Modern Medicine. 2014, Vol. 21, No. 3 : 196-200

Case Report

POSTERIOR PELVIC EXENTERATION FOR ADVANCED, UNRESPONSIVE TO RADIATION THERAPY CERVICAL CANCER – A CASE REPORT

N. Bacalbașa[1], Irina Bălescu[2]

[1]"Carol Davila" University of Medicine and Pharmacy, Bucharest, Romania
[2]"Ponderas" Hospital, Bucharest, Romania

REZUMAT

Exenterație pelvină posterioară pentru neoplasm cervical avansat radiorezistent - prezentare de caz

Deși cancerul de col uterin este relativ ușor de diagnosticat în stadii incipiente, există încă un număr semnificativ de pacienți ce se prezintă în stadii avansate ale bolii anual. În aceste cazuri protocolul standard de tratament consta în radioterapie externă asociată cu brahiterapie și chimioterapie cu Cisplatin, urmat de tratament chirurgical. Uneori chiar și după chimioterapie și iradiere neo-adjuvantă invazia locală este încă prezentă și, mai mult decât atât în unele cazuri creșterea tumorală continuă, neoplazia fiind neresponsivă la tratamentul neo-adjuvant. În aceste cazuri chirurgia este singura opțiune curativă, având ca scop ablația unei tumori agresive. Prezentăm cazul unei paciente în vârstă de 62 ani diagnosticată cu neoplasm de col uterin avansat ce a prezentat progresie tumorală pe parcursul chimio-iradierii. Am efectuat o exenteratie pelvină posterioară cu rezultate postoperatorii bune. La 1 an după exenterație pacienta nu prezintă semne de recurență.

Cuvinte cheie: neoplasm de col uterin avansat, radioterapie, exenterație pelvină posterioară

ABSTRACT

Although cervical cancer is relatively easy to be diagnosed in early stages, there still is an important number of patients who present with locally advanced disease. In these cases the standard protocole consists in neo-adjuvant external radiotherapy and brachytherapy combined with Cisplatin – based chemotherapy followed by surgery. Sometimes even after aggresive neo-adjuvant chemo-irradiation the local invasion is still present and, in rare cases, the tumoral growth continues, the malignancy being unresponsive to neo-adjuvant treatment. In these cases surgery is the only curative option in order to remove a large and in most of the cases aggressive tumor. We present the case of a 62 year old female diagnosed with advanced cervical cancer with tumor progression during chemo-irradiation. We proceeded to a posterior pelvic exenteration with good post-operative results. 1 year after surgery the patient is free of disease.

Key words: advanced cervical cancer, radiotherapy, posterior pelvic exenteration

Corresponding author: Nicolae Bacalbașa, MD
Dimitrie Racoviță Street, no. 2, Bucharest, Romania
E-mail: nicolaebacalbasa@gmail.com

INTRODUCTION

Although pelvic exenterations represent aggressive surgical procedures which might associate physical and psychological problems and a worsened body image, they are the only potential solution with curative intent in centro-pelvic tumors originating from both digestive and gynecologic tract. (1,2,3) In selected cases preoperative oncologic treatment can offer a tumor down-staging or can diminish the tumoral invasion in adjacent organs providing this way the possibility of less aggressive surgical procedures. In other cases this desiderate cannot be obtained; the tumor proves to be unresponsive to neo-adjuvant treatment and multivisceral resections being needed in order to obtain a good control of the disease. Studies have shown that clinical features of the tumor and both molecular and non-molecular biomarkers can be responsible for the poor tumoral response at irradiation. (4) In these cases surgery remains the only treatment with curative intent. We present the case of a 62 year old patient diagnosed with a large cervical tumor in which neo-adjuvant treatment failed to obtain an acceptable control of the disease. She was addressed to our service after augmentation of the tumor under neo-adjuvant treatment; we performed a total hysterectomy en bloc with bilateral adnexectomy, total colpectomy, abdomino-perineal rectal resection and pelvic lymph node dissection with good results.

