformation classifications and proposal of an updated system. Hum Reprod Update. 2011; 17: 693-705.

Acién P, Sánchez Del Campo F, Mayol MJ, Acién M. The female gubernaculum: Role in the embryology and development of the genital tract and in the possible genesis of malformations. European Journal of Obstetrics and Gynecology and Reproductive Biology. 2011;159(2).

Acién P, Bataller A, Fernández F, Acién MI, Rodríguez JM, Mayol MJ. New cases of accessory and cavitated uterine masses (ACUM): a significant cause of severe dysmenorrhea and recurrent pelvic pain in young women. Hum Reprod. 2012;27(3):683-694.

Acién P, Acién M. Accessory and cavitated uterine mass versus juvenile cystic adenomyoma. Vol. 2, F and S Reports. 2021.

Akar ME, Leezer KH, Yalcinkaya TM. Robot-assisted laparoscopic management of a case with juvenile cystic adenomyoma. Fertil Steril. 2010;94(3):e55-e56. doi:10.1016/j.fertnstert.2010.06.001

Alkhateeb HM, Yaseen EM. Twin pregnancy in an accessory cavitated non-communicating uterus. Int J Surg Case Rep. 2015;10:45-8.

ASRM Müllerian anomalies classification 2021. Fertil Steril 2021 Nov;116(5):1238-1252.

Azuma Y, Taniguchi F, Wibisono H, Ikebuchi A, Moriyama M, Harada T. A case report of an accessory and cavitated uterine mass treated with total laparoscopic hysterectomy. Yonago Acta Med. (2021) 64:207–9.

Batt RE, Yeh J. The cavitated accessory uterine mass: a Müllerian anomaly in women with an otherwise normal uterus. Obstet Gynecol. 2011 Mar;117(3):733-734.

Branquinho MM, Marques AL, Leite HB, Silva IS. Juvenile cys- tic adenomyoma. BMJ Case Rep. 2012;2012:bcr2012007006. d

Brosens I, Gordts S, Habiba M, Benagiano G. Uterine cystic adenomyosis: a disease of younger women. J Pediatr Adolesc Gynecol. 2015;28(6):420-426.

Buttram VC Jr, Gibbons WE. Müllerian anomalies: a proposed classification (an analysis of 144 cases). Fertil Steril 1979; 32: 40–46.

Chun SS, Hong DG, Seong WJ, Choi MH, Lee TH. Juvenile cystic adenomyoma in a 19-year-old woman: a case report with a proposal for new diagnostic criteria. J Laparoendosc Adv Surg Tech A 2011; 21: 771–4.

Dadhwal V, Sharma A, Khoiwal K. Juvenile Cystic Adenomyoma Mimicking a Uterine Anomaly: a Report of Two Cases. Eurasian J Med. 2017 Feb;49(1):59-61. doi: 10.5152/eurasianjmed.2017.17028.

Deblaere L, Froyman W, Van den Bosch T, et al. Juvenile cystic adenomyosis: a case report and review of the literature. Australas J Ultrasound Med. 2019;22(4):295-300. doi:10.1002/ajum.12171

Du H, Taylor HS. The Role of Hox Genes in Female Reproductive Tract Development, Adult Function, and Fertility. Cold Spring Harb Perspect Med. 2016 Jan;6(1):a023002.

Emmen JMA, McLuskey A, Adham IM, Engel W, Grootegoed JA, Brinkmann AO. Hormonal control of gubernaculum development during testis descent: Gubernaculum outgrowth in vitro requires both insulin-like factor and androgen. Endocrinology. 2000;141(12).

Fisseha S, Smith YR, Kumetz LM, Mueller GC, Hussain H, Quint EH. Cystic myometrial lesion in the uterus of an adolescent girl. Fertil Steril 2006;86:716–8.

