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Emergency embolization in locally advanced cervical cancer: a case series in a tertiary referral center in Argentina

Abstract

Cervical cancer is the second most common cancer in women in South America. However, it represents the greatest impact on morbidity and mortality in women under 45.

Among the most serious complications of cervical cancer, bleeding occupies a significant place, being the main symptom in advanced stages and leading to high morbidity and mortality.

Uterine artery embolization is a minimally invasive method that consists of injecting an embolizing material into terminal vessels.

The objective of this study is to describe cases of patients with advanced cervical cancer who required embolization of uterine arteries to control massive vaginal bleeding in a tertiary referral hospital.

Materials and methods: This is an observational, retrospective study, conducted at Sanatorio Güemes, Buenos Aires between October 2017 and May 2023. We included patients that required embolization due to severe vaginal hemorrhage and diagnosis of locally advanced cervical cancer. Our Institution is one of the largest third-level centers in the city of Buenos Aires, receiving referrals for cervical cancer from other more disadvantaged regions of Argentina.

Variables such as age, International Federation of Gynecology and Obstetrics stage, hemoglobin level, oncological treatment performed, embolization material, complications and re-embolization were analyzed.

A univariate analysis was performed. The data are expressed in categorical variables in absolute numbers and percentages.

Results: A total of 21 patients were included. Median age was 46 years (range, 24 - 83). The mean hemoglobin level was 7.6 g/dl.

In our study, 95.2% of the patients responded to the first embolization, and 28.5% required a second intervention throughout the oncological treatment, and only one patient (4.76%) needed a third embolization.

Regarding the material used, 66.6% of the patients were embolized with a gelatin sponge, while definitive material was used in the remaining patients (33.3%).

Patients who underwent a second embolization, gelatin sponge was used in 83.33% and definitive material was used in only 1 (16.66%).

The average survival time from diagnosis was 17.8 months, while the time from the first embolization was 9.8 months. 47.6% of the patients died after the first or second episode of embolization.

95.2% of the patients did not present complications and only 1 (4.76%) died two days after the procedure.

Conclusion: Uterine artery embolization is a safe and effective procedure for the treatment of acute hemorrhage in patients with advanced cervical cancer.

However, since it is a procedure that is performed only in tertiary centers, it makes it difficult to have universal access.

Keywords: embolization, cervical cancer, hemorrhage, women

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Introduction

Cervical cancer is the second most common cancer in women in South America.

It was the fourth cause of cancer mortality in women worldwide in 2020, being more common in developing countries.[1] In Argentina, during 2017 the mortality was 7.4 deaths per 100,000 women, with the highest incidence in Misiones, Salta and Chaco.[2]

The prevalence of this disease in developing countries stems primarily from inadequate access to primary prevention measures like HPV vaccination, as well as secondary prevention methods such as cytology and/or HPV testing in screening studies. Additionally,

various risk factors such as low socioeconomic status, multiparity, smoking, and immunosuppressive conditions contribute to its high incidence. Globally, about 35% of cases are diagnosed as locally advanced disease, not being feasible for surgical treatment, with a 5-year overall survival of 60%.[3] In developing countries, the diagnosis in locally advanced stages can reach up to 70% of cases.

Locally advanced cervical cancer is defined by the presence of any of the following findings.[4]

a) Tumor greater than 4 cm in its greatest dimension (Stage IB3 - IIA2)

b) Tumor invading parametria (Stage IIB)

c) Tumor that extends to the lateral pelvic wall, and/or involves the lower third of the vagina, and/or causes hydronephrosis, and/or involves the pelvic and/or para-aortic lymph nodes (Stage III)

d) Tumor that invades bladder or rectum mucosa, or extends beyond the true pelvis (Stage IVA).

Among the worst complications of cervical cancer, bleeding takes over a significant place and it is more frequent in advanced stages (III and IV).[5,6] The bleeding can be massive, being defined as loss of any amount of blood that causes signs of hypovolemia and/or hemodynamic instability.[7]

The importance of this complication lies in the morbidity produced, because it can cause severe anemia requiring multiple blood transfusions and hospitalizations in intensive care units. On the other hand, it causes a delay in the start of radiant treatment, increasing mortality.

Initially, managing massive hemorrhage involves administering solutions like Ringer's lactated or physiological solution to expand the vascular space, along with employing vaginal tamponade. If bleeding persists despite these measures, surgical or minimally invasive approaches, such as uterine artery embolization or hypogastric artery ligation, may be considered.[8,9]

Hypogastric artery ligation was the first method used to prevent massive haemorrhage in oncological patients. This procedure should be performed by qualified gynecologic oncologist surgeons. It can present a high percentage of morbidity due to complications of the procedure, being more important in those patients who have undergone radiotherapy since the normal anatomy is distorted and vital structures can be injured.[10] Furthermore, it is a method that cannot be performed in patients who present with poor functional status or organ failure.

Uterine artery embolization (UAE) is a minimally invasive method that injects an embolizing material into the interior of terminal arteries, mainly uterine arteries. This ultimately translates into a decrease in blood flow and, consequently, a decline in bleeding.

