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PREGNANCY AFTER UTERINE ARTERIAL EMBOLIZATION FOR THE TREATMENT OF FIBROID - CASE REPORT

Kamilla Fernandes Santiago de Araujo Unigranrio University, Rio de Janeiro, RJ. http://lattes.cnpq.br/4874445049934445

Marina Pacheco Robert Pinto

Unigranrio University, Rio de Janeiro, RJ. http://lattes.cnpq.br/9417002610063641

Jussara Mote de Carvalho Novaes Cardoso Fontes Federal Hospital, Rio de Janeiro, RJ.

Michel de Mello Zelaquett

Mioma Center, Rio de Janeiro, RJ. http://lattes.cnpq.br/6846749591873995



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Abstract: Leiomyomas are benign tumors which have a high prevalence in the gynecological routine and great economic impact on the health system. Embolization of the uterine artery represents a less invasive therapeutic proposal in the management of myomatosis, but it still faces resistance in its use, especially in women with a desire to become pregnant in the future. In the literature, there is documentation on the safety and efficacy of EAU in the short term, but further studies are needed on its long-term effects, especially in relation to fertility, since there is a risk of damage to the utero-ovarian collateral circulation and consequent local change in blood flow. during the procedure. The aim of the study is to report the case of gestational success after the approach of myomatosis by uterine artery embolization. The work consists of a descriptive study of the case report type, followed at the Centro de Mioma, RJ, and is based on the analysis of medical records. Due to limited studies on the effects of EAU in the long term, it was not possible to establish the superiority or advantage of the EAU in relation to other therapeutic methods, as well as it was impossible to identify individual and/or external factors that contribute to a greater chance of the patient to preserve her fertility. More scientific studies are needed to assist in choosing the most beneficial invasive leiomyoma treatment method for woman, especially nulliparous women.

Keywords: Leiomyoma, embolization, treatment, fertility and pregnancy.

INTRODUCTION

Leiomyomas are benign hormone-dependent tumors originating in the uterine muscular layer that are frequent in gynecological routine. ¹ They represent an important cause of morbidity due to the negative impact on the female reproductive system. ^{2,3} They are responsible for abnormal

bladder dysfunction uterine bleeding, and obstetric disorders, and can lead to complications such as anemia, urinary incontinence and infertility or abortion, respectively. 4 In addition, they have a great economic impact on the health system given their prevalence. ⁵ Statistics reveal that approximately 35 to 77% of women of reproductive age are affected by this type of uterine fibroma, although the true prevalence is higher, since most are asymptomatic. Among the symptoms, there are pelvic pain, uterine bleeding and infertility, which may be related to mechanical obstruction of the uterine tubes, uterine morphological alteration and receptivity of the endometrium to the embryo. 6

Currently, there are established and successful approaches to the treatment of fibroids: expectant management, symptomatic treatment and hormone therapy, in addition to laparotomy, robotic or hysteroscopic laparoscopic myomectomy, hysterectomy, ultrasound waves (USG) and uterine artery embolization (EAU). ⁷

Uterine artery embolization introduced in 1995 as a non-surgical therapeutic option for symptomatic patients diagnosed with leiomyoma. Since then, fibroid embolization has also been used in the treatment of adenomyosis, postpartum hemorrhage and in cases of uterine vascular malformation, in addition to obstetric complications. hemorrhagic 8,9 Unlike surgical approaches, EAU is minimally invasive and produces necrosis of tumors by ischemia, with temporary occlusion of the vessels in the region through biocompatible particles, through angiography. 5,10 There are several types of embolic agents in interventional radiotherapy, and among the possible options in the EAU are polyvinyl alcohol microparticles (PVA) and tris-acryl gelatin microspheres (TAGM). 11.12