CASE REPORT

The 62 year old female was addressed to our service for pelvic pain and vaginal bleeding. The local exam revealed a large cervical tumor invading the left parametrum. The biopsies revealed a squamous keratinized cervical tumor and the CT scan showed a 73/37 cm cervical tumor with slight invasion of the anterior rectal wall and no distant metastases (Picture 1). The patient was addressed to the oncology service where she was submitted to neo-adjuvant treatment: external beam radiation therapy associated with Cisplatin for 4 months but the patient presented a massive vaginal and rectal bleeding associated with subocclusive syndrome; the CT scan revealed the augmentation of the cervical tumor to 8/4 cm. The rectoscopy confirmed the tumoral invasion on the anterior and left side at 3 cm above the anal margins. The cistoscopy showed no modifications. We decided to perform the surgical procedure

Figure 1. Initial CT scan showing the cervical tumor invading the anterior rectal wall

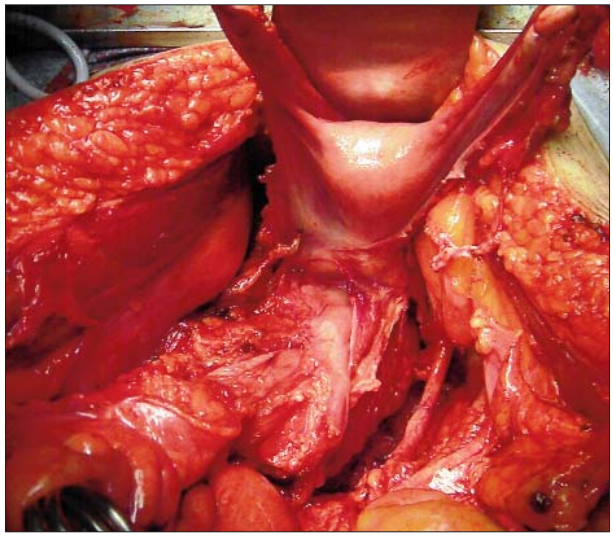

Figure 2. The large cervical tumor invading the anterior rectal wall: intraoperative aspect

which at that moment seemed to be the only potential curative solution. Intraoperatively a large cervical tumor invading the anterior rectal wall was found; a total posterior exenteration with pelvic lymph node dissection was performed (Pictures 2-7); the early postoperative evolution was uneventful, the patient being discharged in the 14th postoperative day. The histopathological study of the specimen: total hysterectomy with bilaretal adnexectomy, total colpectomy and abomino-perineal rectal resection (Pictures 8-9) confirmed the biopsies' results: squamous keratinized well differentiated cervical cancer invading the rectal wall. The patient had a good oncologic outcome, with no signs of recurrence 1 year after surgery.

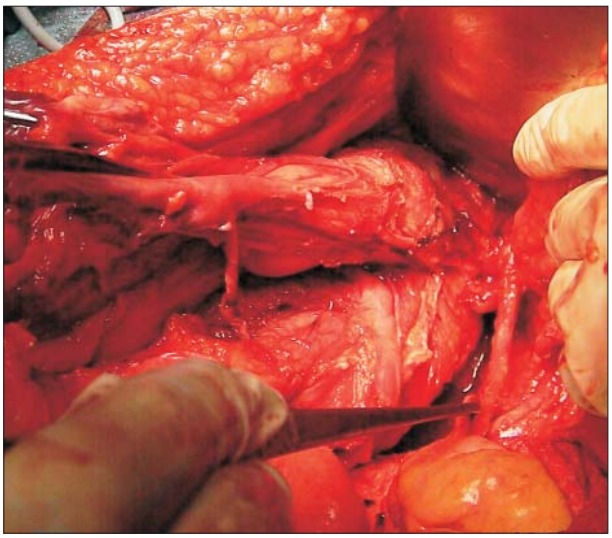

Figure 3. The right ureter is completely dissected

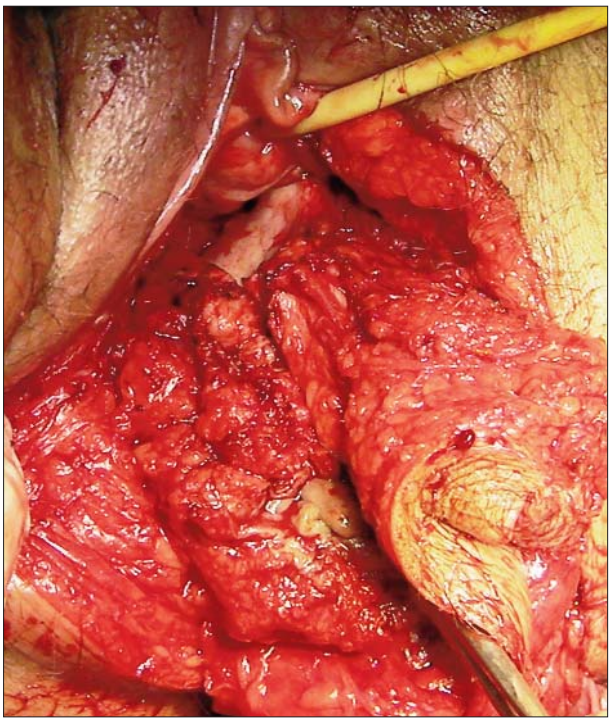

Figure 4. Perineal phase: total colpectomy en bloc with rectal abdomino-perineal resection

