

Clinical and morphological considerations in one case with cervical cancer and right ureterohydronephrosis

CRISTINA GEORGIANA GHIB PARA¹⁾, MIRCEA FLORIN SFERDIAN²⁾, VOICU DAȘCĂU³⁾, LUCIAN PĂIUȘAN⁴⁾, IOAN IOIART⁵⁾

¹⁾Department of Hematology, Faculty of Medicine, Pharmacy and Dentistry, "Vasile Goldiș" Western University of Arad, Romania

²⁾Department of Radiology, Faculty of Medicine, Pharmacy and Dentistry, "Vasile Goldiș" Western University of Arad, Romania

³⁾Department of Obstetrics and Gynecology, Faculty of Medicine, Pharmacy and Dentistry, "Vasile Goldiș" Western University of Arad, Romania

⁴⁾Department of Morphopathology, Faculty of Medicine, Pharmacy and Dentistry, "Vasile Goldiș" Western University of Arad, Romania

⁵⁾Department of Urology, Faculty of Medicine, Pharmacy and Dentistry, "Vasile Goldiș" Western University of Arad, Romania

Abstract

We present the case of a 34-year-old female with cervical cancer and right ureterohydronephrosis. She was admitted to the Urology Clinic of the Emergency County Hospital of Arad, Romania, on November 11, 2015, after previously being diagnosed with stage IIIA cervical cancer in December 2014 and undergoing radio and chemotherapy and laparotomy for staging. At the moment of hospital admission, the patient suffered from fever and right lumbar pain, she was also diagnosed with grade IV right ureterohydronephrosis. The patient was operated at the Urology Clinic of Arad; the intervention involved a total hysterectomy with bilateral adnexectomy and a right obturator neorectomy of the necrotic lymph nodes. However, the evolution was favorable. The purpose was to increase the patient's survival rate and increase the quality of her life by also applying one palliative method including a urethral stent. As a result, the patient's life was extended.

Keywords: cervical, cancer, stent, hysterectomy, ureterohydronephrosis.

Introduction

Worldwide, cervical cancer is the third most common cancer. Although this type of cancer is preventable, most women living in developing countries do not have access to effective screening programs. As a result, more than 70% of cervical cancers occur in these countries [1, 2]. Human papillomavirus (HPV) is central to the development of cervical neoplasia and is detectable in 99.7% of all cervical cancers [3]. The main histological types of cervical tumors are squamous cell carcinoma (69% of cervical cancers) and adenocarcinoma (25% of cervical cancers) [4].

This type of cancer is commonly accompanied by ureterohydronephrosis (UHN), which is a condition characterized by dilation of the renal ureter/pelvis resulting from mechanical or inflammatory urinary tract obstruction, this condition being more frequently associated with more advanced cancer stage, squamous histology and non-surgical treatment of cancer [5]. Unfortunately, early cervical cancer is often asymptomatic, and consequently, screening tests are one of the most important tools for detection of this disease in its earliest and most treatable stages. The first symptoms generally occur when the pre-cancer turns into a true invasive cancer and are associated primarily with abnormal and/or postcoital bleeding and watery, mucous, or purulent and malodorous vaginal discharges, which can be easily mistaken for conditions other than cervical cancer, such as common vaginal infections. Advanced stages are often associated with pelvic or lower back pain, which may radiate along the

posterior side of the lower extremities [6]. The decisive diagnosis of cervical cancer is, however, only made based upon histological evaluation of a cervical biopsy, while physical examination [7], cervical cytology, HPV presence and colposcopy can only arise the suspicion thereof.

The aim of this article is to offer a new vision about the latest steps in the treatment of advanced cervical cancers including palliative methods such as the stent application mentioned in this case, despite all the clinical and morphopathological aspects in advanced disease. Due to all the protocol steps, the patient's life was extended.

Case presentation

We present the case of a 34-year-old woman who was first diagnosed with cervical cancer (stage IIIA), in November 2014, when admitted to the Emergency County Hospital of Arad, Romania, for abdominal pains. A cervical biopsy was used for the initial histopathological diagnosis. Of note, she had a family history of cervical cancer (mother, stage IIB).