In the literature, there is documentation of safety and efficacy of EAU in the short term, but further studies are needed on its long-term effects, such as symptom relief and fertility. In the short term, it demonstrated a reduction in symptoms and greater costeffectiveness when compared to surgical treatment. 13 In previous studies, a significant reduction in the size of the myomas was observed in the third postoperative month. In comparison with hysterectomy, some studies have observed similar therapeutic effects in relation to the improvement of postoperative symptoms such as anemia and dysmenorrhea, and other studies have observed an earlier return to daily activities and a lower degree of postoperative pain in patients undergoing EAU. 3,14 However, there is greater reintervention after EAU within 1-2 years when compared to hysterectomy, which can be explained by incomplete devascularization of the tumors. 15 The comparison between the myomectomy, hysterectomy and EAU methods is presented in the form of a table in Appendix B at the end of the work.

When compared to myomectomy, EAU had a shorter hospital stay, in addition to an earlier return to daily activities. 9,16 There was also an improvement in quality of life, assessed by the Uterine Fibroid Symptomand Quality of Life (UFS-QOL) questionnaire, up to 3-5 years after the procedure. 5,10 Some studies show similar results between the methods and others demonstrate a more significant improvement in quality of life and better reproductive results in myomectomy when compared to EAU. Uterine volume reduction and menstrual bleeding scores remained similar in both. The incidence of complications varied between studies, but there was greater reintervention after EAU during the 2-year follow-up. The main reason was pain. 10,13,14

Regarding ovarian function, there are controversies in the literature regarding the use of EAU as a therapeutic option for women who wish to maintain their fertility, as there is a concern of damaging the utero-ovarian collateral circulation and causing changes in blood flow in the region during the procedure. Therefore, it could compromise the ovarian reserve with consequent amenorrhea, generate implantation difficulties due to endometrial injury or cause deformities of the uterine cavity due to myometrial injury, thus interfering with female fertility. of FSH after EAU, which indicates that the procedure did not result in changes in ovarian function, especially in patients under 45 years of age. 5,7,14

In both hysterectomy and myomectomy there are risks of damage to the ovary. ^{5,9} Myomectomy also results in myometrial injury and whether this influences reproductive outcomes is uncertain. ^{9,10} Even though there are not many studies and certainties about the relationship between EAU and post-procedure fertility in patients who wish to become pregnant in the future, this topic has been the subject of discussions, even though it has shown favorable results for pregnancy. ¹⁴

In recent years, there has been an increase in nulliparous women over the age of 30 with leiomyoma, where surgical treatments can affect female reproductive capacity. Therefore, it is important to have minimally invasive procedures that allow postponing definitive surgeries. ¹⁴ Taking into account that myomatosis has a high prevalence in the gynecological routine and great economic impact on the health system, uterine artery embolization represents a less invasive therapeutic proposal, but which still encounters resistance in being used, especially in women who wish to get pregnant in the future.

The aim of the study is to report a case of gestational success after uterine arterial

embolization myomatosis approach.

THEORETICAL FOUNDATION

Leiomyoma is the most common tumor of women in menacme, especially from the age of 50, when 80% of women become susceptible to its development. When symptomatic, it negatively impacts the lives of patients and depending on its location, size and quantity, it can cause a feeling of heaviness in the lower abdomen, abdominal pain and dyspareunia, in addition to abnormal uterine bleeding. 17 The diagnosis can be made during the physical examination, when the presence of a mass in the pelvic region is verified, associated with a compatible clinical history. Transvaginal ultrasound is the most accessible and accurate complementary method for diagnosis. Prior evaluation of the myoma through radiological examinations such as ultrasound is important to establish the best therapeutic approach in each case. 14 Other tests, such as hysteroscopy and magnetic resonance imaging, may be useful in the differential diagnosis with endometrial polyps and sarcoma. 4