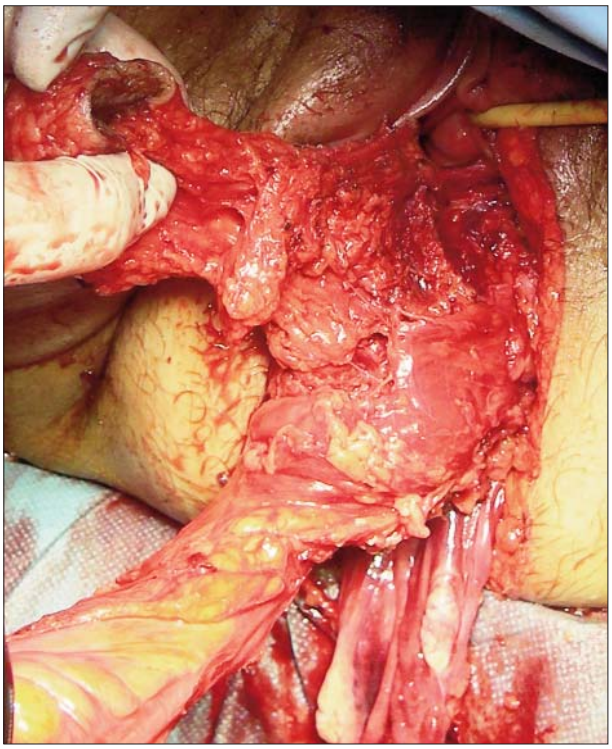

Figure 5. Removing the specimen through the perineal incision

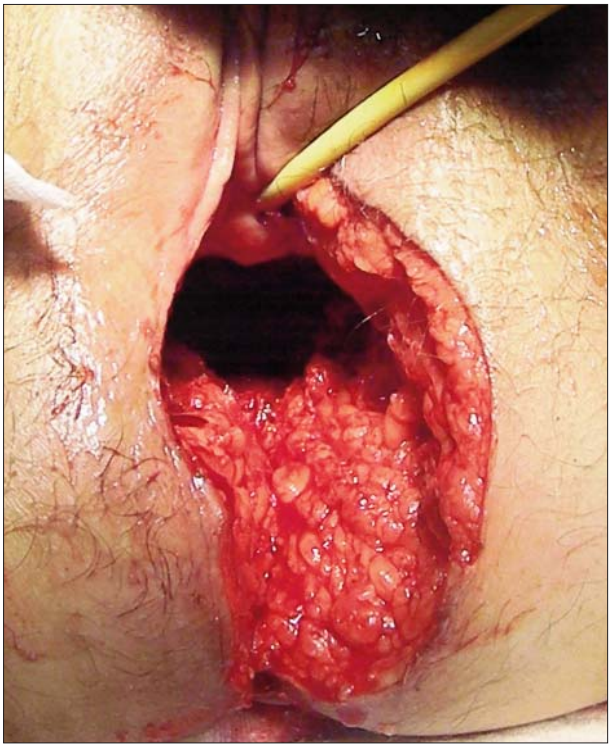

Figure 6. The final aspect of the perineum after resection: posterior exenteration

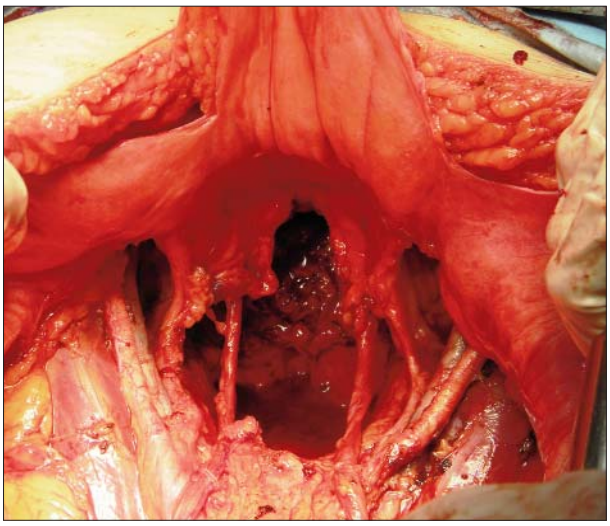

Figure 7. The final aspect after resection and pelvic lymph node dissection

Figure 8. The specimen: total hysterectomy with bilateral adnexectomy, total colpectomy and abdomino-perineal rectal resection

