HYSTEROSCOPY NEWSLETTER

Hysteroscopy is a diagnostic method rarely used in Brazil, despite its effectiveness in the diagnosis and treatment of intrauterine pathologies. In comparison with other tests, such as hysterosalpingography, performed on patients with infertility, it has the advantage of bringing a real image of the uterine cavity, even allowing to perform an endometrial biopsy, when necessary. Unfortunately, many medical professionals still prefer conventional procedures, such as curettage, which, in my view, are blind and can lead to destruction of the endometrium and, consequently, infertility.

Hysteroscopic examinations are becoming less and less painful - as a result of the hysteroscopist's skill and technical knowledge and the advent of technology, such as the improvement and reduction of the diameter of the optics, high-definition video systems, safe and effective means of stretching and new instruments - and are well tolerated by patients, which increases their acceptance and allows their therapeutic performance in an outpatient setting.

Conventional hysteroscopies continue to be performed in a surgical environment, for the treatment of more complex uterine disorders. However, some hysteroscopic surgeries can also be performed in the office.

Currently, there is a new concept called “see and treat”, where some pathologies, when diagnosed on an outpatient basis, are already treated during the exam itself. This concept innovated hysteroscopy, leading to a very large gain for all, as patients no longer need to leave their daily activities to perform a surgical procedure and the health care system costs less. However, such a concept should only be carried out by doctors well qualified with the technique.

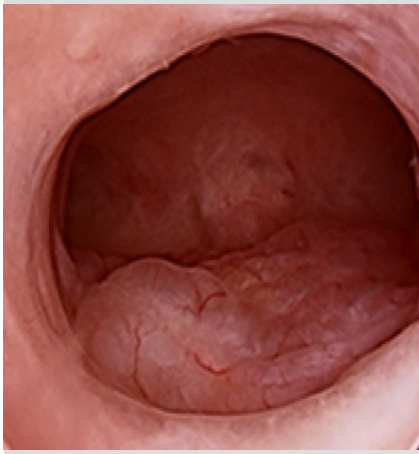
Due to the still slow dissemination of hysteroscopy, as well as the little access to information, it is still natural for patients to arrive with a certain fear to perform the exam, either in the office or in the hospital. For that, I help in the formation of a new generation of able gynecologists, not only to perform hysteroscopy, but also to multiply it.

Currently, I coordinate the Videohysteroscopy sector at the ABC Medical School where, after a two (2) year internship, six professionals leave with a complete hysteroscopy training. In this center, we carry out diagnostic procedures and surgeries of low and high complexity, on an outpatient basis and in an operating room.

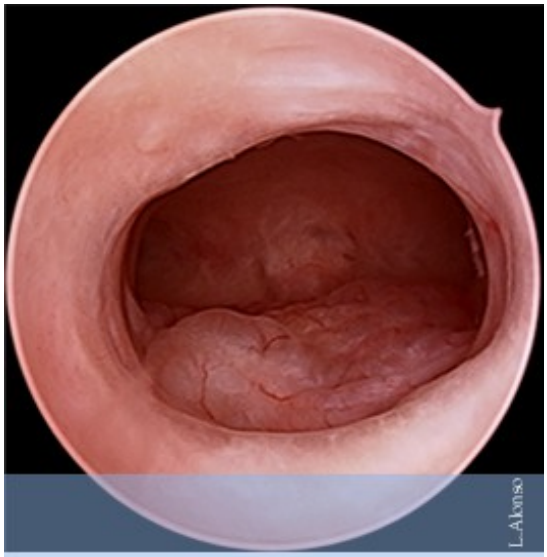
It is gratifying to know that, today, hysteroscopy has been widely discussed worldwide. In Brazil, we continue to fight for its amplified insertion in the public network and for its democratization. Although it is a more accurate examination, it is difficult to access for the Brazilian population since there are few centers that present this technology.

Thomas Moscovitz
Brasil

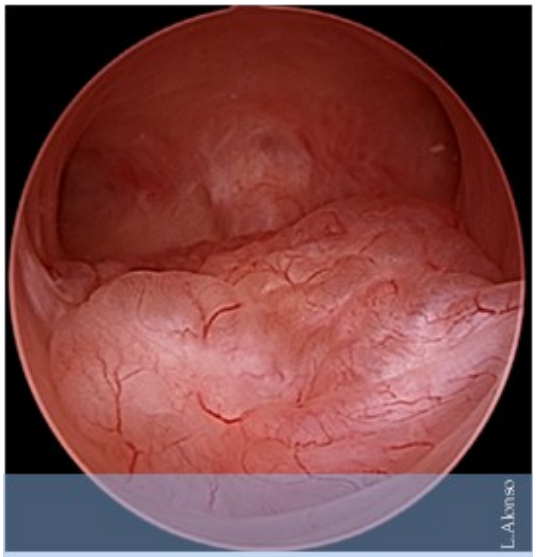
INSIDE THIS ISSUE



HYSTEROSCOPY PICTURES



Cystic polyp in the posterior wall



Detailed view of the cystic glands

*During menopause, there is an atrophy of the endometrium as a result of the low hormonal level. In this situation, can be found atrophyc glands mixed with cystic ones. Endometrial cystic atrophy is an unusual hysteroscopic finding, most often described in postmenopausal women treated with tamoxifen. This is a benign condition and is not related to endometrial hyperplasia, and thus this condition is not associated with an increased risk of endometrial adenocarcinoma. (Cheung, V. Y. T. (2017). "Endometrial Cystic Atrophy." J Minim Invasive Gynecol **24**(5): 711.)*

Tamoxifen is an antineoplastic drug C26H29NO wich competitively inhibits the binding of estradiol to estrogen receptors on the breast cancer cell. It was synthesized in 1962 as a contraceptive pill but later became an essential drug for the treatment of oestrogen-receptor-positive breast cancer. When estrogen enters a cell and binds to an estrogen receptor, activates genes that produce capable of stimulating cell growth. However, in breast cancer cells, when an estrogen receptor is bound to tamoxifen, its properties are altered in such a way that it can no longer activate genes. The result is a decrease in the growth of breast tissue and of breast cancer tissue (Editors of Encyclopaedia Britannica)

If you are interested in sharing your cases or have a hysteroscopy image that you consider unique and want to share, send it to hysteronews@gmail.com

INTERVIEW WITH...

Pushing the boundaries of the surgery in the field of reproductive medicine

Jaime Ferro

Surgical Unit Director

IVI Valencia España

Do you think the uterus is still a big conundrum to discover?

Generally speaking, I think so. Although much progress has been made in recent years especially with the data from the studies regarding their ontogenesis and physiology conducted by the German group of Dr Noe, Kunz and Leyendecker and by the genomics studies conducted by Dr. Simon and many other equally prominent studies that I am probably missing mentioning them now. It is a real shame that the publicity of those studies is not what they deserve.

