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Chapter 6

Etiology, Clinical Manifestations, Evaluation and Management of Uterine Leiomyoma

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Abstract

Uterine fibroids are common, benign, monoclonal tumors developed from myometrial cells. Genetically, 40% of these cells have chromosomal abnormalities, disorganized growth regulatory genes and disarrayed collagen fibers. Estrogen and progesterone stimulate fibroid growth. Conditions associated with high and prolonged exposure to these hormones increase the risk of fibroid development e.g., low parity, early menarche, increased age and increased body mass index. On the contrary, conditions with low hormonal levels decrease the risk of fibroid development, e.g., smoking, exercise and high parity. Additional, risk factors include, genetic susceptibility among family members wherein one member has fibroids; race/ethnicity, specifically among black women; Increased BMI and diets rich in ham and red meat have been well-

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established. In addition to serum levels of ovarian steroidal hormones, local production of factors within the muscle cells are important in the pathogenesis of fibroids like; increasing aromatase levels which causes an increase in the production of estrogen or production of varying growth factors. Fibroids are frequently asymptomatic. However, they can cause serious morbidities and have deleterious effects on the quality of life for women suffering with them. In the hierarchy of fibroid symptoms, abnormal uterine bleeding is the most common symptom associated with myomas. Pelvic pain is only slightly more reported by women with uterine fibroids. Presenting symptoms are normally related to the size and location of the fibroid. Subfertility due to deformity or obstruction caused by uterine fibroids is unusual. Recurrent abortions may be induced by a fibroid occupying the endometrial cavity even though the abortificant effect of fibroids in general is controversial. Red degeneration of a fibroid may develop during pregnancy and results from the fibroids' central hemorrhagic infarction. Consequently, it is able to induce severe pain and occasionally rebound tenderness, low-grade fever, leukocytosis, nausea and vomiting. Obstetric complications commonly associated with fibroids include; pre-term labor, placental abruption, fetal malpresentation, obstructed labor, cesarean delivery and postpartum hemorrhage. Pedunculated submucous or subserous fibroids may undergo torsion and necrosis. Infection of a fibroid at post-partum or post curettage is rarely reported. Severe anemia resulting from menorrhagia and hydronephrosis resulting from mechanical pressure on the ureters are also occasionally seen. Uterine fibroids may be diagnosed by careful examination of the pelvic region or by imaging techniques such as; transvaginal sonography, saline-infusion sonography, hysteroscopy and magnetic resonance imaging. For most women with mild to moderate symptoms, observation is recommended, especially among premenopausal women. If menorrhagia is reported, the endometrium should be evaluated by sonography or biopsy. Nonsurgical treatments currently used for the management of fibroids include; levonorgestrel-intrauterine device, GnRHa with or without add back therapies, aromatase inhibitors, selective estrogen or progesterone receptor modulators, androgens and herbal drugs. However, these drugs are usually used for a limited time period. If symptoms increase in severity or if pressure symptoms are present, surgical intervention by abdominal, laparoscopic or hysteroscopic myomectomy, hysterectomy, uterine artery embolization or magnetic resonance-guided focused ultrasound may be performed.

Introduction

Uterine Leiomyomas or myomas are common, benign, monoclonal tumors which develop from myometrial cells. The extracellular matrix of a myoma is composed of collagen, elastin, fibronectin and proteoglycan [1]. Most myomas are asymptomatic and are diagnosed accidentally.

Uterine fibroids may be present in different locations of the uterus. If a leiomyoma is located immediately under the endometrium and very near the uterine cavity, it is called submucousal. If however, it is located under uterine serosa, it is called subserousal and, if confined to the myometrial layer, it is called intramural. However, if an intramural myoma grows excessively large it may show characteristics of a submucous or subserous myoma. Pedunculated submucous or subserousal myomas may undergo torsion and infarction necrosis. Occasionally, a subserous myoma becomes parasitic and is nourished by blood vessels from omentum or broad ligaments.

Leiomyomas usually grow slowly. A prospective MRI study on 72 premenopausal women showed a growth rate of 9% in 12 months. However, investigators noted that within that same cohort of women, varying rates of growth were present in different fibroids [2].