Its pathophysiology is still unknown, but it is known that the myoma expresses more estrogen and progesterone receptors compared to the adjacent unaffected myometrium. Recent studies demonstrate that estrogen is able to increase the expression of receptors for progesterone. ¹⁸ Factors such as black race, age (over 50 years old), late pregnancy, early menarche, caffeine and alcohol consumption, obesity and a diet rich in red meat are related to the appearance of myoma. However, the parity factor seems to play a protective role, where multiparous women seem to be more protected than nulliparous women. ⁴

There are several classifications of myoma in the literature, all based on the degree of intramural location and/or the degree of distortion of the uterine cavity. Two classifications commonly seen in clinical practice are the one adopted by the ESGE (European Society for Gynecological Endoscopy) and the FIGO classification. The ESGE is more simplified, which denominates G0 for pedunculated intrauterine fibroids, G1 for fibroids with most (> 50%) in the uterine cavity and G2 for fibroids with most (> 50%) in the myometrium. The FIGO classification is more recent and is divided into nine types of myoma (0-8), with 0: intracavitary pedunculated; 1: submucosal or < 50% intramural; 2: submucosal ≥ 50% intramural; 3: 100% intramural in contact with the endometrium; 4: intramural; 5: subserosal ≥ 50% intramural; 6: subserosal < 50% intramural; 7: subserous pedunculate; and 8: other types of myoma. Several types of fibroids may be present at the same time. 4

Patients who present symptoms usually do not respond to pharmacological treatment with GnRH agonists, whose function is to limit fibroid growth and restore hemoglobin levels. 4 In addition, as they have bone mass loss as the main side effect, these drugs must not be prescribed for continuous use, therefore, they are commonly used in the preoperative period. Studies report that its use before surgery is able to reduce the size of the myoma and decrease endometrial adherence and vascularization subsequent improvement in the visualization of the region during the surgical procedure. ⁴ Myomectomy hysterectomy or traditionally been the first choice in the management of symptomatic fibroids. 10

Embolization of the uterine artery emerged as an alternative in the 1990s and is characterized as an interventional radiological procedure, which aims to reach the uterine artery via the vascular route, in order to temporarily interrupt its flow with embolizing agents. For this, a catheter is inserted percutaneously into the femoral artery, accessing the internal iliac artery.

Once in place, the guide wire is passed inside the uterine artery, a branch of the posterior internal iliac artery, and then angiography is performed to visualize the uterine vascularization and define the size of the myoma (Figure 1). Finally, the agent is injected to embolize the artery and stop blood flow to the tumor. ^{7.17}

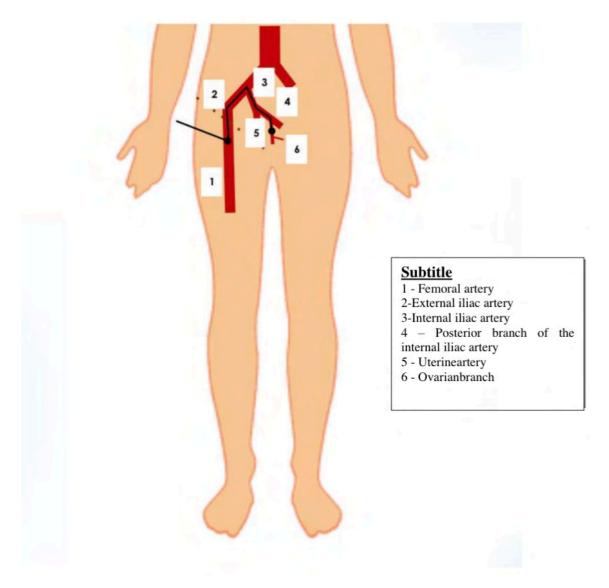
Despite having an advantage in terms of length of hospital stay, the choice of EAU as the initial therapy is still questionable, since during the procedure there is a risk of compromised ovarian function consequent hypoestrogenism with endometrial atrophy, which result in early menopause. This is due to the possibility of the ovarian circulation being affected by particles of embolic material, since the arteries of the uterus and ovary communicate. ^{19,20} However, in practice, the use of particles larger than the diameter of the ovarian vessels reduces the risk of occlusion of these vessels. ¹⁴ The uterine artery, a direct branch of the internal iliac, bifurcates into ascending and descending branches, supplying structures such as the lateral portion of the uterus, the cervix and vagina. The ascending branch, in addition to being responsible for the lateral vascularization of the uterus, is divided into ovarian and tubal branches, which continue the vascularization of the medial ends of the ovary and tube, and anastomoses with the ovarian and tubal branches of the ovarian artery. About it, it can be said that it has its origin in the abdominal part of the aorta, inferior to the renal artery and superior to the inferior mesenteric artery. As it follows, it adheres to the parietal peritoneum and passes anterior to the ureter in the posterior abdominal wall. Upon reaching the lesser pelvis, it crosses the origin of the external iliac vessels and, following medially, divides into an ovarian and a tubal branch, which are responsible for the ovarian and tubal irrigation together with the corresponding branches of the uterine artery. ²¹ In addition, ovarian function may be impaired due to technical failures, such as inadequate embolization of utero-ovarian anastomoses, anatomical variations - ovary irrigated predominantly by uterine arteries - or exposure to ionizing radiation. Other possible complications associated with EAU are the expulsion of the myoma requiring surgical intervention, complications arising from changes in the puncture site, arterial injuries, obstructions caused by the guidewire and improper embolization of other vessels. ²⁰

