

Cervical Cancer - Controversies in Treatment Higher Stages - Case Report - Could be Multi Organ Surgical Approach Benefiting for Patient?

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1. Summary

When cervical cancer happens it's often first treated with surgery to remove the cancer. Other treatments may include medicines to kill cancer cells. Options might include chemotherapy and targeted therapy medicines. Radiation therapy with powerful energy beams also may be used. Sometimes treatment combines radiation with low-dose chemotherapy [1].

2. Introduction

Cervical cancer is a growth of cells that starts in the cervix. The cervix is the lower part of the uterus that connects to the vagina. Various strains of the human papillomavirus, also called HPV, play a role in causing most cervical cancers. You can reduce your risk of developing cervical cancer by having screening tests and receiving a vaccine that protects against HPV infection [1]. In this case report we present 46-year old patient with typical signs of cervical carcinoma – postcoital bleeding, bleeding between periods, painful intercourse and urge of often urination.

3. Symptoms

- Vaginal bleeding after intercourse, between periods or after menopause
- Menstrual bleeding that is heavier and lasts longer than usual
- Watery, bloody vaginal discharge that may be heavy and have a foul odor
- Pelvis pain or pain during intercourse [1].

4. Screening

Screening means checking for a disease before there are symptoms.

There are three main ways to screen for cervical cancer:

- The human papilloma virus [HPV] test check cells for infection with high-risk HPV types that can cause cervical cancer.
- The Pap test [cervical cytology] collects cervical cells so they can be checked for changes caused by HPV. It can also find infections or inflammation.
- The HPV/Pap contest uses an HPV test and Pap test together to check for both high-risk HPV and cervical cell changes.

5. Diagnosis

- Colposcopy
- Biopsy – punch biopsy, endocervical curettage, loop electro-surgical excision procedure, cone biopsy
- PET-CT scan
- Magnetic resonance imaging
- Ultrasound
- Chest x-ray
- Complete blood count
- Oncomarkers
- Blood chemistry study
- Cystoscopy

- Sigmoidoscopy

6. Prognosis

The prognosis for cervical cancer depends on many factors:

- The stage of the cancer [size of the tumor and whether the cancer has spread beyond the cervix]
- The type of cervical cancer [adenocarcinoma or squamous cell carcinoma]
- Age and general health of the patient
- Whether there are other health problems or diseases, including if there are immunocompromised or have HIV
- Whether the cancer is newly diagnosed or has recurred [2].

7. Survival Rates for Cervical Cancer

5-year relative survival rate for cervical cancer diagnosed at an early stage is 91%.

The 5-year relative survival rates for cervical cancer are as follows:

- When cervical cancer is diagnosed at an early stage, the 5-year relative survival rate is 91%
- When cervical cancer is diagnosed after it has spread to nearby tissue, organs, or regional lymph nodes, the 5-year survival rate is 60%
- When cervical cancer is diagnosed after it has spread to a distant part of the body, the 5-year relative survival rate is 19%.
- The 5-year relative survival rate for all people with cervical cancer is 67% [3]

8. Types and grades of cervical cancer

8.1. Types

The type of cervical cancer you have tells you the type the cancer started in. The two main types of cervical cancer are squamous cell cancer and adenocarcinoma.

8.1.1. Squamous Cell Carcinoma: Squamous cells are the flat, skin-like cells covering the cervix's outer surface [the ectocervix].

Between 80 and 90 out of every 100 cervical carcinomas [80 to 90%] are squamous cell cancers.

8.1.2. Adenocarcinoma: Adenocarcinoma is a cancer that starts in the gland cells that produce mucus.

The cervix has glandular cells scattered along the inside of the passage that runs from the cervix to the womb [endocervix]. Is less common than squamous cell cancer, out of every 100 cervical cancers [10 to 20%] are adenocarcinomas.

Adenocarcinoma is treated in the same way as squamous cell cancer of the cervix.

8.2. Grading

The grade of a cancer tells you how much the cancer cells look

like normal cells.

The grade gives your doctor an idea of how the cancer might behave and what treatment you need.