> "...the 3D US is currently the most effective cost-effective option for the accurate diagnosis of uterine cavity malformations and hysteroscopy is the best tool to correct them"

In your experience, what is the role of uterine malformations in reproduction?

Throughout my experience with uterine malformations and especially the uterine cavity, I've been able to observe the different uterine symptomatic behaviors in relation to the patient's age. In women with uterine septum or dysmorphic uterine cavities who sought pregnancy while in their 20s, the problems are more obstetrical in nature, having preterm contractions and/or labor dystocia. The ones a little older, in their 30's usually present with late abortions and those in the late thirties, usually have early and recurrent abortions. From those patients at age forty and older, the most frequent problem is implantation failure.

We have not found for now an explanation to this observation and is most likely multifactorial, perhaps the presence of adenomyosis is one of the possible influencing factors. This is just a personal observation and obviously studies are needed to prove this hypothesis. In the meantime, we're collecting data.

What about adenomyosis?

Adenomyosis has to do with reproductive risk. Well, it is a totally different pathology, first of all, it is known that there is an alteration of uterine dynamics that is evidently related to subfertility. Second, as an inflammatory process that directly influences the normal endometrium it impairs implantation. What is still unclear is whether the severity of the of the disease is correlated with the severity of reproductive impairment.

Is the combination of 3D Ultrasound (3d US) and Hysteroscopy the best option for the study of uterine malformations?

In principle I believe that the 3D US is currently the most effective cost-effective option for the accurate diagnosis of uterine cavity malformations and hysteroscopy is the best tool to correct them. MRI images can be a good alternative for the diagnosis of uterine malformations when more basic imaging modalities such as US is not diagnostic.

Can you tell us any of your "surgical tricks"?

I really don't have any hidden tricks, but if I would say that one of the the most important thing in performing minimally invasive surgery is the discipline in the process, get used to always follow a protocol. Minimally invasive surgery requires a lot of support from technology and this should be personally reviewed first of all to verify that everything is in order to begin. An airplane pilot wouldn't fly without checking pre-aircraft controls.

Any advice for the young colleague starting in the world of minimally invasive surgery?

I would like to tell them that practice makes the expert, and experience is obtained with patience and watching many different techniques with different tools, to summarize, always do all it takes to help your patients!!!

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Original Article

Hysteroscopy Newsletter Vol 6 Issue 2

Uterine Arterio-Venous Malformation (AVM). A rare cause of heavy vaginal bleeding. Case Report.

*Dr. Luis Pablo López Rivero;** Dr. José Negrón Salazar; ***Dr. Enrique David Huaricallo De La Barra
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Keywords:
Arterio-Venous Malformation, Heavy Vaginal Bleeding.

SUMMARY

Uterine Arterio-Venous Malformation (AVM) is a rare event that can cause massive uterine bleeding that is difficult to control. Its diagnosis should be established through an adequate history taking, physical exam and complementary imaging studies, being the most useful transvaginal Doppler ultrasound, CT Angiogram and Angio MRI. THE Treatment will vary depending on the clinical conditions of the patient, size and location of the AVM, age of the patient and future fertility desire. Uterine artery embolization is the first line in treatment, however hysterectomy still plays an important role in those patients with hemodynamic instability due to the heavy vaginal bleeding.

INTRODUCTION

Uterine Arterio-Venous Malformation (AVM), also known as arterio-venous fistula, is a rare poorly known pathology, sometimes being fatal. Dubreuil and Loubat reported the first case of Uterine AVM in 1926, currently there are fewer than 100 cases reported in the medical literature. (1,2,5)

The incidence ranges from 0.6% to 4.5% in patients with abnormal uterine bleeding. (3,5)

It is an extension in the intervellous space in the thickness of the myometrium, with direct flow from the artery to the venous system, without the participation of capillaries. (2)

There are wo types of AVM identified. One congenital and one acquired have been described, both of which could lead to heavy uterine hemorrhage. (1)

Acquired uterine AVM can be caused by previous uterine procedures including: uterine trauma, pregnancy-related conditions (some authors point out that pregnancy would play an important role in its pathogenesis), infections, pelvic surgery (cesarean section, myomectomy, uterine curettage), exposure to Diethylstilbestrol and treatment of gestational trophoblastic disease among others.

Congenital uterine AVM, which is even rarer, arises from the stopping of capillary plexus vascular development, which results in multiple communications between arteries and veins. (1, 2, 4)

Differential diagnoses include retained products of conception, gestational trophoblastic disease, abnormal placentation during the first trimester. (1)

Among the studies frequently used to establish the diagnosis are:

1- Transvaginal ultrasound + Color Doppler

2- Lab Beta hCG

3- Pelvic CT Angiogram

4- Angio-Pelvic MRI Magnetic Resonance Image

Ultrasound findings are heterogeneous, could be described as a mass with multiple hypoechogenic cysts or tubular structures. The color Doppler demonstrates an area of increased vascularization inside the myometrium, with vessels that can even reach the endometrium. AV-SHUNTS, with low resistance flow and high flow rates. All these findings suggest the diagnosis of AVM, however, they are not definitive. (2, 5)

Clinical sign and symptoms of uterine AVM may present chronically or acutely. The most common symptom is abnormal uterine bleeding that may be minimal (spotting) or heavy (massive), other symptoms include recurrent pregnancy loss, abdominal or pelvic pain, dyspareunia and/or anemia. (1,2,5)

It is thought that bleeding occurs in menstrual bleeding because the AVM is exposed due to endometrial shedding, or iatrogenic during a dilation and curettage procedure. (3.2)

Treatment depends on different clinical conditions (1,4,5) that should be considered:

- Hemodynamic conditions
- Size and location of the AVM
- Amount of Bleeding
- Patient's age
- Desire of future fertility
- Previous episodes of bleeding

Hysterectomy and/or uterine artery embolization (UAE) have been the main treatment of uterine AVM. Uterine artery embolization is the first choice in cases of women of reproductive age with a desire for fertility preservation, 71-93% success rates are reported, however, up to 32% of the patients require multiple uterine artery embolization procedures.(3) It should be noted that there is not yet sufficient evidence regarding follow-up of patients following in relation to pregnancy outcomes, obstetric complications. (1) On the other hand, there are publications pointing out that there is not yet sufficient evidence regarding the follow-up of patients following UAE regarding to future pregnancy outcomes, and obstetrical complications. (1) Also, there are publications recommending the use of hysteroscopy as an alternative in the treatment of uterine AVM, and also other surgical procedures such as hypogastric artery ligation, uterine artery ligation. (3.4, 5)

Complete obliteration of the AVM nest is critical to achieve full resolution of the symptoms. Failure to achieve this could result in reformation of the AVM even larger than the previous one. Some authors point out that the simple ligation of the feeding vessels of the AVM without their cleavage could result in collateral growth and faster growth of the AVM, and that vessel ligation could prevent access to proper embolization. (5)

In 1988 a review carried out by Beller et al, of cases with uterine AVM and its subsequent follow-up, recommended avoiding pregnancy, because pregnancy increases blood flow and vessel proliferation, which would lead to complication in the management of the uterine AVM, predisposing to complications during pregnancy or postpartum. (5)

CASE REPORT

We report the case of a 32-year-old patient, who presented with low abdominal cramping pain. An ultrasound revealed the presence of an intrauterine pregnancy of 11 weeks with 2 days, with a visualized fetal pole and positive fetal cardiac activity. She was diagnosed with threatened abortion, ultrasound reported a low implanted gestational sac and the presence of a marked heterogeneous decidual reaction, marginal chorionic hematoma with a volume of 12 ml.