MATERIAL AND METHODS DESIGN

The work consists of a descriptive study of the case report type, with a qualitative variable, about a successful pregnancy after treatment of myoma through uterine artery embolization, case followed up at the Myoma Center, Center of Rio de Janeiro - RJ. For the study, an analysis of the medical records was performed, including clinical data, complementary exams and actions taken, after the patient's formal authorization by signing the free and informed consent form (FICF), whose CAAE number is 52159921.3.0000.5283e whose date of approval by the Research Ethics Committee (CEP) was January 28, 2022.

BIBLIOGRAPHIC RESEARCH METHODOLOGY

The literature search was carried out on *Pubmed*, *Cochrane and Lilacs platforms*, using the following descriptors: leiomyoma, embolization, treatment, fertility and pregnancy. Only articles in Portuguese and English were selected, with a time frame from 2011 to 2021, in the last 10 years, due to the small amount of bibliographic material on the topic addressed. Clinical trial studies, metanalysis, literature review and systematic review were selected. At the end of the



Vascular anatomy image shows EAU puncture site in the femoral artery, heading towards the external iliac artery as it passes through the inguinal ligament and reaching the internal iliac artery. From the posterior branch of the internal iliac artery, the uterine artery is reached. The uterine artery in turn gives off several branches, including the ovarian branches.

Figure 1: Vascular pathway during uterine arterial embolization for uterine artery access. Source: Prepared by the author.

research, a total of 28 articles were obtained, of which 20 were used in the project. Articles that do not match the study proposal were excluded, such as those that addressed post-EAU pain management; which brought comparisons regarding the embolic agents used in the procedure or comparisons between other minimally invasive techniques for the treatment of myomatosis, in addition to studies that reported types of extrauterine myomatosis. Finally, the book "Clinically Oriented Anatomy" by Keith L. Moore, seventh edition, was also used to complement the theory on the subject.

CASE REPORT

Patient, DM, 23 years old, female, sought gynecological care in January 2009 complaining of urinary frequency and weight in the lower abdomen. He also reported mild dysmenorrhea relieved with analgesics. She denied changes in menstrual flow. Nulliparous, nulliparous, menarche at age 11. Date of last menstrual period (DUM) 01/07/2009. Diagnosed with fibroids 4 years ago, without treatment, she used homemade teas in an attempt to reduce the fibroid. Previous use of oral contraceptives (OAC) in 2008, with headache and emesis for 2 months after starting medication. He denied using OAC at the time. He denied too many comorbidities and medications for daily use. He denied hospitalizations or previous surgeries. Social drinker. In view of the clinical history, the diagnostic hypothesis of leiomyoma was raised. Magnetic resonance imaging (MRI) of the pelvis (12/09/2008) with diagnosis of an enlarged uterus measuring 446.7 cm ³ and the presence of transmural, intramural and subserosal fibroids, with the largest measuring 8.6 cm. Embolization of the uterine artery was indicated as a treatment for being nulligest.