After undergoing 22 external radiotherapy sessions, the patient was subjected to laparoscopy, converted to laparotomy, during March 2015, which revealed an inoperable cancer. Those methods were selected for a better view of the tumoral limits. This was followed by 10 chemotherapy sessions and, respectively, one brachytherapy session. These sessions resulted in lumbar pain and loss of appetite. In January 2015, she also received a right ureteral stent at the Clinic of Urology, Emergency County Hospital of Timișoara, Romania.

The last hospital admission was on November 11, 2015, at the Emergency County Hospital of Arad. A simple urinary radiograph was performed on this occasion, which showed a ptosis of the right kidney and the presence of a right ureteral stent. Computed tomography (CT) scanning revealed a moderate increase of uterus size and a slightly heterogeneous aspect of the cervix in the hypocaptant area. We noticed oversized annexes of bilateral volume, mainly on the right side; emphasis on a lesion with polycystic aspect with contrast peripheral plug; most probably related to the secondary dissemination of cancer. Several bilateral necrotic adenopathies, located primarily in the internal iliac and right-side obturator regions. This led to a compression/invasion of the right distal ureter, with suprajacent distension of ureterohydronephrosis type, 3rd degree. Also, we observed there, a minimal liquid reaction in the Douglas recess.

The presence of ureterohydronephrosis was established after detailed urinary analysis, which included the measurement of the levels of urea, creatinine, and uric acid, abdominal ultrasound examination, renal radiography and CT exams (Figures 1 and 2).

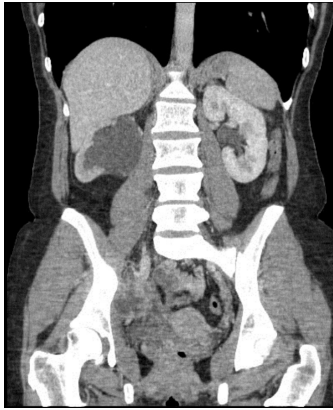


Figure 1 – Computed tomography: coronal view.



Figure 2 – Computed tomography: sagittal view.

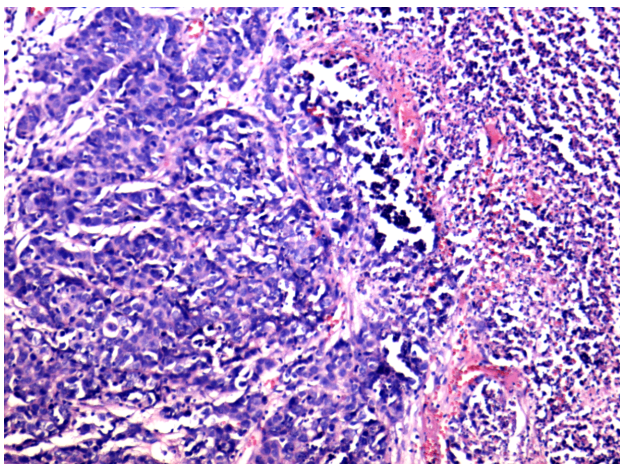


Figure 3 – Large squamous cell mass with hemorrhagic necrosis; stroma with moderate lymphocyte infiltration (HE staining, ×100).

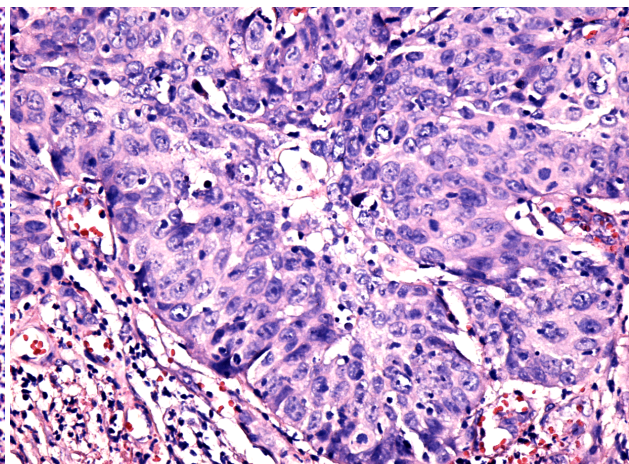


Figure 4 – Malignant cells with prominent nucleoli and atypical mitoses; perivascular tumoral infiltration (HE staining, ×200).