The patient had significant history of 1 previous elective surgical abortion that resulted in heavy bleeding during the procedure. 2 days later, a repeated ultrasound revealed no fetal cardiac activity with persistent marked heterogeneity of the decidual reaction.

Dilation and curettage was scheduled with prior administration of misoprostol. The procedure is carried out at the conclusion of the procedure, there was massive uterine hemorrhage, which was controlled with compression, administration of uterotonics (ergometrine, oxytocin, misoprostol), administration of tranexamic acid, required transfusion of 2 units of packed red blood cells, and insertion of an intrauterine Foley balloon inflated with 20 ml to provide compression.

After 12 hours, the patient spontaneously expulsed the intrauterine Foley balloon, the patient remained stable and without bleeding. Ultrasound revealed minimal amount of blood inside the uterine cavity. (**See photo 1)**

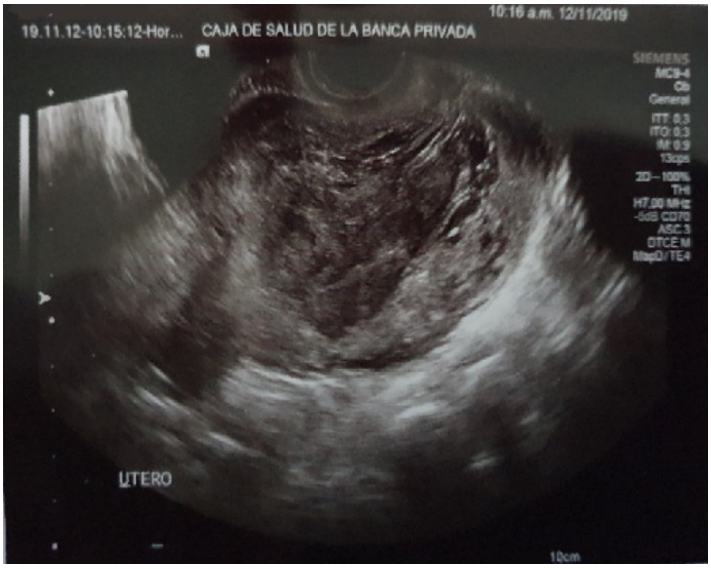

Photo 1. Ultrasound that indicated the presence of hematometra.

AMEU Aspiration of the hematometra is recommended under ultrasound guidance, which is performed obtaining a large amount of blood clots. At the conclusion of the procedure a massive uterine hemorrhage occurs again, which could not be controlled with measures used in previous episode of bleeding, so it is decided to perform emergency laparotomy, with uterine arteries ligation (O'Leary stich), after the bleeding was controlled, a second Foley catheter was placed inside the uterus inflated with 30 ml of sterile solution. The blood loss was 1000 ml, so 3 more units of PRBC were transfused. It should be noted that fertility preservation measures were attempted, because the patient had no children and had expressed desire of future fertility.

At 36 hours the intrauterine balloon spontaneously came out, the patient was stable and ultrasound control described little hematomera and clots in the endometrial cavity.

Thinking that the cause of bleeding was due to a low implantation pregnancy (cervical ectopic) or the likelihood of a case of abnormal placentation (first trimester acretism), administration of methotrexate intramuscularly was performed. Patient had great response and no additional methotrexate was given.

The last check performed a month and a half after hospital discharge, Beta hCG was 67 IU/L, and the repeated ultrasound reported endometrium of 6.3 mm. Doppler revealed preserved circulation, vascular flow with dilation and right varicocele 6 mm, left greater than 10 mm with turbulent flow circulation.

The clinical course of the patient was great, she restarted regular menstrual bleeding, albeit in small amounts. Ten days after her last follow up control, the patient again had massive vaginal hemorrhage, of approximately 1000 ml. She arrived at the hospital with blood pressure 70/40 mmHg, pulse 104 per minute, conscious, pale, hemoglobin of 7.3 g/dl. At the arrival, the vaginal bleeding decreased, she was transfused 2 more units of PRBC. A pelvic ultrasound scan revealed a AVM of 85x50x65 mm, presence of vascular dilations in the posterior wall of the uterus. Quantitative beta hcg was 0.3 IU/L

Pelvic Angio CT scan reported the presence of a Uterine Arteriovenous Malformation (AVM) on the posterior uterine wall. It was determined that the patient did not meet criteria to perform an embolization of uterine arteries, one of the main reasons was the hemodynamic instability of the patient. (**See photo 2)**

Due to recurrent episodes of heavy bleeding, it is decided to proceed with a hysterectomy, which is performed without complications. The specimen revealed the presence of the AVM on the posterior uterine wall. (**See photo 3)** Patient had uneventful postoperative course and was discharged home in stable conditions.

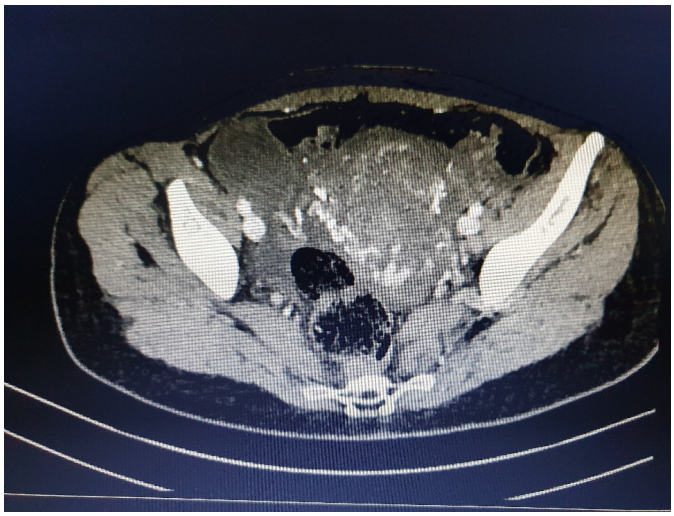

Photo 2. Pelvic Angio CT scan cross-section showing dilated vessels in the posterior uterine wall.