Grimbizis GF, Gorts S, Di Spiezio SA, et al. The ESHRE/ESGE consensus on the classification of female genital tract congenital anomalies. Human Repord. 2013; 28: 2032-44

Gruenwald P. The relation of the growing müllerian duct to the wolffian duct and its importance for the genesis of malformations. Anat Rec. 1941;81(1).

Jones WS. Congenital anomalies of the female genital tract. Trans N Engl Obstet Gynaecol Soc. 1953; 7:79-94

Kives, S. (2016). Müllerian Anomaly Classification Systems. In: Pfeifer, S. (eds) Congenital Müllerian Anomalies. Springer, Cham.

Kiyak H, Seckin KD, Karakis L, Karacan T, Ozyurek ES, Asoglu MR. Decidualized juvenile cystic adenomyoma mimicking a cornual pregnancy. Fertil Steril 2020;113:463-5.

Kriplani A, Mahey R, Agarwal N, Bhatla N, Yadav R, Singh MK. Laparoscopic management of juvenile cystic adenomyoma: four cases. J Minim Invasive Gynecol. 2011;18(3):343-348. doi:10.1016/j. jmig.2011.02.001

Liu X, Wang J, Liu Y, Luo S, Yan G, Yang H, Wan L, Huang G. High Intensity Focused Ultrasound Ablation for Juvenile Cystic Adenomyosis: Two Case Reports and Literature Review. Diagnostics (Basel). 2023 May 1;13(9):1608.

Merviel P, Lelievre C, Cambier T, Thomas-Kergastel I, Dupré P-F. The first ethanol sclerotherapy of an accessory cavitated uterine mass. Clin Case Rep. 2021;9(1):19-22. doi:10.1002/ccr3.3371

Mondal R, Bhave P. Accessory cavitated uterine malformation: Enhancing awareness about this unexplored perpetrator of dysmenorrhea. Int J Gynaecol Obstet. 2023 Aug;162(2):409-432. doi: 10.1002/ijgo.14681.

Munro MG, Critchley HOD, Broder MS, et al. FIGO classification system (PALM-COEIN) for causes of abnormal uterine bleeding in nongravid women of reproductive age. Int J Gynaecol Obstet 2011; 113:3–13. 9.

Naftalin J, Bean E, Saridogan E, Barton-Smith P, Arora R, Jurkovic D. Imaging in gynecological disease: clinical and ultrasound characteristics of accessory cavitated uterine malformations. Ultrasound Obstet Gynecol 2021;57:821–8.

Oppelt P, Renner SP, Brucker S, et al. The VCUAM (Vagina Cervix Uterus Adnex-associated Malformation) classification: a new classification for genital malformations. Fert Steril. 2005; 84: 1493-7.

Paul PG, Chopade G, Das T, Dhivya N, Patil S, Thomas M. Accessory Cavitated uterine mass: a rare cause of severe dysmenorrhea in young women. J Minim Invasive Gynecol. 2015;22(7):1300-1303. doi:10.1016/j.jmig.2015.06.007

Persson J, Bossmar T, Teleman P (2010) Robot-assisted laparoscopic surgery for a rudimentary uterine horn with two non-communicating cavities. J Robot Surg 4:137-140.

Peyron N, Jacquemier E, Charlot M, et al. Accessory cavitated uterine mass: MRI features and surgical correlations of a rare but under recognised entity. Eur Radiol. 2019;29(3):1144-1152. doi:10.1007/ s00330-018-5686-6

Potter DA, Schenken RS. Non-communicating accessory uterine cavity. Fertil Steril. 1998;70(6):1165-1166. doi:10.1016/ s0015-0282(98)00380-x

Sánchez-Ferrer ML, Acién MI, Sánchez del Campo F, Mayol-Belda MJ, Acién P. Experimental contributions to the study of the embryology of the vagina. Human Reproduction. 2006;21(6).