Incidence

The incidence of uterine myoma increases with advanced age. In one study which evaluated the prevalence of uterine fibroids by ultrasound scanning, a rate of 4% in 20-30 years, 11-18% in 30-40 years and 33% in 40-60 years old women was reported [3]. In another study, by age 50 nearly 70% of white and more than 80% of black women were found to have myomas by ultrasound scanning [4]. In gross serial sections of uterine specimens at 2-mm intervals 77% of women who had hysterectomy were found to have uterine myomas [5].

Almost 8 women in 1000 per year will require surgery for uterine myomas. The peak age of surgery is about 45 years of age [6].

Etiology

Myomas are produced by a single progenitor smooth muscle cell. The exact growth stimulator(s) in uterine myomas is not yet known. However, genetic susceptibility, ovarian steroid hormones and growth factors have been suggested as etiologic factors for uterine fibroid growth.

1. Genetics

It is hypothesized that a muscle cell loses its normal growth regulation probably due to a somatic chromosomal mutation [7]. Chromosomal abnormalities are currently found in 40% of myomas and include; translocations between chromosomes 12 and 14, trisomy of chromosome 12 and deletions of chromosome 7 [8]. More than 100 genes are suggested to have different expressions by uterine fibroid cells [9]. The presence of multiple myomas with higher recurrence rates and a 2.5 fold increase in the risk of developing myomas in first degree relatives, point to a genetic predisposition [10]. Uterine myomas are 2-3 times more frequently seen in black women [4].

Hereditary uterine and cutaneous leiomyomatosis as well as renal cell carcinoma are known as autosomal dominant syndrome. The affected gene, *fumarate hydratase*, is responsible for the coding of an enzyme in the Krebs cycle. It is used to screen for this mutation in families with cutaneous leiomyomatosis. 10-16% of the affected women will develop renal cell carcinoma [11, 12].

2. Hormones

The literature clearly supports the notion of leiomyomas being hormone sensitive due to the fact that the majority of observed growth is seen during the reproductive years and typical regresses after menopause. Additionally, gonadotropin-releasing hormone agonists (GnRHa) usually decrease the size of myomas. Both estrogen and progesterone stimulate the growth of myomas. Peak mitotic activity of a fibroid cell is seen in the luteal phase which suggests a stimulatory role for progesterone [13, 14].

Immunohistochemical studies on the proliferative indexes of human uterine leiomyoma cells grafted onto mice showed a basic and major role for progesterone but a supportive and permissive action for estrogen by increasing progesterone receptor production [15, 16, 17].

Evidence suggests that the microenvironment within a myoma is more estrogenic [18, 19, 20]. Also aromatase gene and enzyme expression are increased in myomas [21].

3. Growth Factors (GFs)

Various growth patterns of different myomas in the same uterus support the theory of local stimulatory effect of growth factors along with the hormones. Several GFs such as; Epidermal GF, Transforming GF β, Insulin GFI and II, basic fibroblast GF and vascular endothelial GF, are highly expressed by myoma cells [22, 23, 24, 25].

It has been suggested that these GFs are produced locally by smooth muscle cells or fibroblasts and are able to stimulate mitosis in cells with synthesis of extra cellular matrix and angiogenesis [26]. Parathyroid hormone-related protein and prolactin are produced more in myoma cells as compared to normal myometrial cells and act as GFs [27]. Hematopoiesis was also reported in degenerating myomas [28].

Presence of abnormal vasculature and dilated veins that resemble an abnormal angiogenesis are stimulated by abnormal vascular growth factors such as fibroblast and vascular endothelial growth factors. These changes may be responsible for heavy abnormal uterine bleeding [29].

Regulation of these GFs by controlling responsible genes is the basis of the idea for gene therapy. So, possibly in the future, specific altered genes that are delivered to myoma cells may regulate genes and prevent excessive cellular growth [30].