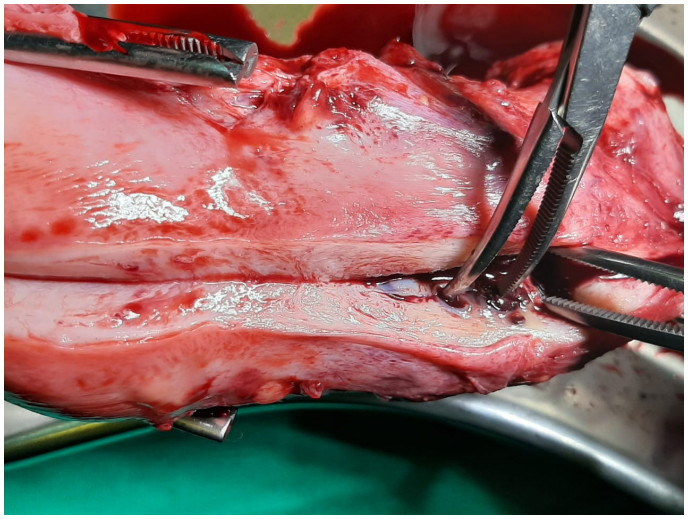

Photo 3. Operative part uterus that in sagittal cut shows aberrant and dilated vessels in intimate contact with endometrial/endocervical channel

CONCLUSION

Any woman of reproductive age who has abnormal uterine bleeding and a negative pregnancy test, could potentially have a uterine AVM, as stated by the American College of Obstetrics and Gynecology (ACOG) in the acronym PALM COEIN, would not be classified in anatomical alterations of the uterus (PALM) so it should be taken into consideration the uterine MAV at the time of establishing possible diagnoses of anatomical alterations of the uterus that present with abnormal uterine bleeding. Its management depends on the clinical conditions, currently prefers a management that takes into account the preservation of fertility, uterine arteries embolization being the treatment of first choice, however, in cases such as the one just presented, hysterectomy remains a valid option for its definitive treatment.

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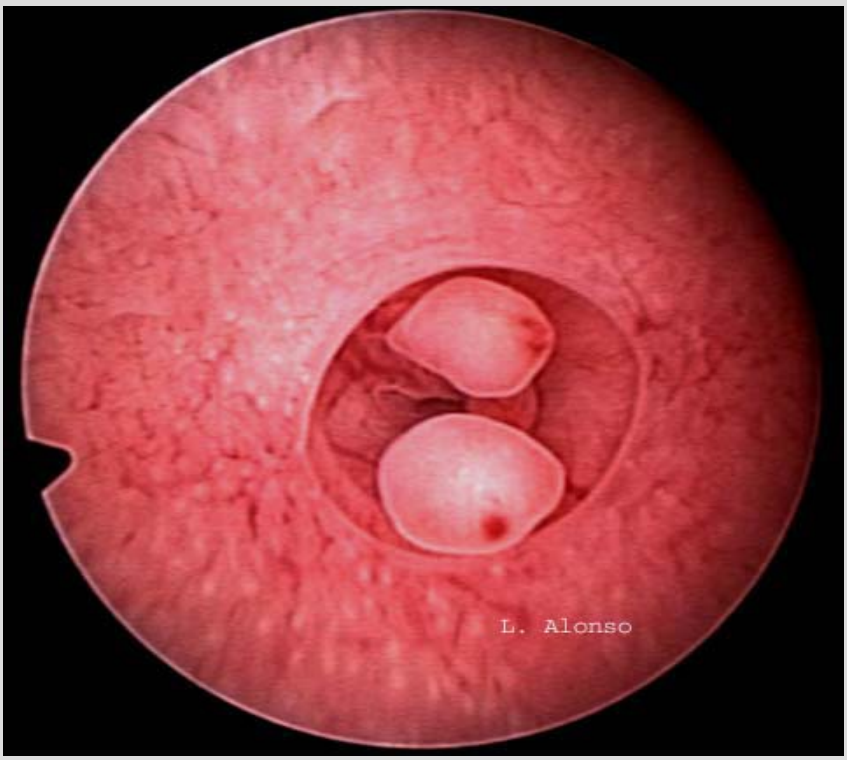
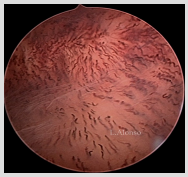
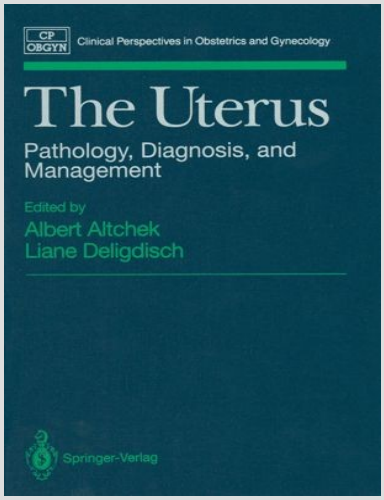
What's Your Diagnosis?





Respuesta al número anterior:

Distrofia Vascular



The Uterus
Pathology, Diagnosis and Management

Albert Altchek, Liane Deligdisch

Springer 1991

446 páginas

Inglés

Talking About

Hysteroscopy Newsletter Vol 6 Issue 2

Robert's Uterus

Luis Alonso. Centro Gutenberg. Spain

RESUMEN: Even today there are some surprising uterine malformations either because they are very infrequent or because of the difficulty in their diagnosis and treatment. An example is Robert's uterus, which is a variant of the septate uterus, although with certain peculiar connotations.

In the following text we will discuss about this malformation from different points of view : clinical, diagnosis and treatment. It is very important to achieve a correct diagnosis, differentiating it from the unicornuate uterus with functional non-communicating horn, because the management of these two uterine malformations is very different.

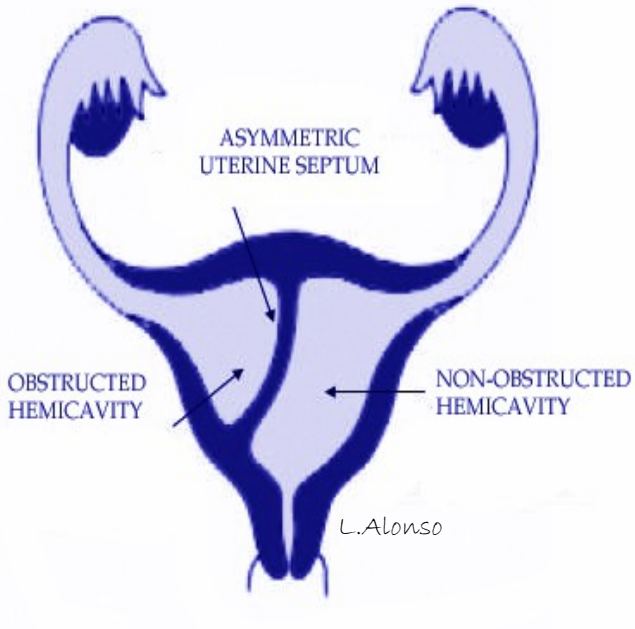
PALABRAS CLAVE:
Robert's uterus, Útero septo, Hemicavidad obstruida

Robert's uterus is a rare uterine malformation of which there are only a few reported cases. In this type of malformation, it is very important to establish a previous diagnosis as well as an appropriate treatment that allows to reconstruct the morphology and functionality of the uterus.