Steinkampf MP, Manning MT, Dharia S, Burke KD. An accessory uterine cavity as a cause of pelvic pain. Obstet Gynecol. 2004;103(5 Pt 2):1058-1061. doi:10.1097/01.AOG.0000127944.68645.58

Strassmann P. Die operative vereinigung eines doppelten uterus. Zentralbl Gynaekol. 1907; 31:1322

Strug M, Christmas A, Schoonover A, Romero VC, Cordoba M, Leary E, Thakur M. Impact of an accessory cavitated uterine mass on fertility: case presentation and review of the literature. F S Rep. 2023 Sep 28;4(4):402-409. doi:10.1016/j.xfre.2023.09.001].

Supermaniam S, Thye WL. Diagnosis and laparoscopic excision of accessory cavitated uterine mass in young women: two case reports. Case Rep Womens Health 2020;26:e00187.

Takeda A, Sakai K, Mitsui T, Nakamura H. Laparoscopic management of juvenile cystic adenomyoma of the uterus: report of two cases and review] of the literature. J Minim Invasive Gynecol. 2007 May-Jun;14(3):370-4. doi: 10.1016/j.jmig.2007.01.005.

Takeuchi H, Kitade M, Kikuchi I, Kumakiri J, Kuroda K, Jinushi M. Diagnosis, laparoscopic management, and histopathologic findings of juvenile cystic adenomyoma: a review of nine cases. Fertil Steril. 2010;94(3):862-868.

The AFS classification of adnexal adhesions, distal tubal occlusion, tubal occlusion secondary to tubal ligation, tubal pregnancies, Müllerian anomalies and uterine adhesions. Fertil Setil 1988; 49: 944–955.

Timmerman S, Stubbe L, Van den Bosch T, Van Schoubroeck D, Tellum T, Froyman W. Accessory cavitated uterine malformation (ACUM): A scoping review. Acta Obstet Gynecol Scand. 2024 Jun;103(6):1036-1045.

Zhao X, Yang Y. Ultrasound-guided transvaginal aspiration and sclerotherapy for uterine cystic adenomyosis: case report and literature review. Front Med (Lausanne). 2022;9:764523.

Zhou XJ, Zhao ZM, Liu P, Zhao CY, Lin YJ, Liu Y, Wang M, Tian C, Li HY, Hou CX, Li XM, Zhao ZY, Zhou YJ. Efficacy of high intensity focused ultrasound treatment for cystic adenomyosis: a report of four cases. Ann Palliat Med. 2020 Nov;9(6):3742-3749.