The grades of cancer cells are from 1 to 3:

- Grade 1 [low grade] look most like normal cells. They tend to grow more slowly than higher grades.
- Grade 2 look a bit like normal cells. These cells may grow a bit quicker.
- Grade 3 [high grade] look very normal and not like normal cells. They tend to grow more quickly which means they are more likely to spread. Grade 3 cancer might need more intensive treatment than lower grades.

8.3. Staging

8.3.1. Stage I Cervical Cancer

Stage 1 cervical cancer – in stage I, cervical cancer has formed and is found in the cervix only. It is divided into stages IA and IB, based on the size of the tumor and the deepest point of tumor invasion.

Stage IA is subdivided based on the deepest point of tumor invasion, the cancer is not more than 3 millimeters deep. In stage IA2, the cancer is more than 3 but not more than 5 millimeters deep.

Stage IB1 – the tumor is 2 centimeters or smaller and the deepest point of tumor invasion is more than 5 millimeters.

Stage IB2 – the tumor is larger than 2 centimeters but not larger than 4 centimeters.

Stage IB3 – the tumor is larger than 4 centimeters.

8.3.2. Stage II Cervical Cancer

In stage II, cervical cancer has spread to the upper two-thirds of the vagina or to the tissue around the uterus. Stage II is subdivided based on how far the cancer has spread.

Stage II: Cancer has spread from the cervix to the upper two-thirds of the vagina but has not spread to the tissue around the uterus. Stage IIA is further divided based on the size of the tumor:

- Stage IIA1: the tumor is 4 centimeters or smaller.
- Stage IIA2: the tumor is larger than 4 centimeters.
- Stage IIB: cancer has spread from the cervix to the tissue around the uterus.

8.3.3. Stage III Cervical Cancer

In stage III cervical cancer has spread to the lower third of the vagina and/or to the pelvic wall, and/or has caused kidney problems, and/or involves lymph.

Stage III is subdivided based on how far the cancer has spread.

- Stage IIIA: cancer has spread to the lower third of the vagina but has not spread to the pelvic wall.
- Stage IIIB; cancer has spread to the pelvic wall; and/or the tumor has become large enough to block one or both ureters or has caused one or both kidneys to get bigger or stop working.

- Stage IIIC is divided into stages IIIC1 and IIIC2, based on the spread of cancer to the lymph nodes

8.3.4. Stage IV Cervical Cancer

In stage IV, cervical cancer has spread beyond the pelvis, or has spread to the lining of the bladder or rectum, or has spread to other parts of the body.

Stage IV is subdivided into stages IVA and IVB, based on where the cancer has spread.

- Stage IVA: cancer has spread to nearby pelvic organs, such as the bladder or rectum

- Stage IVB: cancer has spread to other parts of the body, such as the liver, lungs, bones, or distant lymph nodes.

Stage IV is also called metastatic cancer traveling through the lymphatic system or blood and form tumors in other parts of the body.

8.3.5. Recurrent Cervical Cancer

Recurrent cervical cancer is cancer that has recurred after it has been treated. The cancer may comeback in the cervix or as metastatic tumors in other parts of the body. Tests will be done to help determine where the cancer has returned in your body, if it has spread, and how far. The type of treatment that you have for recurrent cervical cancer will depend on how far it has spread.

8.4. Cervical Cancer Treatment by Stage

The cancer stage is an important factor in deciding the best treatment.

An important factor for some patients is fertility preservation. Such treatments may be an option for some small cancers that are only in the cervix.

8.4.1. Treatment of Stage IA Cervical Cancer

Treatment of stage IA1 cervical cancer may include

- Cold knife conization, a fertility-sparing procedure, for some small cancers
- Total hysterectomy with or without bilateral salpingo/oophorectomy, for patients whose cancer has a high risk of coming back

8.4.2. Treatment of Stage IA2 Cervical Cancer May Include

- Modified radical hysterectomy and removal of lymph nodes
- Radical trachelectomy, a fertility-sparing surgery, and removal of lymph nodes
- Internal radiation therapy, for patients who cannot have surgery

8.4.3. Treatment of Stages IB and IIA Cervical Cancer

Treatment of these stages may include:

- Radiation therapy given at the same time as chemotherapy
- Radical hysterectomy and removal of pelvic lymph nodes with or without radiation therapy to the pelvis, plus chemotherapy
- Radical trachelectomy, a fertility-sparing surgery
- Radiation therapy alone

When radiation is used, it may be given as external radiation therapy only or as a combination of external and internal radiation therapy. Chemotherapy drugs, such as cisplatin or carboplatin, may be given at the same time as radiation therapy and it helps the radiation therapy work better.