It was first described by Héléne Robert under the name "Asymetrical bifiditis with unilateral menstrual retention". It is actually an asymmetric variant of the septated uterus and is characterized by having a complete uterine septum that divides the uterine cavity asymmetrically from the fundus up to the Internal Cervical Os (ICO) resulting in a non-communicating hemi-uterine cavity and another hemiuterina cavity with unicorn uterus appearance, all in a uterus with a normal external morphology.

As a result of the presence of a non-communicating hemi-cavity, hematometra, hematosalpinx and, due to the existence of retrograde menstrual flow, there may also be associated endometriosis peritoneal implants.

According to the new classification of ESGE-ESHRE, this type of malformation can be defined as U6 or unclassified uterine malformation although some group has defined it as a complete septated uterus (U2b) with unilateral cervical aplasia (C3) and normal vagina (V0)



Robert's Uterus

3 types of Robert's uterus have been described based on the characteristics of the existing hematometra inside the blind hemicavity at the time of diagnosis:

Type I: With gran hematometra

Type II: Without hematometra

Type III: With small hematometra

Usually hematometra and its associated dysmenorrhea are usually of increasing severity over time due to increased tension and size of the blind hemicavity. In cases without hematometra, patients do not usually suffer from severe dysmenorrhea, in these circumstances the most common complaint is recurrent pregnancy loss, since the communicated hemi-uterus behaves like a unicornuate uterus.

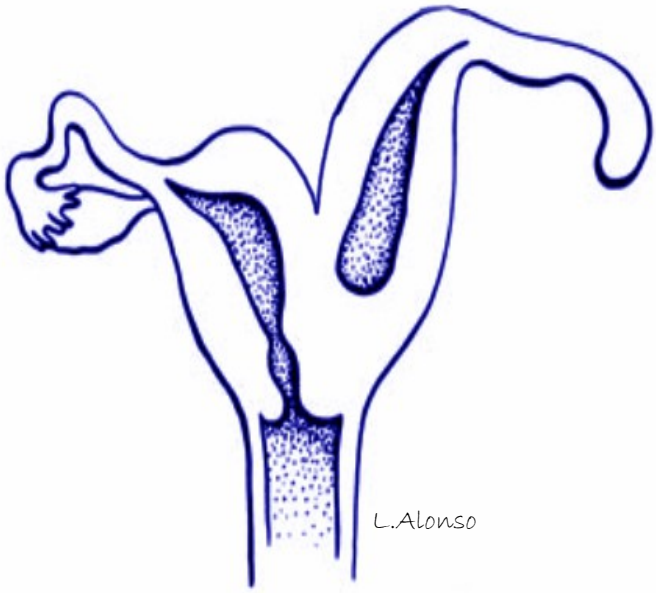
Diagnosing this complex Mullerian malformation is difficult resulting in frequent misdiagnosis, often mistaken for a unicorn uterus with a non-communicating rudimentary cavity.

Within the different imaging tests that can be used to establish the diagnosis, 2D ultrasound has low sensitivity, usually misdiagnosing it as unicornuate uterus. Using hysterosalpingography it appears as a fusiform image of the unicorn uterus with visualization of a single fallopian tube.

Magnetic Resonance Imaging (MRI) in the coronal view is the best imaging modality to diagnose Robert's uterus, demonstrating the uterine septum, the presence of hematomera in the blind cavity and the existence of a normal uterine contour. 3D ultrasound provides similar results to MRI.

The gold standard for diagnosis is the combination of hysteroscopy and laparoscopy that demonstrate a unicorn uterus in the case of hysteroscopy and the existence of a normal morphology of the uterine contour at laparoscopy.

The way to differentiate while performing a laparoscopy a unicorn uterus from a Robert's uterus is that in Robert's the uterine contour is normal or with a small indentation of 1 cm while the unicornuate uterus has a greater indentation (Larger than 1 cm).



Unicornuate uterus with functional non-communicating horn

The only treatment available is surgical, having established two surgical options, on the one hand the realization of a hysterotomy of the dilated hemicavity with drainage of the hematometra, thus avoiding the recurrence. The other surgical alternative is metroplasty with communication of the two hemicavities, this communication can be performed by laparoscopic after hysterotomy of the dilated blind hemicavity or by transcervical route, performing a hysteroscopic metroplasty.

Unfortunately, due to miss-diagnosis and confusion with a non-communicating rudimentary horn, often these patients undergo a total resection of the non-communicating hemiuterus, with the functional impact that comes with such a mutilating procedure.

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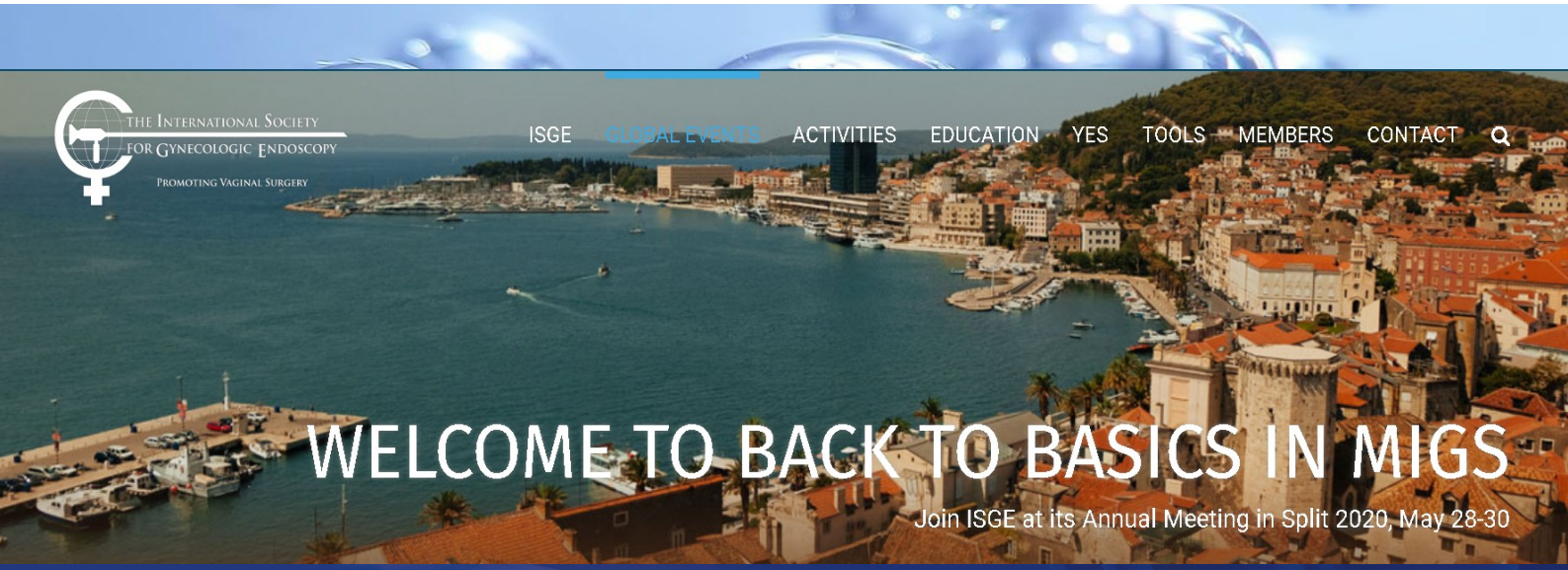
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Update