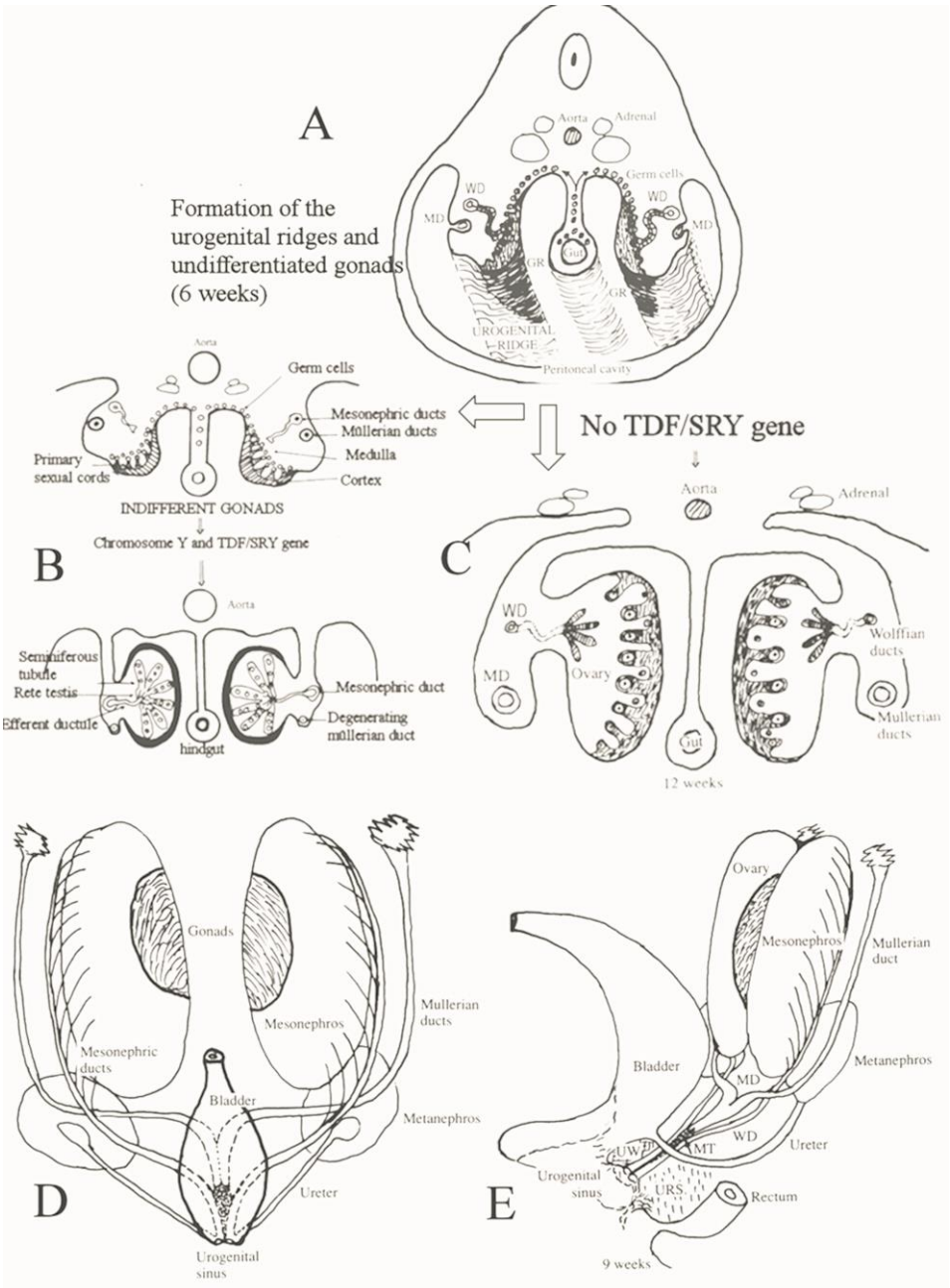

Figure 1. A. Urogenital ridge and undifferentiated gonads. B. Development of the gonads and Wolffian ducts in the male, and the Müllerian ducts in the female in C. D. Development of the genital ducts in the female. The formation of the uterine primordia and opening of the mesonephric ducts to the urogenital sinus is shown. E. Lateral view showing the urorectal septum (URS) and the urogenital wedge (UW). (Taken from Acién P. and Acién MI. Hum Reprod Update, Supplementary data I. 2011;17:693–705, with permission).