8.4.4. Treatment of Stages IIB, III, and IVA Cervical Cancer

Treatment of these stages may include:

- Radiation therapy given at the same time as chemotherapy
- Surgery to remove pelvic lymph nodes followed by radiation therapy with or without chemotherapy

Most people with these stages will receive a combination of external and internal radiation therapy. With combination giving chemotherapy at the same time helps the radiation therapy work better.

8.4.5. Treatment of Stage IVB Cervical Cancer

Treatment of stage IVB may include:

- Radiation therapy as palliative therapy, to stop bleeding caused by the cancer.
- Chemotherapy and the targeted therapy drug bevacizumab as palliative therapy. There are many chemotherapy drugs used as palliative therapy for stage IVB cervical cancer, including cisplatin, carboplatin, ifosfamide, irinotecan, gemcitabine, paclitaxel, and topotecan. These drugs may be given alone or in combination.

Palliative therapy is treatment meant to improve the quality of life of patients who have a serious or life-threatening disease, such as cancer. Many of the same treatments for cancer, such as chemotherapy or other kinds of drugs and radiation therapy, can also be used for palliative therapy to help a patient feel more comfortable [3].

8.4.6. Treatment of Recurrent Cervical Cancer

This treatment may include:

- The immunotherapy drug pembrolizumab.
- Radiation therapy and chemotherapy given at the same time, for cancer that has come back in the pelvis. Radiation may be given as external radiation therapy only or as a combination of external and internal radiation therapy. Many different chemotherapy drugs are used to treat recurrent cervical cancer, including cisplatin, carboplatin, ifosfamide, irinotecan, gemcitabine, paclitaxel, topotecan, and vinorelbine. These drugs may be given alone or in combination.
- Chemotherapy and the targeted therapy drug bevacizumab as palliative therapy. Many different chemotherapy drugs are used as palliative therapy for recurrent cervical cancer, including cisplatin, carboplatin, ifosfamide, irinotecan, gemcitabine, paclitaxel, topotecan, and vinorelbine. These drugs may be given alone or in combination.
- Palliative therapy is treatment meant to improve the quality of

life of patients who have a serious or life-threatening disease, such as cancer. Many of the same treatments for cancer, such as chemotherapy or other kinds of drugs and radiation therapy, can also be used for palliative therapy to help a patient feel more comfortable.

- Pelvic exenteration, for certain patients who cannot have radiation therapy. The goal of pelvic exenteration is to cure the cancer by removing it from all the organs to which it has spread [3].

9. Case Report

In 2015 patient underwent all diagnostic methods with conclusion of histologically proven squamocellular advanced cervical carcinoma with infiltration of the basis of urinary bladder in convolut with right ureter with II. grade hydronephrosis. Oncomarkers CEA, CA 125 and CA 19-9 were positive. The blood work showed microcytary anaemia. The staging was T4 [1 -2 ?, urinary bladder and rectum ?], N1, M0. During rectoscopy signs of redness in depth of 10 centimeters from anus [sample without histological signs of malignancy]. Enlarged right parailiacal lymph nodes around 1 centimeter. Patient had implanted double J-stent. She underwent complete neoadjuvant radio and chemotherapy in full possible doses in the whole pelvic area.

Then she was observed on effectiveness of radio and chemotherapy for 3 months. After that time the complete restaging of disease [CT, MRI, PET CT] excluded distant metastases in liver, lungs, brain and bones. She showed N1 lymphonopathy, reduced hydronephrosis but pathological mass of cervix with it's volume reduction but persistent contact to rectum and urinary bladder.