Figure 9. The specimen: cervical tumor invading the anterior rectal wall

DISCUSSIONS

After almost 7 decades since Brunchwig reported the first exenterations performed at that moment with palliative intent, pelvic exenteration became the gold standard in treating advanced pelvic malignancies. Once the surgical techniques developed and the postoperative intensive care improved the evolution of these patients significantly improved. In order to make this surgical procedure more efficient in terms of survival attention was focused on the capacity of neoadjuvant treatment to better control the extent of the disease. In this way a large number of patients undergo neoadjuvant chemo-irradiation but unfortunately not all of them present benefits at the end of that treatment. Studies have shown that there are some features of the tumor which might predict a poor response. (4) The tumor's diameter seems to be strongly correlated with the response to irradiation. A large tumor can reflect a long period between the moment of occurrence and the time of diagnostic but it can also predict the presence of an aggressive biology of the malignant cells which will be associated in time with a poor prognostic and an unfavorable evolution in terms of survival. (4,5) Another important tumoral biomarker which influences the response to irradiation is tumor hypoxia. Hypoxic malignant cells are defined as having $pO2 < 10$ mmHg and seem to have a higher capacity of spreading (both locally and distant – through the lymphatic drainage) and also a high resistance to radiation therapy. (6,7,8) Unfortunately, some of these cases might also have a poor prognosis even after surgery due to the the malignant cells' high capacity of dissemination. (7)

An indirect sign which might predict tumoral hypoxia is the decreased number of red blood cells. The presence of anemia seems to be associated with a poor prognosis because it contributes to tumoral hypoxia (9,10,11). In their study Bush et al demonstrated that patients with cervical cancer and hemoglobin levels higher than 12 g/dL had a better evolution when compared to those with chronic anemia. (11) However other studies failed to demonstrate the utility of erythropoietin to correct anemia preoperatively in order to correct tumoral hypoxia. (12) Further studies are still needed to establish

which are the best options to correct this parameter.

Other biological markers which might be correlated with tumor response to irradiation are thrombocytosis and leukocytosis. Increased number of white blood cells (more than 10.000/μL is observed to be associated with poor response to radiotherapy; this fact can also signal a tumoral abscess which results in a delayed radiation treatment. Association between thrombocytosis (> 400.000 / μL), leukocytosis (>10.000/μL) and unresponsive tumor to irradiation can be associated with the presence of a high level of tumor derived growth factor synthesized by the aggressive malignant cells. These factors proved to have predictive value in identifying the patients with worse prognostic and high risks of recurrence. (13,14,15)

In our case the patient presented chronic anemia which probably produced secondary tumoral hypoxia; this fact might explain the tumor resistance at radiation therapy. Although as we have already mentioned tumoral hypoxia is usually associated with aggressive cells with high capacity of migration into the lymphatic flow and secondary poor outcome even after radical surgery (7) we decided to perform the surgical procedure in order to remove the hemorrhagic tumor invading the rectal wall, producing subocclusive syndrome. The indications for pelvic exenteration in case of large cervical tumors invading the rectal wall have been widely researched in clinical studies. (16,17, 18,19) When it comes about overall survival after exenteration, the most important factors seem to be negative margins and complete surgical resection. (20,21,22) Among patients with negative margins it would be interesting to find out which is the smallest distance between the negative margins and the tumor' s limit in order to establish how far should we go with the resection. (21)

CONCLUSIONS

Pelvic exenteration remains the only curative solution in locally invasive cervical cancer. Although nowadays the standard protocol consists in neoadjuvant chemo-irradiation, there are cases in which the tumor does not respond to this therapy, the most important factors associated with non responsive to irradiation tumors being anemia and secondary hypoxia and large dimensions of the tumor. Even in these cases, in which usually the tumor is a very aggressive one surgical treatment may be tried with curative intent.