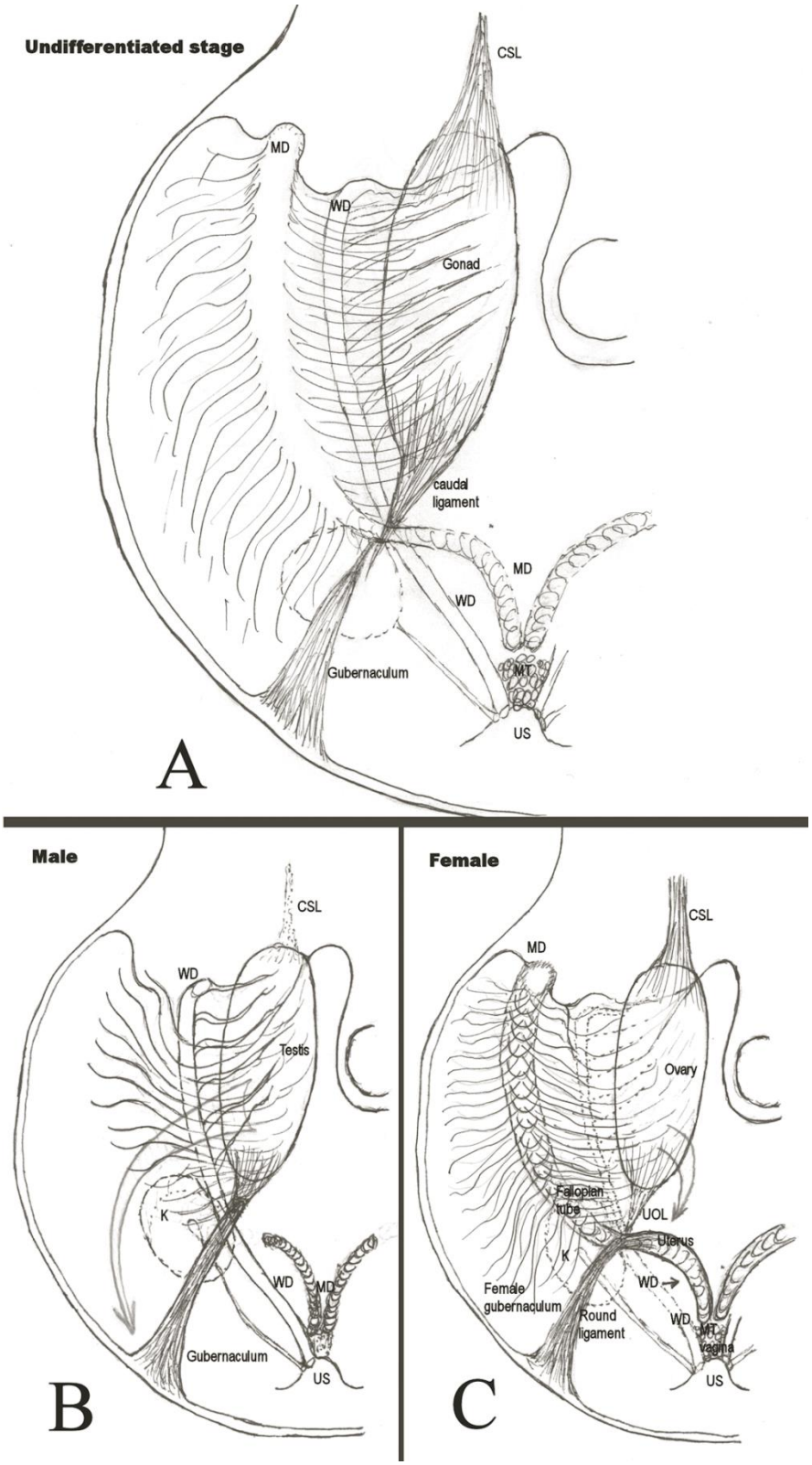

Figure 2. Schematic illustration of the possible development of the gubernaculum. A. At an Undifferentiated Stage. B. In Males. C. In Females. CSL, cranial suspensory ligament. WD, Wolffian duct. MD, Müllerian duct. MT, Müllerian tubercle. US, urogenital sinus. K, kidney. UOL, uteroovarian ligament (caudal ligament of the gonad). (Taken from P. Acién et al. Eur J Obstet Gynecol 2011;159:426-32, with permission)

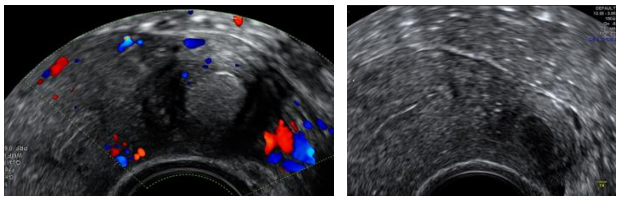

Figure 3a & b. 2D Ultrasond images of ACUMs in the left lateral myometrium showing the myometrial mantle and haemorrhagic content that can be hyperechogenic (3a) or ‘groundglass’ in appearance (3b)