The correct selection of the embolic agent to use depends on the objective of the desired treatment. Arterial occlusion can be permanent or temporary and also distal or proximal.

Among the embolic agents used, the most common is the Gelatin sponge, a substance derived from porcine subcutaneous adipose tissue. It is a substance that generates temporary occlusion through mechanical obstruction, generating a foreign body that is then reabsorbed between 3 weeks to 3 months after embolization.

On the other hand, as a permanent embolizing agent we have Polyvinyl Alcohol (PVA) particles and microspheres. PVA particles are inert particles that generate permanent occlusion at the embolization site due to mechanical obstruction by a foreign body. They are marketed in spherical or uneven shapes and in sizes from 50 to 1200 µm in diameter. Microspheres are a set of spherical particles formed from acrylics, hydrogels, resins, polymers, etc, that also generate mechanical obstruction due to a foreign body. They have the particularity that medications such as chemotherapeutic agents can be added to them. They are marketed in sizes from 40 to 1200 µm and in dry or suspension form and have the advantage of greater compressibility, generating more uniform embolization when compared to PVA particles. As a disadvantage, they present a greater risk of ischemia or infarction.[10]

The objective of our study is to describe cases of patients with advanced cervical cancer who required uterine artery embolization in the context of acute hemorrhage in a tertiary institution.

Material and methods

This is an observational, retrospective study, conducted at "Sanatorio Güemes" during period of time between October 2017 and May 2023.

The medical records of patients diagnosed with cervical cancer were analyzed and those that have complicated with severe hemorrhage, defined by the presence of anemia requiring transfusion and/or hemodynamic instability, requiring embolization of uterine arteries were included.

In each case were recorded: age of the patients, FIGO stage of the disease, hemoglobin level prior to embolization, previous oncological treatment, type of material used in embolization and the occluded vessel,clinical outcome as well as the presence of complications or the need for re-embolization. Post-diagnosis and post-embolization survival in months was also recorded.

The data analysis was made using the statistical software Epi Info. Upon admission, all patients have provided signed informed consent for the use of their data.

Results

We studied 21 cases of patients diagnosed with advanced and metastatic cervical cancer (IIA2-IVB) who required UAE due to an episode of severe acute hemorrhage. The average age of the patients was 45.8 years, with an age range at the time of the procedure of 24 to 83 years.

Of the patients included in the study, it was observed that 1 patient (4.76%) was in stage IIA2, 2 patients (9.52%) in stage IIB, 5 patients (23.8%) in stage IIIB, 6 patients (28.5%) in stage IIIC1, 5 patients (23.8%) in stage IVA and, finally, 2 patients (9.52%) in stage IVB at the time of diagnosis (Table 1).

The majority of patients (66.6%, 14 patients) began their illness with an episode of severe acute vaginal bleeding, therefore, they had not started the standard treatment at the time of embolization. On the other hand, 3 patients (14.28%) had received treatment with concurrent chemoradiotherapy and brachytherapy, while 4 patients (19.04%) received only chemoradiotherapy without brachytherapy. Among these patients, one had received two prior chemotherapy regimens with carboplatin and paclitaxel, in addition to immunotherapy with pembrolizumab, due to disease progression.

A complete blood count was performed before the procedure in all patients, where an average hemoglobin level of 7.6 g/dl. The minimum value recorded was 5.3 g/dl, while the maximum value was 9.8 g/dl.

Table 1 Clinical characteristics and technical aspects

Characteristics	N° of patients (%)
Age: years (Range)	45.8 (24-83)
FIGO stage	
IIA2	1 (4.76%)
IIB	2 (9.52%)
IIIB	5 (23.8%)
IIIC1	6 (28.5%)
IVA	5 (23.8%)
IVB	2 (9.52%)
Primary treatment of cancer	
Concurrent chemo-radiotherapy	3 (14.28%)
Concurrent chemo-radiotherapy + brachytherapy	3 (14.28%)
Chemotherapy + Pembrolizumab	1 (4.76%)
Without treatment	14 (66.66%)
Pre embolization hemoglobin	7.6
Embolized artery	
Both uterine arteries	16 (76.19%)
Uterine artery left or right	2 (9.52%)
Hypogastric artery	1 (4.76%)
Embolizing agent	
Gelatin sponge	14 (66.6%)
PVA particles/microspheres	7 (33.3%)

Regarding UAE, the majority of patients (95.2%, 20 patients) had responded to the first embolization. However, some of these patients (28.5%) required a second intervention throughout treatment, and only one patient (4.76%) required a third embolization. In one patient (4.76%), a bleeding episode occurred after the first embolization procedure, requiring a hemostatic flash with additional radiotherapy after 48 hours.

In 16 patients (76.1%), embolization of both uterine arteries was carried out, while in 2 patients (4.76%) embolization was unilateral. Regarding the material used during the procedure, most patients were embolized with a gelatin sponge (66.6%) while definitive material was used in the remaining patients (33.3%). Of the total number of patients who had undergone a second episode of embolization, temporary material (gelatin sponges) had been used in 83.33% and definitive material (PVA microparticles) in 16.66%.