We were trying to find international guidelines for this case because generally oncogynecologists recommend palliative chemotherapy on bases of 5-FU. But this therapy patient declined. After multidisciplinary consultation of gynecologist, surgeon and urologist, according to the age of patient and the fact of lacking distant metastases we decided for surgical treatment which could end up just like probatory laparotomy or potential radical multi organ operation. We performed en-block hysterectomy with trachelectomy, resection of rectosigma and resection of urinary bladder with reimplantation of both ureters on double J-stents, paraaortocaval lymphonodectomy, omentectomy and appendectomy. Peroperationally we were performing histology and according to the findings during surgery we were extending radicality of operation – distal radial resection line of rectosigma, with high descendent-recto anastomosis and ligature a.mesenterica inferior, resection line of urinary bladder and parametrial areas which were negative for malignancy. In definitive histology the finding was squamocellular carcinoma of cervix with infiltration of rectosigma up to tunica muscularis mucosae and infiltration of urinary bladder. Operation was without complications so was post-operative period and patient was discharged on 15th post-operative day. After 2 years she underwent resection of single metachronic lung lesion in right lungs as wedge resection of peripheral metastasis approximately 17 millimeters.

Patient is until now with only complication of recurrent stenosis of reimplanted left ureter, otherwise she is without any other complications and without any signs of metastatic and recurrence of the disease (Figure 1-6).

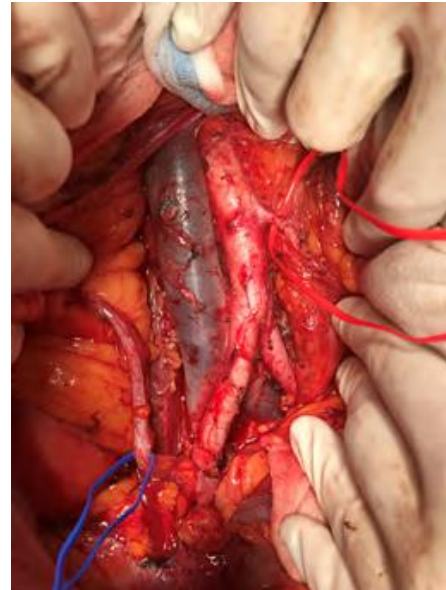


Figure 1: Preparation of anatomical structures, blue tape – right ureter with double J-stent, red tape a.mesenteric artery

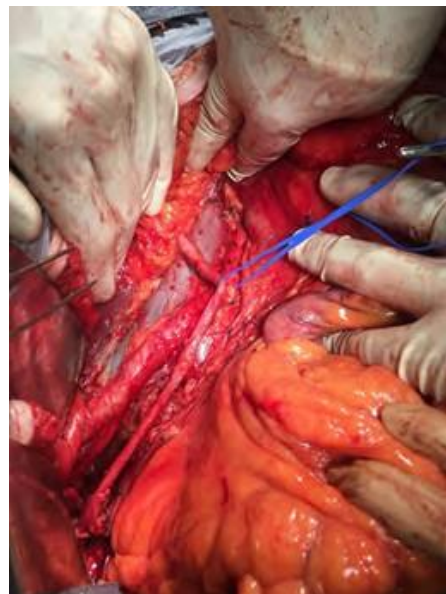


Figure 2: Pararectal preparation on the right

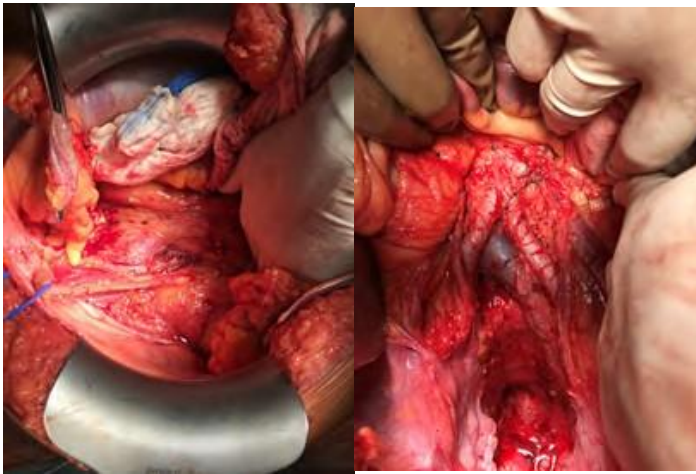


Figure 3 and 4: Status post en-block resection, radical hysterectomy and trachelectomy with high ligation of a.mesenterica inferior