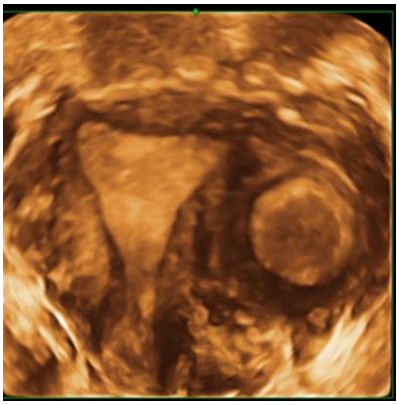

Figure 4. 3D ultrasound image of ACUM in the left lateral myometrium

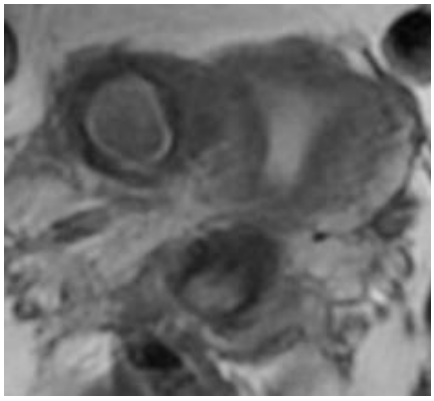

Figure 5. MRI image of ACUM in the right lateral myometrium

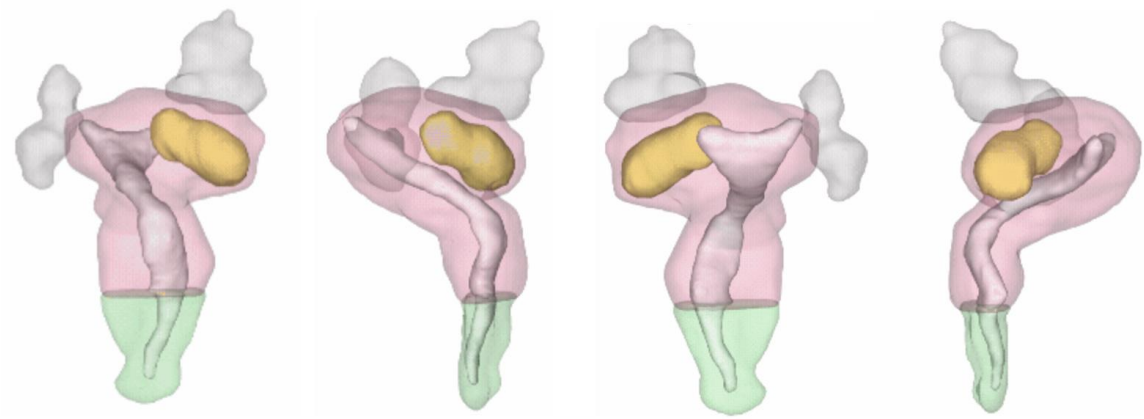

Figure 6. Three-dimensional reconstruction of ACUM based on MRI images

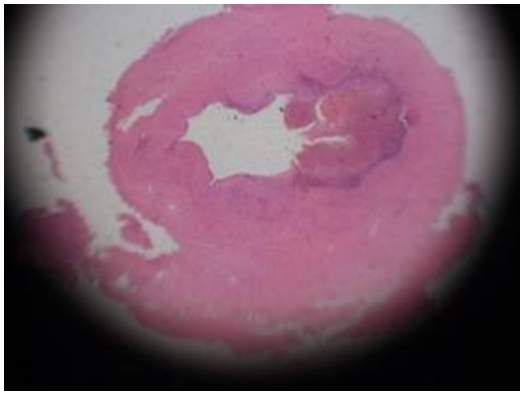

Figure 7. Microscopic pathologic image of ACUM