Risk Factors

1. Ethnicity and Family History

Chromosomal abnormalities are present in 40% of myomas. Moreover, first degree relatives of women with uterine fibroids are 2.2 times more likely to develop myomas within their lifetime. The fact that myomas are 2-3 times more frequent in black women as compared to white women suggests for genetic predisposition [4, 7, 10, 31]. It is believed that a genetic susceptibility may exist for uterine fibroids in certain families or ethnicities.

2. Hormones:
a-Endogenous Hormones

Factors associated with higher exposure to estrogens include: obesity, early menarche and low parity increase the risk of developing myomas while factors that decrease estrogen exposure such as smoking, leanness and higher parity decrease risk [32].

Pregnancy:

During pregnancy high levels of hormones are produced by the placenta and cause significant physiologic changes in the mother. It can therefore be logically concluded that these hormones should induce the stimulatory effect on fibroid growth during pregnancy.

However, the behavior of a myoma during pregnancy is not accurately predictable. Leo-Toaff et al. reported that in the first trimester myomas either grew or remained unchanged. This is explained by a possible response to the increase in hormonal levels.

However, in the second trimester, smaller myomas (2-6 cm) remained unchanged or decreased in size and the larger myomas became smaller and were thought to be related to the down regulation of hormonal receptors.

More interesting still, in the third trimester, all of the myomas either became smaller or remained unchanged which was explained by receptor down regulation. Most of myomas decrease in size after delivery [33].

b-Exogenous Hormones

Oral contraceptive pills (OCPs):

It has been suggested that the use of OCPs increase the risk of developing myomas. However, several studies report neither increase in fibroid growth nor the formation of new fibroids during the use of low-dose OCPs [34, 35, 36].

Menopausal Hormone Replacement Therapy:

Studies evaluating postmenopausal women with uterine myomas remain controversial. For instance, in one study, researchers showed an average of 0.5cm growth in the size of myomas after receiving oral progesterone and estrogen transdermal patches for 12 months [37]. However, other studies have shown no increase in the size of uterine fibroids [38]. Overall, it can be concluded that for most postmenopausal women with myomas, hormone replacement therapy will not induce growth.

3. Age

With advanced age, the incidence of leiomyomas increases. An almost five-fold increase in the incidence of myomas was observed among women 40-44 years of age as compared to women 22-29 years of age [2].

4. Body Mass Index

Studies show a positive relationship between symptomatic uterine Leiomyomas and increased BMI or low physical activity [39, 40].

Diet

Diets rich in beef, ham and red meat also show an increased risk for the development of leiomyomas; whereas diets rich in vegetables show a decreased risk [41].

5. Endometrial Cell Injury

Although repetitive injuries to endometrium or inflammation caused by infection, hypoxia or menses have been implicated as inducing smooth muscle cell proliferation and development of myomas, no increase in the incidence of myomas has been reported in women documented as having had a prior history of sexually transmitted infections or intrauterine device implantations.

Clinical Manifestations

Myomas can induce morbidity and decrease quality of life yet mortality due to myomas is very rare. Clinical symptoms caused by uterine myomas largely depend on the size and location of the myoma.

Historically, the classification of myomas has been performed by one of the three following systems: primary, secondary or tertiary. The tertiary system was first described by Wamsteker et al. and was based on the locations of myomas as submucousal or subendometrial [43]. Finally, the Federation of International Gynecologists and Obstetricians (FIGO) classification system (PALM-COEIN) developed a methodology for the classification of abnormal uterine bleeding caused by myomas which included subclassifications. The system evolved to include 8 categories or types based on the localization of the tumor [44]. The final classification is as follows [42]:

Type 0: intracavitary (pedunculated submucous)

Type 1: > 50% of the diameter is in the uterine cavity

Type 2: $\leq$ 50% of the diameter is in the uterine cavity

Type 3: adjacent to the endometrium without intracavitary portion.

Type 4: completely intramural.

Type 5: subserousal $\geq$ 50% of the diameter is intramural.

Type 6: subserousal < 50% of the diameter is intramural.