In September 2009, she returned for consultation with a complaint of

stranguria, frequency, low back pain and mild dysmenorrhea, denying any change in menstrual flow. He denied using OAC. A new MRI was requested, which showed an enlarged uterus of 665 cm ³ and multiple fibroids, with the largest measuring 11.6 cm. Open myomectomy was indicated.

Open myomectomy was performed in December 2009 with the excision of 6 myomas, without complications. In February 2011, he presented with a transvaginal USG with the uterus in retroversion flexion, measuring 7.6 cm in length, 4.5 cm in width, 4.2 cm in thickness, with regular contour and heterogeneous echotexture, presenting hypoechoic nodules with posterior intramural myomatous appearance with 0.8 cm and 0.6 cm.

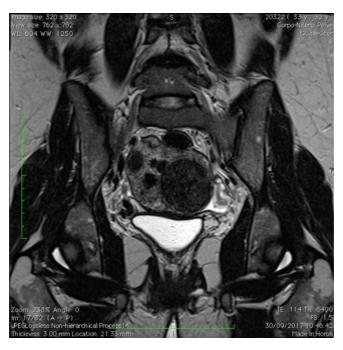
In February 2017, he sought gynecological complaining again of care dysmenorrhea, bulging of the right iliac fossa and frequent dyspareunia, reporting a single episode of sinus bleeding. He denied urinary changes. Upon vaginal examination, the uterus was slightly enlarged, mobile and painless. Painless attachments. Pelvic MRI revealed a uterus measuring 160 cm 3, in slight retroflexion, with a bulged contour, with a heterogeneous sign at the expense of multiple myomas, the largest being 4 cm, intramural, with a slight intraserosal component, tangential to the endometrium. Uterine cavity with preserved minimally distorted in the middle third by fibroids. (Figures 1 and 2). Embolization of the uterine artery is indicated to approach the fibroids.

In October 2017, fibroid embolization was performed with a right femoral puncture and diagnostic arteriographies showing large and tortuous uterine arteries, when multiple uterine fibroids were visualized. Catheterization of each uterine artery for embolization with BeadBlock microparticles (PVA). Control



2017 MRI in sagittal view shows uterus of 160 cm3, in slight retroflexion, with bulged contour, with heterogeneous signal at the expense of leiomyomas (indicated by white arrow), intramural dominants with a discrete intraserosal component, tangent to the endometrium, the largest of them measuring 4 cm. Uterine cavity with preserved shape, minimally distorted in the middle third by fibroids.

Figure 2: Real-time print of pelvic MRI in sagittal view. Source: Myoma Center - RJ, 2017.



2017 MRI in coronal section showing an enlarged uterus with the presence of hypoechoic images (indicated by the white arrow), suggestive of myomatosis.

Figure 3: Real-time print of pelvic MRI in coronal section.

Source: Myoma Center - RJ, 2017.

arteriography showing adequate vascular exclusion of fibroids. At the end, removal of the systems, manual compression of the puncture site for 10 minutes and occlusive and compressive dressing. No post-procedure complications were reported.

The patient presented with moderate dysmenorrhea up to 15 days after the procedure. DUM 11/01/17, lasting 5 days, normal flow and few clots. He denied urinary or intestinal alterations. Refers to reduced abdominal volume in the right iliac fossa. Laboratory tests and MRI were requested and a return scheduled in February 2018 for follow-up.