The final diagnosis was cervical cancer with necrotating right obturator fossa with the presence of adenopathy and right ureterohydronephrosis 4th degree. As a result, the patient was operated during the same day, *i.e.*, total hysterectomy with bilateral adnexectomy and a right obturator necrosectomy of lymph nodes. As a palliative measure, the right ureteral stent was replaced with a new one. The post-operative evolution of the patient appeared favorable.

The sample for histopathological diagnosis was collected from the adjacent area of the external orifice of the endocervical canal, *via* a curettage technique.

Macroscopic examination emphasized fibrin-hematic clots and numerous tissue fragments less than one mm. Two larger tissue fragments with the maximum size of 2/4 mm and 4/10 mm, respectively, were also identified.

All the received material was taken in work, formalin fixed, paraffin embedded and stained with Hematoxylin–Eosin (HE).

Further, microscopic examination showed numerous tissue fragments, originating from the exocervical and transitional area.

We identified compact tumor proliferation masses composed of large polymorphic polyhedral malignant cells, with evident elements of atypia and frequent atypical mitotic figures, but without formation of keratin pearls. Large areas of necrosis and a diffuse lymphocyte infiltration in the stroma were also observed (Figure 3).

Malignant cells present indefinite cell borders, prominent nucleoli and frequent atypical mitoses. Perivascular invasion was also identified (Figure 4).

The tumor penetrative depth could not be precisely assessed because the sample contained only elements from the superficial area of cervix.

Overall, the diagnosis was a large non-keratinizing infiltrative squamous carcinoma cell (G3) with an unspecified tumor stage, originating probably from the transitional area of the cervix.

Discussion

Non-adherence to regular screening is considered to be a major risk factor for late diagnosis of cervical cancer

[8–14]. This was also the case of most patients diagnosed with advanced cancers at the Clinic of Urology, Emergency County Hospital of Arad. Cervical cancer screening detects precancerous lesions and the early-stage of the

disease, the treatment of which reduces the incidence of cervical cancer-induced mortality. Cytological screening for cervical cancer with Papanicolaou (Pap) test has never been evaluated in a randomized trial, but there are multiple observational studies showing a significant decrease in cervical cancer incidence and mortality as screening has been implemented [15–22]. In our case, the patients were tested subsequently, but most of them very late considering their pathology.

In women aged less than 30 years, doctors recommend that the Pap test should be made alone every three years, without having a primary HPV co-testing [23]. In older patients, cancer screening should be similarly performed (*i.e.*, once every three years), and if the results are negative, both Pap test and primary HPV co-testing should be performed every five years after that [24]. This additional step is related to the fact that HPV infection in women older than 30 years is more likely to be persistent, and therefore, has a greater likelihood of clinical significance [25]. The patient investigated did adhere to these recommendations, which, unfortunately, caused serious health consequences.

Here, cervical cancer was associated with severe ureterohydronephrosis. This association is well documented in the specialty literature. For example, a recent multicenter study made in Italy, included 2024 patients with invasive cervical cancer, which underwent radical surgery preceded by radiotherapy application; the results revealed complications in 873 patients, of which most cases (341, *i.e.*, more than 40%) had urinary and other related problems [26]. Similarly, a small cohort study (43 patients) conducted at the same hospital revealed a close association between cervical cancer and adverse urinary conditions. Thus, not only that ureterohydronephrosis was frequently observed in patients with advanced cervical neoplasia, but also the stage of cervical cancer was moderately associated with its incidence.

For early-stage of cervical cancer, a modified radical hysterectomy with pelvic lymphadenectomy is preferred over primary chemotherapy and radiotherapy. According to most studies, surgery generally results in a definitive treatment, significantly increases survival rates compared to primary radiation therapy (RT) and provides a better quality of life [27–29]. For women with locally advanced cervical cancer, primary chemotherapy and radiotherapy is indicated, although the benefits of treatment are higher for earlier stages (stages IB to IIB) than for more advanced stages (stages III to IVA) [10–12]. The type of treatment used depends on the cancer stage and consists of a combination of surgical and non-surgical methods, including radical hysterectomy [28, 29], extrafascial hysterectomy or conization [30], fertility-sparing surgery [31], hysterectomy after chemotherapy and radiotherapy treatment [32, 33], primary radiation therapy, and adjuvant therapy indications [9].