Hysteroscopy Newsletter Vol 6 Issue 2

Hysteroscopic Assessment of Endometrial Premalignal Lesions

MD Lara Domínguez, R Oña López, C García-Salmones
Virgen de Valme University Hospital. Sevilla, Spain.

INTRODUCTION

Endometrial premalignant lesions have been recognized as Endometrial Hyperplasia (HE). This term refers to a proliferation or excessive and pathological growth of the endometrial glands. There is an increased endometrial glands/stroma ratio. Endometrial hyperplasia encompasses a series of lesions ranging from some lesions with minimal malignant potential to others that are premalignant with elevated risk of progression to cancer.

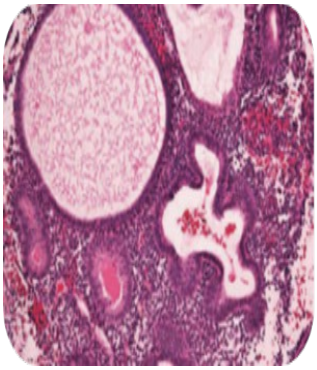
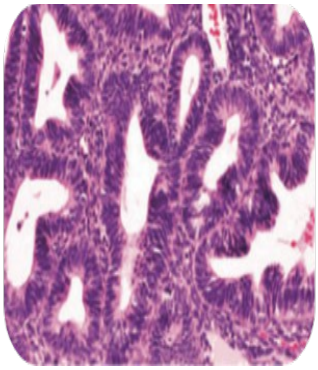
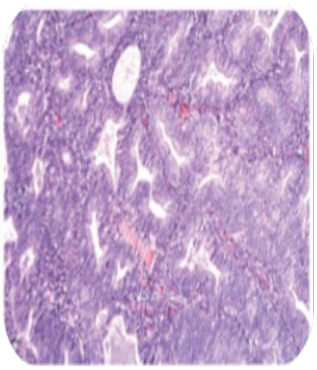
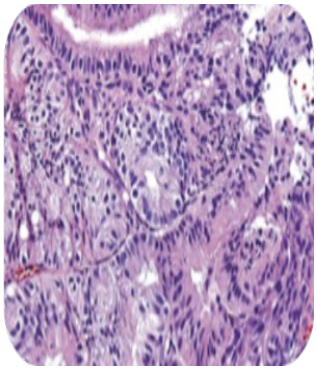
It is essential to always consider the presence of HE, since it is present in 8/1000 asymptomatic patients and in 10% of patients with Abnormal Uterine Bleeds (AUB) and / or Heavy Menstrual Periods (HMP). They are also responsible for 15% of the cases of post-menopausal bleeding. We should suspect this pathology in patients who have risk factors, such as increased estrogen without progesterone opposition, either by exogenous treatments, anovulation, polycystic ovarian syndrome or obesity; as well as Tamoxifen therapy or hereditary risk such as Lynch II or HNPCC.

Ultrasound assessment of the thickened endometrium can raise suspicion for this diagnosis, especially in post-menopausal patients or those taking Tamoxifen, which will lead to perform an endometrial biopsy by aspiration or curettage first. When the diagnosis is inconclusive, a hysteroscopy will be chosen to evaluate the uterine cavity and obtain targeted endometrial biopsies.

CLASSIFICATION

There are several published proposed classifications for Endometrial Hyperplasia. There has been controversy with each one of them and they have not been widely accepted, so multiple updates have been made over the years. The last one was published in 2014.

The first classification of premalignant endometrial lesions was that of the World Health Organization (WHO) in 1994, based on a publication by Kurman et al published in 1985 and endorsed by the Royal College of Obstetricians and Gynaecologists (RCOG). This classification is merely histological, based on the complexity of the glandular architecture and especially in the presence of cytological atypia. It identifies 4 categories:

Simple hyperplasia without atypia (SH)

It presents an increased gland/stromal ratio, minimal stromal decrease, simple-looking cystic dilated glands that are grouped in clusters. Minimal changes in complexity and glandular density. There are no atypical cells. It is also known as cystic hyperplasia.

Complex hyperplasia (CH)

There is greater increase in the gland/stroma ratio, greater number of glands, more clustered and overcrowded. Greater complexity of glandular, tubular structures with folds. Appearance of intraluminal papillae, pseudostratification. There are no atypical cells.

Simple hyperplasia with atypia (ShwA)

Remarkably increased gland/stroma ratio, only minimal stroma present. There are cystic dilations. Atypical cells lining the glandular lumen.

Complex hyperplasia with atypia (CHwA)

Very high gland/stroma ratio with minimal stroma, crowded, branched glands, very complex packed epithelium with atypical cells lining the glands.

The presence of cellular atypia is the most important prognostic factor for progression to endometrial carcinoma in the WHO classification. The risk of progression to malignancy was defined for each of the HE. In the case of SH, the risk would be 1.07%, for CH 3.4%, 6% for SHwA and 23% risk of carcinoma for CHwA. The average time for progression to cancer has been defined in 10 years for hyperplasia without atypia and in 4 years for cases with atypia.

Because this classification is subjective and entails some interobserver variability, a group of experts proposed a new classification system that introduced the Endometrial Intraepithelial Neoplasm nomenclature (EIN) in the year 2000. This histomorphological classification was endorsed by the American College of Obstetricians and Gynecologists (ACOG) and the Society of Gynecologists Oncologists (SGO).