REFERENCES

1. Marnitz, S., Kφhler, C., Móller, M., Behrens, K., Hasenbein, K., Schneider, A., Indications for primary and secondary exenterations in patients with cervical cancer, Gynecologic Oncology 103 (2006) 1023–1030
2. Hawighorst-Knapstein S, Fusshoeller C, Franz C, Trautman K, Schmidt M, Pilch H, et al. The impact of treatment for genital cancer on quality of live and body image – Results of a prospective longitudinal 10-year study. Gynecol Oncol 2004;94:398–403.
3. Roos EJ, de Graeff A, van Eijkeren MA, Boon TA, Heintz APM. Quality of live after pelvic exenteration. Gynecol Oncol 2004;93: 610–4.
4. Klopp, A., Eifel, P., Biological Predictors of Cervical Cancer Response to Radiation Therapy, Semin Radiat Oncol 22:143-150 © 2012 Elsevier Inc
5. Eifel PJ, Jhingran A, Levenback CF, et al: Predictive value of a proposed subclassification of stages I and II cervical cancer based on clinical tumor diameter. Int J Gynecol Cancer 19:2-7, 2009
6. Fyles AW, Milosevic M, Wong R, et al: Oxygenation predicts radiation response and survival in patients with cervix cancer. Radiother Oncol 48:149-156, 1998
7. Hockel M, Schlenger K, Aral B, et al: Association between tumor hypoxia and malignant progression in advanced cancer of the uterine cervix. Cancer Res 56:4509-4515, 1996
8. Fyles A, Milosevic M, Hedley D, et al: Tumor hypoxia has independent predictor impact only in patients with node-negative cervix cancer. J Clin Oncol 20:680-687, 2002
9. Grogan M, Thomas GM, Melamed I, et al: The importance of hemoglobin hemoglobin levels during radiotherapy for carcinoma of the cervix. Cancer 86:1528-1536, 1999
10. Thomas G: The effect of hemoglobin level on radiotherapy outcomes: The Canadian experience. Semin Oncol 28:60-65, 2001
11. Bush RS: The significance of anemia in clinical radiation therapy. Int J Radiat Oncol Biol Phys 12:2047-2050, 1986
12. Thomas G, Ali S, Hoebers FJ, et al: Phase III trial to evaluate the efficacy of maintaining hemoglobin levels above 12.0 g/dL with erythropoietin vs above 10.0 g/dL without erythropoietin in anemic patients receiving concurrent radiation and cisplatin for cervical cancer. Gynecol Oncol 108:317-325, 2008
13. Hockel M, Schlenger K, Aral B, et al: Association between tumor hypoxia and malignant progression in advanced cervical cancer
14. Hernandez E, Donohue KA, Anderson LL, et al: The significance of thrombocytosis in patients with locally advanced cervical carcinoma: A Gynecologic Oncology Group study. Gynecol Oncol 78:137-142, 2000
15. Mabuchi S, Matsumoto Y, Isohashi F, et al: Pretreatment leukocytosis is an indicator of poor prognosis in patients with cervical cancer. Gynecol Oncol 122:25-32, 2011
16. Goldberg JM, Piver S, Hempling RE, Aiduk C, Blumenson L, Recio FO. Improvement in pelvic exenteration: factors responsible for reducing morbidity and mortality. Ann Surg Oncol 1998;5: 399–406.
17. Lambrou NC, Pearson JM, Averette HE. Pelvic exenteration of gynecologic malignancy: indications, and technical and reconstructive considerations. Surg Oncol Clin N Am 2005;14:289–300.
18. Stanhope CR, Symmonds RE. Palliative exenteration – What, when, and why? Am J Obstet Gynecol 1985;152:12–6.
19. Symmonds RE, Pratt JH, Webb MJ. Exenterative operations: experience with 198 patients. Am J Obstet Gynecol 1975;121(7):907–18.
20. Fleisch MC, Pantke P, Beckmann MW, Schnuerch HG, Ackermann R, Grimm MO, et al. Predictors for long-term survival after interdisciplinary salvage surgery for advanced or recurrent gynecologic cancers. J Surg Oncol May 1, 2007;95(6):476–84
21. Westin SN, et al, Overall survival after pelvic exenteration for gynecologic malignancy, Gynecol Oncol (2014), http://dx.doi.org/ 10.1016 /j.ygyno.2014.06.034
22. Shingleton HM, Soong SJ, Gelder MS, Hatch KD, Baker VV, Austin Jr JM. Clinical and 356 histopathologic factors predicting recurrence and survival after pelvic exenteration 357 for cancer of the cervix. Obstet Gynecol Jun 1989;73(6):1027–34