The particularities: almost all the patients with advanced genital cancer have severe complications and the palliative treatment is not so easy to be applied. The patients with cervical cancers could present vaginal bleeding, vaginal discharge, obstructive uropathy, symptomatic anemia [34].

Several peculiarities of this case include: the relatively

young age at which the advanced cervical cancer was diagnosed, the family history of cervical cancer and the fact the young woman's life was prolonged by more than a year by using palliative, non-surgical, as well as surgical methods in an aggressive regimen, the patient being able to endure all of them without significant complications and side effects thereof.

☒ Conclusions

The proper therapeutic approaches were applied to prolong the patient's life despite the advanced stage of cervical cancer and its association with a severe ureterohydronephrosis. This approach was developed by cumulating all the results obtained from the medical investigations. The morphopathological, imaging, and biological data, as well as the clinical symptoms have led to the conclusion that the combined treatment applied, *i.e.*, total hysterectomy with bilateral adnexectomy, right obturator neurectomy of the necrotic lymph nodes and replacement of right ureteral stent has helped increase the patient's life span and quality.

Conflict of interests

The authors state that they have no conflicts of interests.

References

- [1] Siegel R, Ward E, Brawley O, Jemal A. Cancer statistics, 2011: the impact of eliminating socioeconomic and racial disparities on premature cancer deaths. *CA Cancer J Clin*, 2011, 61(4):212–236.
- [2] Torre LA, Bray F, Siegel RL, Ferlay J, Lortet-Tieulent J, Jemal A. Global cancer statistics, 2012. *CA Cancer J Clin*, 2015, 65(2): 87–108.
- [3] Walboomers JM, Jacobs MV, Manos MM, Bosch FX, Kummer JA, Shah KV, Snijders PJ, Peto J, Meijer CJ, Muñoz N. Human papillomavirus is a necessary cause of invasive cervical cancer worldwide. *J Pathol*, 1999, 189(1):12–19.
- [4] Kurman RJ, Norris HJ, Wilkinson EJ. Atlas of tumor pathology: tumors of the cervix, vagina, and vulva. 3rd edition, Armed Forces Institute of Pathology (AFIP), Washington, DC, 1992, 245.
- [5] Patel K, Foster NR, Kumar A, Grudem M, Longenbach S, Bakkum-Gamez J, Haddock M, Dowdy S, Jatoi A. Hydronephrosis in patients with cervical cancer: an assessment of morbidity and survival. *Support Care Cancer*, 2015, 23(5): 1303–1309.
- [6] Hughes RR, Brewington KC, Hanjani P, Photopoulos G, Dick D, Votava C, Moran M, Coleman S. Extended field irradiation for cervical cancer based on surgical staging. *Gynecol Oncol*, 1980, 9(2):153–161.
- [7] Partridge EE, Abu-Rustum NR, Campos SM, Fahey PJ, Farmer M, Garcia RL, Giuliano A, Jones HW 3rd, Lele SM, Lieberman RW, Massad SL, Morgan MA, Reynolds RK, Rhodes HE, Singh DK, Smith-McCune K, Teng N, Trimble CL, Valea F, Wilczynski S; National Comprehensive Cancer Networks. Cervical cancer screening. *J Natl Compr Canc Netw*, 2010, 8(12):1358–1386.
- [8] Sedlis A, Bundy BN, Rotman MZ, Lentz SS, Mudderspach LI, Zaino RJ. A randomized trial of pelvic radiation therapy *versus* no further therapy in selected patients with stage IB carcinoma of the cervix after radical hysterectomy and pelvic lymphadenectomy: a Gynecologic Oncology Group Study. *Gynecol Oncol*, 1999, 73(2):177–183.
- [9] Lindegaard JC, Fokdal LU, Nielsen SK, Juul-Christensen J, Tanderup K. MRI-guided adaptive radiotherapy in locally advanced cervical cancer from a Nordic perspective. *Acta Oncol*, 2013, 52(7):1510–1519.
- [10] Rijkmans EC, Nout RA, Rutten IH, Ketelaars M, Neelis KJ, Laman MS, Coen VL, Gaarenstroom KN, Kroep JR, Creutz-