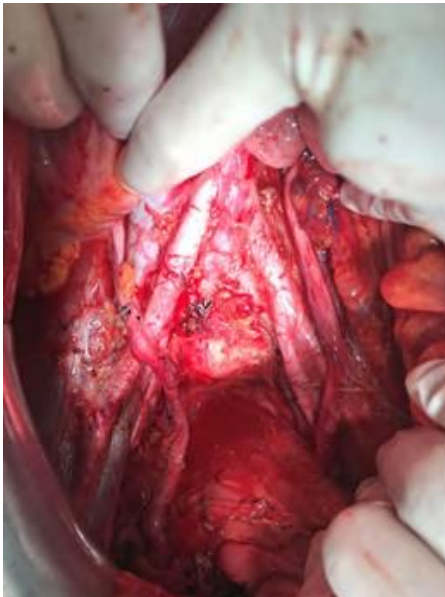


Figure 5: Status post reimplantation of both ureters and test of sufficiency of anastomosis with fluid filling of the rest of urinary bladder.

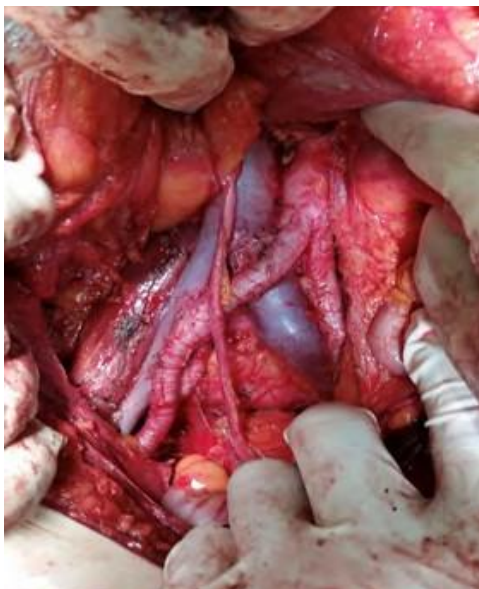


Figure 6: Complete view of the finished operation.

10. Discussion

No standard treatment is available for patients with stage IVB cervical cancer compared with locally advanced cervical cancer. International guidelines propose cisplatin-based combination chemotherapy for widespread metastatic disease with possible addition of bevacizumab. Chemotherapy is useful for the treatment of recurrent or stage IVB cervical cancer who are not candidates for radiation or extensive surgery. However, either bevacizumab or traditional chemotherapy have shown unsatisfactory effect on eliminating the primary cervical cancer and metastases [4]. However, the role of surgery in treating stage IVB patients is still in controversy and has not been fully illustrated. There were selected patients who both underwent chemotherapy and radiotherapy. Surgery procedure was classified as surgery of primary site and surgery of metastatic sites. Surgery procedure of primary site including Loop Electrocautery Excision Procedure, local tumor excision, total hysterectomy without removal of tubes and ovaries, total hysterectomy with removal of tubes and/or ovaries, radical or extended hysterectomy including modified radical or extended hysterectomy, radical hysterectomy and extended radical hysterectomy, hysterectomy and pelvic exenteration [5].

11. Conclusion

In population-based database SEER in years between 2010 – 2015, a total of 1,139 stage IVB cervical cancer patients receiving chemotherapy were included in this retrospective study. Within post-matching cohort, the median duration of overall survival in stage IVB cervical cancer patients receiving chemotherapy was 22 months. Surgery of primary sites combined with chemotherapy tended to prolong the survival of stage IVB cervical cancer patients compared with chemotherapy, especially for patients without visceral metastasis. In conclusion, patients with stage IVB cervical cancer may achieve their best outcomes through chemotherapy combined with surgery or primary sites. However, it deserves larger scale prospective clinical trials to confirm [6].

Until now, the optimal treatment of stage IVB cervical cancer patients still remains controversial. Lack of case numbers and the diversity of clinical manifestations of stage IVB patients leads to deficiency of related researches. Furthermore, the available studies found that survival advantage significantly favors patients who underwent surgery plus chemotherapy compared with chemotherapy alone, revealing the important role of surgery in stage IVB cervical cancer patients [4,6].

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