All patients underwent femoral artery puncture, and a 5Fr Cobra Catheter was utilized for the procedure. Hemostasis was achieved by applying compression with a bandage for 24 hours. No complications were reported at the access site.

Among the total patients, 10 patients (47.6%) died after the first or second episode of embolization and 5 patients (23.8%) were missed to follow up, while the remaining patients (28.5%) remain alive until the end of the study. The average survival time from diagnosis was 17.8 months, while the time from the first embolization was 9.8 months (Figure 1).

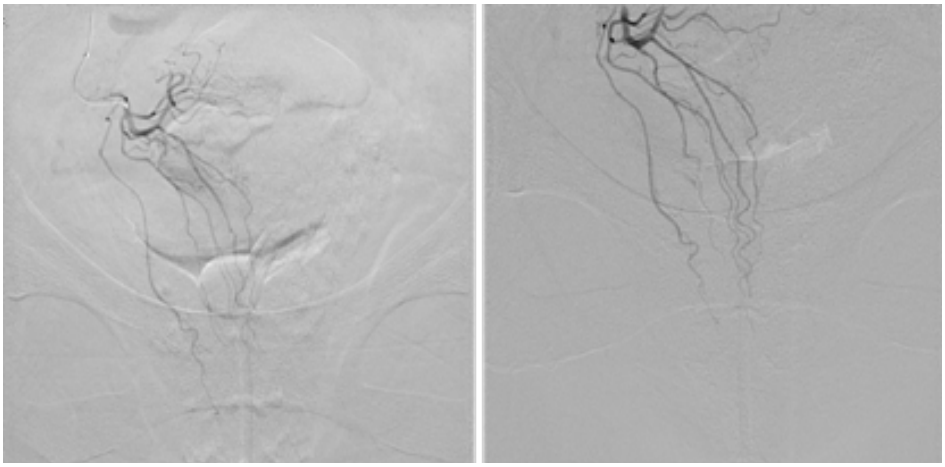

Figure 1 Multiple vessels of distal neovascularization/hypervascularization are identified with involvement of vaginal branches with a predominantly right.

Discussion

Acute hemorrhage in locally advanced cervical cancer is a common complication that presents high morbidity and mortality.

Previously, the gold standard for massive hemorrhage in locally advanced cervical cancer was ligation of the hypogastric arteries, presenting a highly variable success rate between 40% and 100%.[11,12] However, this procedure has a high mortality and morbidity.

The first documented appearance of the transcatheter arterial embolization procedure in both gynecology and obstetrics dates back to the mid-1970s, when it was used to control pelvic hemorrhage in patients with gynecological malignancies.[9,11,13] This therapeutic approach was quickly accepted due to its reduced mortality and morbidity rates.

Various studies have been carried out to highlight the beneficial role of this procedure. Pisco et al.[9] carried out embolization of the internal iliac arteries in 108 patients with uncontrollable bleeding in pelvic neoplasms (39 cases of cervical cancer, 16 cases of ovarian cancer, 50 cases of bladder cancer and 3 cases of prostate). The results of this study showed complete control of bleeding in 69% of patients and partial control in 21% of patients. On the other hand, Yamashita et al.[14] reported 100% temporal bleeding control in 17 patients with malignancies. Mihmanli et al.[15] demonstrated successful ceasing of vaginal bleeding by arterial embolization in 6 patients with gynecological malignancies.

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From these limited literature, it can be inferred that arterial embolization plays a crucial role in the urgent control of massive bleeding in gynecological malignancies and it is a safe procedure.[16] In our study, the observed efficacy of the treatment was 95.2% coinciding with the literature.[17,18]

However, undesirable complications have also been described such as neurological alterations, bladder ischemia, fistulas, and muscle necrosis, among others.[19] This is more common with agents that cause permanent vascular occlusion such as PVA particles or microspheres.

This is because, in those cases in which selective embolization of the vessels that nourish the tumor cannot be performed, vessels that also supply other structures can be occluded.

In our work, of the total of patients, only one patient did not respond to embolization and died two days after the procedure. The rest of the patients (20) did not present complications.

On the other hand, the most frequent mild adverse reaction described in other works was pelvic pain related to the ischemia performed.[20,21] However, a limitation of our study was that this reaction was not described in the clinical records, making its analysis not feasible. Additional complications mentioned include post-embolization syndrome, manifesting as fever, nausea, and leukocytosis, along with less common outcomes like uterine, rectal, or bladder necrosis, abscess formation, sepsis, or sexual dysfunction.[22]

The average number of months from initial diagnosis to death was 17.87 months. Although it was not the main objective of this work, a disadvantage is that the 5-year follow-up of all patients was not performed to evaluate overall survival.

Conclusion

UAE is a safe and effective procedure for the treatment of acute bleeding in patients with advanced cervical cancer.

However, as it is a procedure that is performed only in tertiary centers and the obstacles involved in obtaining definitive embolization materials, it is difficult for its universal access.

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Conflicts of interest

There is no competing interests between the authors.

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