- berg CL. Improved survival of patients with cervical cancer treated with image-guided brachytherapy compared with conventional brachytherapy. *Gynecol Oncol*, 2014, 135(2): 231–238.
- [11] Macdonald OK, Chen J, Dodson M, Lee CM, Gaffney DK. Prognostic significance of histology and positive lymph node involvement following radical hysterectomy in carcinoma of the cervix. *Am J Clin Oncol*, 2009, 32(4):411–416.
- [12] Han K, Milosevic M, Fyles A, Pintilie M, Viswanathan AN. Trends in the utilization of brachytherapy in cervical cancer in the United States. *Int J Radiat Oncol Biol Phys*, 2013, 87(1): 111–119.
- [13] Grigsby PW, Lu JD, Mutch DG, Kim RY, Eifel PJ. Twice-daily fractionation of external irradiation with brachytherapy and chemotherapy in carcinoma of the cervix with positive para-aortic lymph nodes: Phase II study of the Radiation Therapy Oncology Group 92-10. *Int J Radiat Oncol Biol Phys*, 1998, 41(4):817–822.
- [14] Varia MA, Bundy BN, Deppe G, Mannel R, Averette HE, Rose PG, Connelly P. Cervical carcinoma metastatic to para-aortic nodes: extended field radiation therapy with concomitant 5-fluorouracil and cisplatin chemotherapy: a Gynecologic Oncology Group study. *Int J Radiat Oncol Biol Phys*, 1998, 42(5):1015–1023.
- [15] Small W Jr, Winter K, Levenback C, Iyer R, Hymes SR, Jhingran A, Gaffney D, Erickson B, Greven K. Extended-field irradiation and intracavitary brachytherapy combined with cisplatin and amifostine for cervical cancer with positive para-aortic or high common iliac lymph nodes: results of Arm II of Radiation Therapy Oncology Group (RTOG) 0116. *Int J Gynecol Cancer*, 2011, 21(7):1266–1275.
- [16] Grigsby PW, Heydon K, Mutch DG, Kim RY, Eifel P. Long-term follow-up of RTOG 92-10: cervical cancer with positive para-aortic lymph nodes. *Int J Radiat Oncol Biol Phys*, 2001, 51(4):982–987.
- [17] Dueñas-González A, Zarbá JJ, Patel F, Alcedo JC, Beslija S, Casanova L, Pattaranutaporn P, Hameed S, Blair JM, Barraclough H, Orlando M. Phase III, open-label, randomized study comparing concurrent gemcitabine plus cisplatin and radiation followed by adjuvant gemcitabine and cisplatin *versus* concurrent cisplatin and radiation in patients with stage IIB to IVA carcinoma of the cervix. *J Clin Oncol*, 2011, 29(13):1678–1685.
- [18] Rose PG, Degeest K, McMeekin S, Fusco N. A phase I study of gemcitabine followed by cisplatin concurrent with whole pelvic radiation therapy in locally advanced cervical cancer: a Gynecologic Oncology Group study. *Gynecol Oncol*, 2007, 107(2):274–279.
- [19] Neoadjuvant Chemotherapy for Locally Advanced Cervical Cancer Meta-analysis Collaboration. Neoadjuvant chemotherapy for locally advanced cervical cancer: a systematic review and meta-analysis of individual patient data from 21 randomised trials. *Eur J Cancer*, 2003, 39(17):2470–2486.
- [20] Ryzewska L, Tierney J, Vale CL, Symonds PR. Neoadjuvant chemotherapy plus surgery *versus* surgery for cervical cancer. *Cochrane Database Syst Rev*, 2012, (1):CD007406.
- [21] Janerich DT, Hadjimichael O, Schwartz PE, Lowell DM, Meigs JW, Merino MJ, Flannery JT, Polednak AP. The screening histories of women with invasive cervical cancer, Connecticut. *Am J Public Health*, 1995, 85(6):791–794.