The term EIN would encompass the atypical HE cases of the previous classification, being defined as a precancerous lesion; the rest of the hyperplasias would be classified as benign endometrial hyperplasias and the third group would belong to the well-differentiated endometrioid adenocarcinoma type I.

This nomenclature is defined by an objective assessment criterion and several subjective criteria, so they offer better reproducibility and sensitivity when discerning between low and high risk of progression to cancer. In this classification the irregularity of the glandular profile is the most relevant factor in the diagnosis of premalignant lesions.

Objective Criteria. Computerized morphometric evaluation (d-score): Measurement of stroma volume with respect to total tissue (stroma + epithelium + glandular lumen)

Subjective Criteria:

- Architecture: Glandular aggregation (glandular/stroma > 55%)
- Cytology: Cytological differences with the adjacent endometrium
- Size of the lesion > 1 mm
- Exclusion of benign lesions
- Exclusion of lesions suggestive of cancer

Table 1. Diagnostic Criteria for Endometrial Intraepithelial Neoplasia*

Nomenclature	Topography	Functional Category	Treatment
Benign endometrial hyperplasia	Diffuse	Prolonged estrogen effect	Hormonal therapy, symptomatic
Endometrial intraepithelial neoplasia	Focal progressing to diffuse	Precancerous	Hormonal therapy or surgery
Endometrial adenocarcinoma, endometrioid type, well differentiated	Focal progressing to diffuse	Malignant	Surgery, stage based

*Previously known as atypical endometrial hyperplasia.

Data from Baak JP, Mutter GL, Robboy S, van Diest PJ, Uyterlinde AM, Orbo A, et al. The molecular genetics and morphometry-based endometrial intraepithelial neoplasia classification system predicts disease progression in endometrial hyperplasia more accurately than the 1994 World Health Organization classification system. Cancer 2005; 103:2304–12 *and* Mutter GL. Endometrial intraepithelial neoplasia (EIN): will it bring order to chaos? The Endometrial Collaborative Group. Gynecol Oncol 2000;76:287–90.

This classification was also not widely accepted because the computerized morphometric analysis was expensive and its use was not routinely adopted, in addition to the difficulty in its interpretation and the lack of specificity when reporting high-grade premalignant lesions.

Subsequently, a new update of this nomenclature was published by WHO in 2014, in order to unify the terms of the two previous classifications to minimize confusion. It continues to recognize the differences between the histological terms Simple (Slightly crowded glands, cystic dilation and scarce mitosis) and Complex (Very crowded glands> 50%, luminal widening and presence of mitosis) but does not take them into account in the classification. In this latest update, only two recognized categories are:

Hyperplasia WITHOUT atypia: defined as non-neoplastic lesions.

Hyperplasia WITH atypia: they correspond to the EIN pathology of the previous classification which are considered premalignant lesions.

In the latter classification nuclear atypia is the main prognostic factor for the progression to endometrial carcinoma and is characterized by an enlargement and rounding of the nucleus, increase in stratification with loss of polarity, nuclear pleomorphism, hyperchromatic nuclei, prominent nucleoli, chromatin with lumpy appearance and increased core/cytoplasm ratio. Due to the presence of nuclear atypia they have greater specificity in the diagnosis of high-grade premalignant lesions.

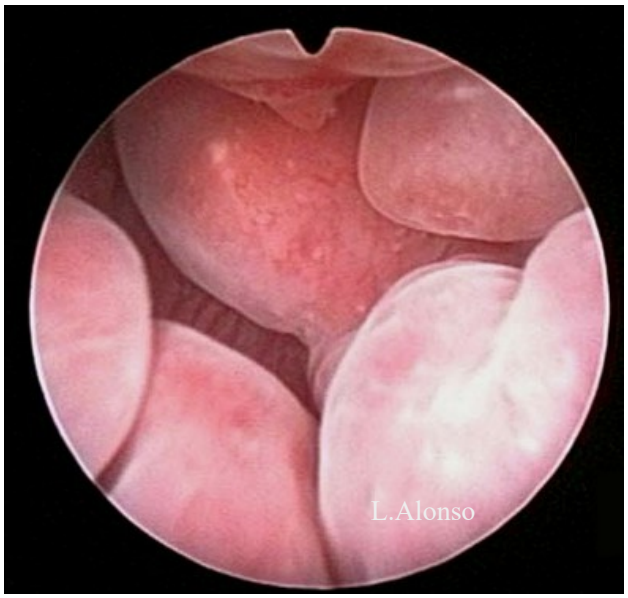
DIAGNOSIS

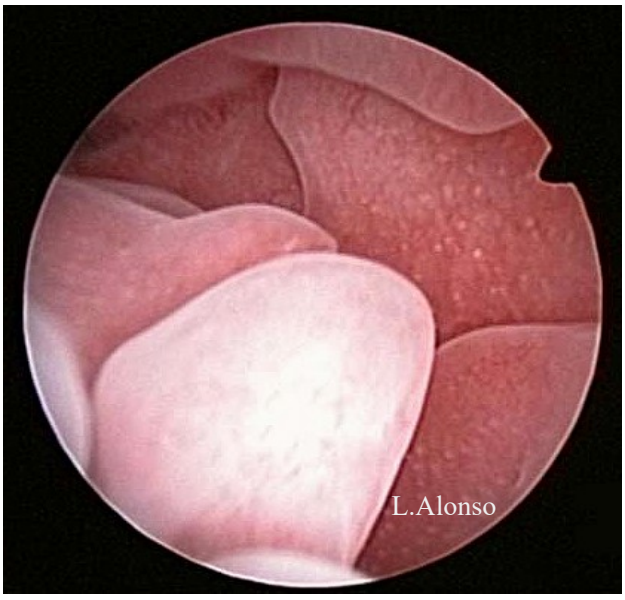
Hysteroscopy is considered the gold standard technique for the evaluation of the uterine cavity and the early diagnosis of this pathology. Premalignant lesions can be focal or diffuse in the endometrium, so with blind biopsy by aspiration or curettage it is possible to miss the diagnosis in cases of focal disease. With direct visualization through the hysteroscope the sensitivity and specificity for the diagnosis of focal lesions increases. 15-43% of EH with atypia coexist with an endometrial adenocarcinoma.

Since the publication of Mencaglia in 1995, several definitions have emerged of what the hysteroscopic images characteristic of this premalignant pathology should be; but today there is still a lack of consensus when defining these images.