Type 7: pedunculated subserousal

Type 8: No myometrial component (cervical, parasitic or those located in the round or broad ligament)

1. Abnormal Uterine Bleeding

The most frequent symptom induced by myomas is excessive menstrual bleeding [45]. When myomas grow they are supplied by an abnormally dilated venous plexuses, thought to be caused by vascular angiogenesis factors such as vascular endothelial or fibroblast growth factors. These vascular changes have been implicated as being responsible for heavy menstrual bleeding of submucous myomas [29]. Increased endometrial surface area and associated endometritis may also contribute to menorrhagia.

A study performed on women between 35-49 years of age showed that gushing of blood during menses was more frequently reported by the women with fibroids as compared to those without fibroids. It was also shown that women who had fibroids measuring 5 cm or more in diameter experienced more gushing of blood and used more pads [46].

In cases of abnormal uterine bleeding, the clinician or healthcare provider should keep the possibility of endometrial hyperplasia or neoplasia at the forefront of his/her mind and resolve to having an appropriate tissue diagnosis and pathologic evaluation completed. There are reports that associate myomas, endometrial hyperplasia, and endometrial carcinomas with the pathophysiologic mechanism of localized and systemic hyperestrogenic conditions [47].

2. Pain

Pain is not a common symptom for uterine fibroids. In a population-based cohort study conducted among 635 women screened by transvaginal ultrasound scanning, 96 women were diagnosed as having myomas with only slightly more moderate or severe dyspareunia or noncyclic pelvic pain being reported. In addition, of those women participating in this study with fibroids, none reported having experienced a higher incidence of dysmenorrhea as compared to women without fibroids [48]. Fibroid degeneration caused by rapid growth, ischemia and cell death can induce pain. Fibroid degenerations are pathologically classified as; hyaline, hemorrhagic, calcification and cystic degenerations that do not differ in presenting symptoms [49].

Acute pain can also be induced by torsion of a pedunculated myoma.

3. Mechanical Pressure Symptoms

Large myomas place pressure on surrounding structures and may show related symptoms such as; partial or complete obstruction of ureters, urinary frequency or urgency and difficulty in bowel habits. Even respiratory failure has been described as a consequence of uterine myomas [50, 51].

Diagnosis

1. Pelvic Examination

A careful pelvic examination reveals an irregularly enlarged, firm, non-tender uterus in subserousal or intramural myomas with considerable size.

2. Transvaginal Sonography (TVS)

TVS is the most accessible and cost-effective diagnostic procedure utilized as a first step when there is suspicion of a space occupying pathology in the pelvis. TVS is reported to be a reliable tool in evaluating the uterus containing less than four fibroids with less than 375 CC volume [52].

3. Saline Infusion Sonohysterogram (SIS)

In this method, saline is infused into the endometrial cavity and the anechoic contrast provided by the saline gives a better visualization of submucous fibroids. It is recommended that SIS be performed in the routine evaluation of infertile women to reduce implantation failure by diagnosing and treatment of endometrial abnormalities also for the cases of abnormal uterine bleeding [53, 54]. However, many clinicians prefer to start with TVS and reserve the SIS procedure for those who are suspected to have submucous myomas versus polypoid lesions or other endometrial pathologies [55].

4. Magnetic Resonance Imaging (MRI)

MRI has the best sensitivity and specificity for confirmation of the number, size and location of all kinds of uterine myomas with the least inter-observer variability [56, 57].

5. Hysteroscopy

Hysteroscopy can also be used for the diagnosis of uterine myomas, especially for the submucosal types. In a comparative study it was reported that mapping of uterine myomas is more precise by transvaginal sonography as compared to hysteroscopy.

However, differentiation between endometrial polyps and submucousal myomas could be better performed via hysteroscopy [58].

Leiomyoma and Reproduction

Leiomyomas rarely cause infertility by obstruction, cavity distortion, mechanical compression or complete obstruction of the cervical canal or tubes. Rather, the current hypothesis is framed around the idea that distortion in the shape of the uterine cavity which can be induced by intracavitary, submucous or intra mural myomas may interfere with normal implantation [59].

For women with no any other etiologic factors for infertility or recurrent abortions, removal of the myomas has been recommended [60].