- [22] Coleman DV, Poznansky JJ. Review of cervical smears from 76 women with invasive cervical cancer: cytological findings and medicolegal implications. *Cytopathology*, 2006, 17(3):127–136.
- [23] Abed Z, O'Leary M, Hand K, Flannelly G, Lenehan P, Murphy J, Foley M. Cervical screening history in patients with early stage carcinoma of the cervix. *Ir Med J*, 2006, 99(5):140–142.
- [24] Ponka D, Dickinson J. Screening with the Pap test. *CMAJ*, 2014, 186(18):1394.
- [25] Jemal A, Simard EP, Dorell C, Noone AM, Markowitz LE, Kohler B, Ehemann C, Saraiya M, Bandi P, Saslow D, Cronin KA, Watson M, Schiffman M, Henley SJ, Schymura MJ, Anderson RN, Yankey D, Edwards BK. Annual Report to the Nation on the Status of Cancer, 1975–2009, featuring the burden and trends in human papillomavirus (HPV)-associated cancers and HPV vaccination coverage levels. *J Natl Cancer Inst*, 2013, 105(3):175–201.
- [26] Zola P, Maggino T, Sacco M, Rumore A, Sinistrero G, Maggi R, Landoni F, Foglia G, Sartori E, De Toffoli J, Franchi M, Romagnolo C, Sismondi P. Prospective multicenter study on urologic complications after radical surgery with or without radiotherapy in the treatment of stage IB–IIA cervical cancer. *Int J Gynecol Cancer*, 2000, 10(1):59–66.
- [27] Querleu D, Morrow CP. Classification of radical hysterectomy. *Lancet Oncol*, 2008, 9(3):297–303.
- [28] Bansal N, Herzog TJ, Shaw RE, Burke WM, Deutsch I, Wright JD. Primary therapy for early-stage cervical cancer: radical hysterectomy *vs* radiation. *Am J Obstet Gynecol*, 2009, 201(5): 485.e1–485.e9.
- [29] Piver MS, Rutledge F, Smith JP. Five classes of extended hysterectomy for women with cervical cancer. *Obstet Gynecol*, 1974, 44(2):265–272.
- [30] ***. National Comprehensive Cancer Network (NCCN). http://www.nccn.org/professionals/physician_gls/pdf/cervical.pdf (Accessed on July 9, 2012).
- [31] ***. NCCN Clinical practice guidelines in oncology. National Comprehensive Cancer Network (NCCN), http://www.nccn.org/professionals/physician_gls/f_guidelines.asp (Accessed on February 27, 2016).
- [32] Morice P, Rouanet P, Rey A, Romestaing P, Houvenaeghel G, Boulanger JC, Leveque J, Cowen D, Mathevet P, Malhaire JP, Magnin G, Fondrinier E, Berille J, Haie-Meder C. Results of the GYNECO 02 study, an FNCLCC phase III trial comparing hysterectomy with no hysterectomy in patients with a (clinical and radiological) complete response after chemoradiation therapy for stage IB2 or II cervical cancer. *Oncologist*, 2012, 17(1):64–71.
- [33] Darus CJ, Callahan MB, Nguyen QN, Pastore LM, Schneider BF, Rice LW, Jazaeri AA. Chemoradiation with and without adjuvant extrafascial hysterectomy for IB2 cervical carcinoma. *Int J Gynecol Cancer*, 2008, 18(4):730–735.
- [34] Mishra K. Gynaecological malignancies from palliative care perspective. *Indian J Palliat Care*, 2011, 17(Suppl):S45–S51.

Corresponding author

Mircea Florin Sferdian, Lecturer, MD, PhD, Department of Radiology, Faculty of Medicine, Pharmacy and Dentistry, "Vasile Goldiș" Western University of Arad, 86 Liviu Rebreanu Street, "Vasile Goldiș" University Campus, 310045 Arad, Romania; Phone +40723–319 316, e-mail: mirceasf@gmail.com

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