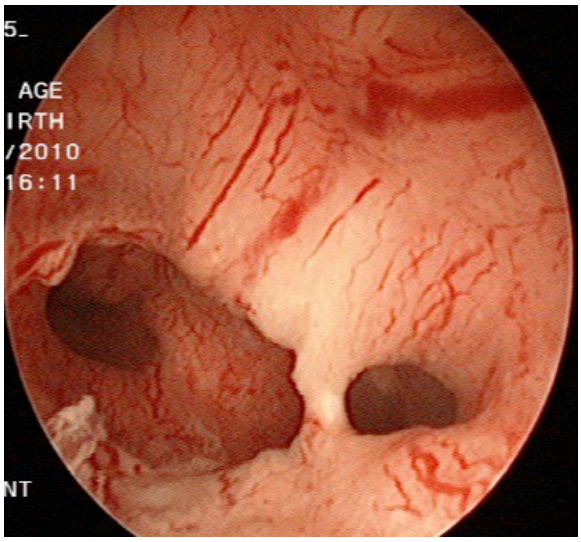
After an exhaustive review we have been able to collect the following characteristics:

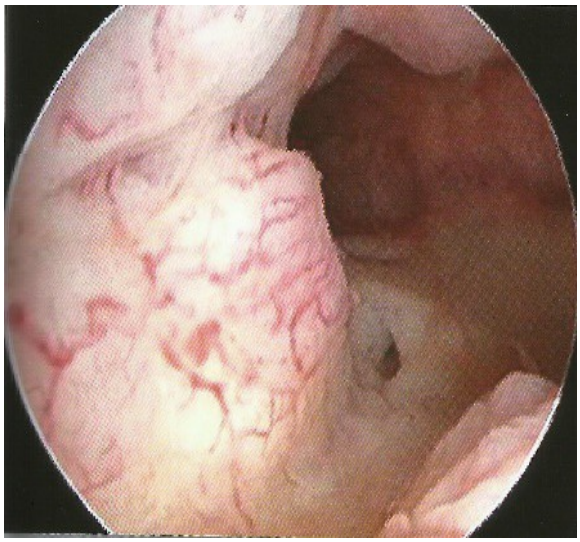
1- Simple Endometrial hyperplasia without atypia. (SH w/o Atypia)



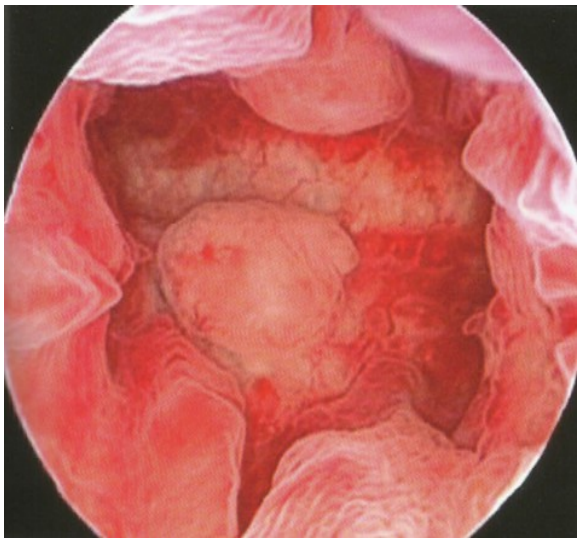


2- Complex Endometrial Hyperplasia without atypia. (CH w/o Atypia)

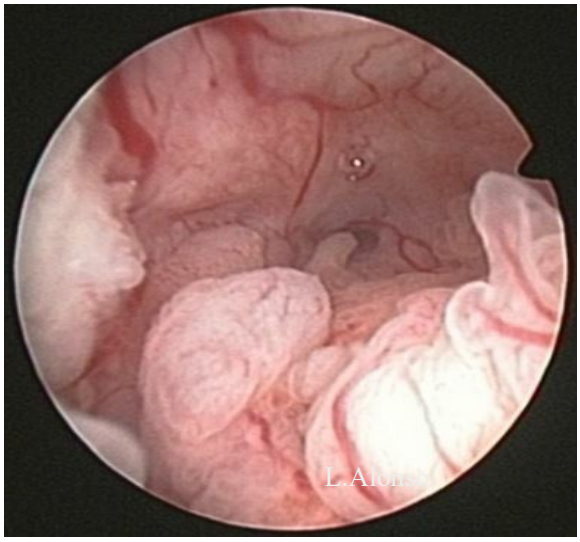


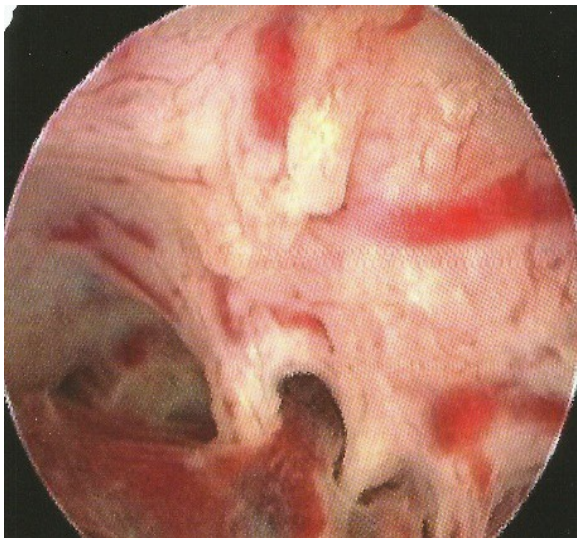


Simple Endometrial hyperplasia with atypia. (SH w Atypia)



4- Complex Endometrial Hyperplasia with atypia. (CH w Atypia)





TREATMENT

1- Endometrial Hyperplasia without atypia

Medroxyprogesterone Acetate 10 mg / day or Levonorgestrel IUD. Biopsy every 6-12 months according to published studies.

There are authors who favor the use of the Levonorgestrel releasing IUD to ensure greater therapeutic compliance and higher regression rate. There are publications that support performing endometrial biopsy every 12 months due to the slow progression of these pathologies and their high regression rates; others, however, argue that the biopsy should be performed every 6 months given the possibility of false negatives results.

If the patient currently has fertility desire, shopuld undergo ovulation induction with endometrial biopsy performed every 6 months until conception.

2- Endometrial Hyperplasia with Atypia

Hysterectomy is the treatment of choice in patients without desire of future fertility.

In patients with desire of future fertility: Megestrol Acetate 40-160 mg / day is a strong progestin and is considered the chemotherapeutic agent of choice for this pathology. Another option would be the use of Levonorgestrel releasing IUD. Also, some authors favor the IUD for best therapeutic compliance, but Megestrol Acetate seems to have higher regression rates in this case.

Endometrial biopsies directed with hysteroscopy would be indicated every 3 months while the presence of atypia continues.

CONCLUSIONS

In the case of premalignant endometrial pathology, the suspicious of the diagnosis and performing an endometrial biopsy are important in all cases. Endometrial biopsy and hysteroscopy are the procedures of choice for the diagnosis.

Hysteroscopists should be familiar with these images of premalignant lesions.

A consensus defining the characteristic hysteroscopic images of premalignant endometrial lesions should be created.

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