Leiomyoma and Pregnancy

The incidence of myomas during pregnancy ranges between 0.65% and 11%, depending on the targeted population and methods of screening. For instance, the incidence among African American women has been documented as being as high as 18% [61]. The behavior of myomas during pregnancy is not accurately predictable [33].

Most pregnancies with myomas will progress to full-term labor without complications [62, 63]. However, a pregnancy with myomas has an increased risk of spontaneous abortion, malpresentation, red degeneration, pre-term birth, and cesarean delivery [62, 63, 64].

In addition to these risks, there is an increased likelihood of placenta previa and post-partum hemorrhage [63]. Central hemorrhagic necrosis of the myoma may develop in a pregnant uterus, also known as "red degeneration". Red degeneration occurs in about 5% of pregnancies with a preexisting fibroid [33]. Pain is the most frequently reported symptom. However, rebound tenderness, leukocytosis, low-grade fever, nausea and vomiting may also develop [65]. Most myomas decrease in size after delivery. The risk of uterine rupture at the site of a previous abdominal myomectomy is reported to be about 0.2% [66]. The risk of uterine rupture during pregnancy after laparoscopic myomectomy is not well reported [67].

Leiomyomatosis Peritonealis Disseminate

Multiple smooth muscle tumors resemble disseminated carcinomatosis. It seems that estrogen stimulates the development of mesenchymal cells to smooth muscle cells. Approximately 50% of reported cases were diagnosed during pregnancy and usually regress after delivery [68].

Potential for Malignant Transformation of Uterine Sarcoma

In previous studies, the rate of sarcomatous transformation of a myoma was suggested to be about 0.13-0.23% [69]. Recently, the idea about the possibility of sarcomatous transformations in a benign myoma has been challenged because it is observed that myomas and sarcomas have different cellular genetic characteristics and origins [70].

For accurate preoperative distinction and differentiation of uterine leiomyosarcoma vs. Leiomyoma, measurement of serum LDH and gadolinium-enhanced diethylenetriamine penta-acetic acid (Gd-DTPA) is recommended. Sarcomas show increased enhancement and vascularity with gadolinium as compared to degenerating fibroids and usually present with the chief complaints of pain and bleeding [71].

Treatment Options

Treatment options include, observation, medical therapy, surgical therapy and radiological interventions. The best therapeutic method depends largely on the woman's age; childbearing desire; intensity of symptoms; the size, number, and location of myomas; the presence of other complicating medical conditions and/or comorbidities; and the woman's desire to preserve her uterus.

1. Observation

Women with mild to moderate symptoms may be followed by serial evaluations of the size and the symptoms of the fibroids. This option may be particularly attractive to women nearing menopausal age, given that the cessation of menses is typically associated with an overall decrease in the size and associated symptoms of myomas. Women with mild symptoms who want to become pregnant may also find this option beneficial.

2. Medical Therapy

Medical treatment of uterine fibroids may be a temporary treatment option for women who are premenopausal or who have high surgical risks or desire future pregnancies.

a- Oral Contraceptive Pills (OCP)

OCP consumption may help to control abnormal uterine bleeding. However, this treatment option remains controversial in part, because of the widely accepted notion that these hormones are able to stimulate fibroid growth [34, 35, 36, 38, 72].

b- Other Medical Treatments

Several medical modalities are suggested for the treatment of uterine fibroids such as; Levonorgestrel-Releasing Intrauterine Devices [73-75], Gonadotropin-releasing hormone agonists [76-79], GnRH Antagonists [79], Aromatase Inhibitors [80-89], Selective Estrogen Receptor Modulators [90, 94], Progesterone Receptor Modulators [95, 96], Androgens [97-99] and Miscellaneous Agents [79, 100-104]. Complete discussion about the options currently available for the medical treatment and prevention of uterine fibroids are provided in two other chapters of this book.