Pregnancy confirmed in September 2018. Twin pregnancy, without complications, daughters born by cesarean section.

DISCUSSION

The case presents the success of pregnancy after different approaches to myoma, including EAU. In the first consultation, uterine artery embolization was indicated due to the not very expressive size of the myomas, where the largest measured 8.6 cm. In 2009, when the case report started, there was no scientific evidence pointing to a risk of ovarian failure after EAU. Therefore, at the time, despite the patient's age and her desire to become pregnant in the future, embolization was the most appropriate option due to its less invasive nature and the patient's condition.

In the second search for medical care, myomectomy was indicated due to the rapid growth of the myoma in less than 1 year, which is now 11.6 cm. In this case, due to the significant increase in the myoma, EAU would not be as effective in reducing its size and providing significant improvement in symptoms.

In the third moment, the EAU was performed so that there was no need for a surgical approach again via the abdomen, since the formation of fibrotic tissue by the previous myomectomy would harm a new surgery. In addition, the size of the fibroids was adequate for the method, with the largest measuring 4 cm.

After the procedures, the patient progressed clinically well and there was no impairment of her fertility.

It is known that in the literature there are limited studies on the long-term effects of EAU, so it is not possible to establish protective or risk factors in order to determine better or worse outcomes for each patient. There is no scientific basis to assist in choosing the most appropriate invasive treatment method for myomatosis for each case.

It is understood that in the short term, all invasive methods of approaching fibroids lead to a significant improvement in symptoms and generate a positive impact on the quality of life of these patients. Regarding re-approach, there is evidence of greater reintervention in the EAU from the second year after the procedure, with the main reason being the recurrence of symptoms, especially pain. 13,15 In the case report, the patient achieved complete improvement of symptoms, without recurrence, and there was no need for a new approach. However, follow-up was discontinued in 2018, one year after the procedure, and therefore, it is not possible to confirm that the result was sustained.

The indication of the EAU for women who wish to become pregnant in the future is questionable due to the limitation of studies on the subject. This is due to the risk of damage to the utero-ovarian collateral circulation during the procedure. However, in the studies carried out, significant damage to ovarian function was not documented when compared to other methods, especially in women under 45 years of age, since there was no difference between the levels

of biomarkers of ovarian function. ^{5,10,14} Furthermore, in myomectomy, myometrial healing may be related to impaired fertility, even though there are still uncertainties. ¹⁰

The main limitations of the research were the lack of studies on the long-term effects of EAU and the limited sample of women in the studies found in the literature. In addition, there was also a limitation, as the patient in the case report was only followed up to 1 year after the embolization.

The work aims to raise discussions about the main methods for approaching myomatosis in women who want to get pregnant, their advantages and disadvantages in relation to EAU, based on published clinical studies and to encourage new studies on the subject, since the existing ones are limited in the literature.

FINAL CONSIDERATIONS

EAU is an alternative and less invasive method for the treatment of leiomyoma, but it is not suitable for women who wish to become pregnant in the future due to the concern of damage to the utero-ovarian collateral circulation during the procedure and the consequent impairment of endometrial, myometrial and ovarian blood flow. ovarian reserve, although there are not many studies about the relationship between EAU and post-procedure infertility.

At the end of the research, it was not possible to establish a superiority or advantage of EAU in relation to other methods of approaching symptomatic myoma, as well as it was not feasible to identify individual and/ or external factors that contribute to a greater chance of the patient to preserve her fertility, this because there is no scientific study in the literature that addresses the benefit or harm of the EAU for women who wish to conceive in the future in an individualized way. Despite the gestational success obtained in the case

report, it is not possible to identify factors that have contributed to this favorable result.

Thus, the aim of the study is to report the case of a successful pregnancy after the uterine artery embolization approach to myomatosis, in order to encourage further studies on the long-term effects of EAU in relation to female fertility and provide new evidence. so that there is the safest indication of the method, especially for those who wish to become pregnant in the future.

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