3. Surgical Treatment Options

Serious to severe symptoms of uterine fibroids include: severe anemia associated with chronic menorrhagia, ureteral obstruction, pelvic pain or pressure, urinary frequency and/or incontinence. Recurrent bouts of these symptoms typically result in patients choosing a surgical option.

a. Myomectomy

Myomectomy is a conservative and widely accepted option for the treatment of uterine myomas. Patient benefits associated with this option include, lower intraoperative risks as compared to hysterectomy [105] and preservation of the uterus. However, women should be fully informed of the risks of this procedure which include the possibility of recurrence and developing a new fibroid in the same uterus which may implicitly require repeated treatments. The risk of developing new fibroids after myomectomy increases with advancing age and number of fibroids. It has been warned by some researchers that the preoperative use of GnRHa may increase the risk of developing new fibroids in the future [2, 106].

1. Abdominal Myomectomy

During an abdominal myomectomy the volume of blood loss should be carefully noted. Surgical techniques are available to limit blood loss such as; tourniquets, vasoconstrictive agents (*vasopressin*), careful planning of uterine incision to keep a safe margin from uterine cornue or great vessels and ligation of both uterine arteries if needed. It seems that uterine incisions made transversely may reduce bleeding because they are parallel to arcuate vessels. Decreasing the number of uterine incisions and using cell savers are other methods to reduce bleeding. Cell savers are used in cardiac and neurological operations and may be used for myomectomy. This device collects blood and after heparinization, red blood cells are washed, filtered, processed and transfused back to the patient if clinically necessary [107].

Appropriate hemostasis is vital for the prevention of adhesion formation. Adhesions on posterior wall incisions are more severe as compared to anterior wall incisions. Adhesion barriers may also be used [108].

2. Laparoscopic/Robotically Assisted Laparoscopic Myomectomy

Superficial subserous or pedunculated myomas are most appropriate for Laparoscopic/robotically assisted laparoscopic myomectomy. Deep intramural or submucous myomas (types 2, 3 and 4) should be laparoscopically operated only in expert hands to perform appropriate approximation and suturing at least in 2-3 layers. Comparative studies of abdominal myomectomy versus laparoscopic route, reveal that though laparoscopic myomectomy has a longer operating time, it remains a preferred method due to less blood loss and increased patient comfort [109].

Major complications are comparable. However, it should be noted that inadequate approximation of myometrium during operation can progress to uterine perforation in a subsequent pregnancy.

3. Hysteroscopic Myomectomy

Ideally, submucous fibroids that induce infertility and abnormal bleeding are operable hysteroscopically. Submucous myomas that are pedunculated or have more than 50% intracavitary volume (types 0-1) can be safely removed by hysteroscopic surgery after cervical dilation and by using cutting loop.

Perforation of the uterus while dilating the cervix or by deep myometrial resection may occur. Intravascular absorption of the distending media may cause pulmonary edema, hyponatremia and heart failure; therefore, careful monitoring of fluid deficit and the use of diuretics and timely termination of the procedure are life saving. Electrolyte levels should also be monitored and corrected.

b. Laparoscopic Myolysis and Cryomyolysis

Coagulation and cryotherapy of myoma, or myolysis is possible under laparoscopic visualization to induce destruction of myoma cells and reduce blood supply [110, 111]. About 50% reduction in fibroid volume was reported. However, severe adhesion formation and uterine rupture during pregnancy are possible complications that have since made this method an inappropriate option [112, 113].

c. Hysterectomy

An investigation of hysterectomy rates revealed that hysterectomy with the indication of uterine myoma decreased slightly during the years 2000-2004. However, leiomyomas remain the leading cause for hysterectomies [114].

When symptoms are severe enough and no future fertility is desired, women may decide to have hysterectomy. The symptoms may be exhausting with profound uterine bleeding, severe anemia, pelvic pain or pressure symptoms and ureteral compression.

Which One-Abdominal, Vaginal or Laparoscopic Hysterectomy?

To choose the best method of hysterectomy via abdominal, vaginal or laparoscopic access, the patient's condition, the facilities that are available and the surgeon's skills should be considered.

A recent Cochrane review concluded that vaginal hysterectomy is the preferred method of hysterectomy. This review concluded that vaginal hysterectomy has the best outcomes with the least complications. When vaginal hysterectomy is not technically possible, laparoscopic hysterectomy has advantages over the abdominal method [115].

The eVALuate study included two randomized multicenter trials. One trial compared laparoscopic with abdominal hysterectomies and the other compared laparoscopic with vaginal hysterectomies. The results of these trials showed almost similar complication rates between all groups. However, lower urinary tract complications were three times more frequent in the laparoscopic group as compared to vaginal or abdominal groups [116].

Short-term preoperative treatment with GnRHa is associated with a reduction in myoma size and may be beneficial when the desired effect is to increase hemoglobin concentrations or in instances when the decision is made to switch from an abdominal hysterectomy to a vaginal method [77].

4. Radiologic Interventions

Uterine Artery Embolization (UAE)

UAE was first described in 1995 for diversion of blood supply from a uterine myoma. UAE is performed by canulation of femoral artery and embolization of the uterine artery and its branches by injection of gelatin sponges, polyvinyl particles, gelatin microspheres performed by a trained radiologist. Tissue hypoxia after UAE induces pain postoperatively. Most patients experience pain, nausea, a low-grade fever and leukocytosis for 1-2 days. Hysterectomy may be needed due to complications like pyometra and sepsis.

In one study of the 88 patients undergoing UAE, 23 (28.4%) women needed hysterectomy due to dissatisfaction with improved symptoms within the first 2 years [117]. Study results have shown that complications associated with UAE include decreased ovarian reserve, earlier menopause and increased pregnancy complications [118, 119].

Another comparative study between laparoscopic myomectomy and embolization demonstrated that miscarriage, abnormal placentation, preterm birth and postpartum hemorrhage were increased among women who underwent UAE [120]. The American College of Obstetricians and Gynecologists (ACOG) considers the UAE procedure to be investigational and relatively contraindicated for the women who desire future fertility [121].

Magnetic Resonance-Guided Focused Ultrasound (MRgFUS)

Ultrasound energy if affixed to a focal point, can produce temperatures high enough to induce cellular death. The use of MRI helps to target the organ and monitor the temperature of the tissue. However, of noteworthy mentioning, small reductions in fibroid volume and high rates of recurrence have been reported in the use of MRgFUS [122]. In addition, risk of thermal injury to the skin and normal tissue are possible complications. Further studies are needed to confirm the efficacy and better understanding the risks associated with MRgFUS. This treatment was approved by the United States Food and Drug Administration (FDA) in 2004. As a treatment modality, MRgFUS is most appropriate for fibroids classified as type 1 and 2 [123].

Summary in the Management of Uterine Myomas

Multiple treatment options exist for fibroid treatment. Treatment options can be personalized based on patient's conditions. For asymptomatic women that do not desire fertility, observation is the best option. Those patients should be scheduled 2-3 times per year for an evaluation of symptoms, performance of a pelvic examination, and if needed, ultrasound scanning. If they desire pregnancy and intracavitary pressure is suspected, uterine cavity should be evaluated by SIS, hysteroscopy or MRI. If the cavity is not deformed surgery should not be considered. However, if the cavity is deformed myomectomy may be the best option.

For symptomatic women who desire fertility but suffer from abnormal uterine bleeding, an assessment of hemoglobin levels and an endometrial biopsy is needed. Evaluation of the uterine cavity by SIS, hysteroscopy or MRI may also help in deciding the most appropriate

treatment method. If mechanical pressure symptoms and pain are present myomectomy should be considered.

For symptomatic women that are perimenopausal, careful observation is considered a suitable treatment option. However, if symptoms of uterine sarcoma such as abnormal bleeding, pain and rapid growth of myoma persist, MRI-gadolinium and LDH are indicated. In cases of menorrhagia with normal endometrial biopsy, GnRH agonist for a few months, levonorgestrel IUD or hysteroscopic myomectomy or endometrial ablations are considered appropriate treatment options. Moreover, if pressure symptoms are present with no desire for future fertility, myomectomy, hysterectomy, UAE or focused ultrasound may be suitable treatment options.

Finally, women suffering from myoma associated symptoms should be concealed about the different treatment options. Also the benefits and probable complications of each treatment method should be explained, to help the patient make the best decision.

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