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Review Article

Radical Abdominal Trachelectomy Followed Neoadjuvant Chemotherapy in Cervical Adenocarcinoma Figo Stadium Ib2-A Case Report and Review of Literature

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Keywords

- "Bulky" cervical cancer
- Fertility preserving surgery
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Abstract

Introduction: During the last three decades fertility preservation are established as a new treatment modality for young patients with early cervical cancer using different surgical approaches and techniques such as vaginal or abdominal simple or radical trachelectomy, total laparoscopic or robotic trachelectomy even large conisation with laparoscopic lympadenectomy. A further goal for gynecological oncology is to try to consider fertility-preserving approach in these patients with bulky cervical cancer not compromising the oncology outcome.

A case report: A 25-year-old patient with cervical adenocarcinoma, FIGO stage IB2, was diagnosed with tumor size more than 40 mm. Preoperative magnetic resonance (MR) was performed and patient received neoadjuvant chemotherapy protocol, Cisplatinum/Doxorubicin, three cycle in 10 days interval followed abdominal radical trachelectomy with pelvic and paraaortic lymphadenectomy. All findings on the follow-up visit after 24 months showed no sign of disease recurrence and patient's menstrual cycles were regular.

Until know small case control studies point on acceptable approach with neoadjuvant chemotherapy followed conservative fertility spare surgery in young patients with bulky cervical tumor who respond well on chemotherapy but we still need more evaluation and data in these group of patients.

INTRODUCTION

Approximately 45% of surgically treated stage IB cancers occur in women under the age of 40 years [1]. The general eligibility criteria for radical trachelectomy include the following: women under 40 years of age who have a strong desire to preserve fertility, no clinical evidence of impaired fertility, lesion size less than 2 cm, International Federation of Gynecology and Obstetrics (FIGO) stages IA2 –IB1, no involvement of the upper endocervical canal, and negative regional lymph nodes [2]. Since Prof D. Dargen presented the fertility preserving approach in early stage of cervical cancer in young women at the end of the last century many publications confirmed safety in oncology outcomes and good pregnancy outcome. In technical approach, nowdays few techniques were established such as vaginal and abdominal trachelectomy and laparoscopic and robotic approach but all with similar oncological outcomes. According to good oncology outcomes, some authors proposed more conservative treatment such as cervical conization or simple trachelectomy and pelvic lymphadenectomy for low-risk patients with tumor size less than 2 cm, absence of lymph vascular space invasion, negative sentinel node [3]. The papers showed some differences in pregnancy outcomes comparing the different technique but success rates are acceptable in all of them. [2,4-7].

A CASE REPORT

A 25-year-old patient came to the Clinical Center of Vojvodina, Novi Sad for a routine gynecological examination. She underwent punch biopsy and FIGO stage IB2 cervical adenocarcinoma, G2, was diagnosed without lympho-vascular involvement and perineural tumor infiltration; tumor size was 45 mm and proliferation index was not measured. The patient was referred to the Oncology Institute of Vojvodina, Sremska Kamenica for further disease management. The patient expressed a strong wish to preserve the fertility. The MR examination of pelvis and abdomen was performed Figure 1.

In the discussion with the patient, she was informed that there are few literature data about the similar cases. No randomized trials have been conducted so far that can confirm the benefits of fertility preserving and oncological outcomes among these high-risk patients and this approach are still an experimental. The laparoscopic pelvic lymph node dissection concerning the suspicion of positive pelvic lymph node by MR was not performed because of lack of the experience in laparoscopy. However, the patient did not want to change her mind about fertility preserving. The patient was informed about the treatment procedure and after signing the informed consent, she started the administration of neoadjuvant chemotherapy (NACT). The performance status of 0–2 was required. Patients did not have other malignancy in their history.

Chemotherapy protocol

She received a combination of cisplatinum (dose, 75 mg/m^2) and doxorubicin (dose, 35 mg/m^2) in three cycles at the interval of 10 to 12 days, according to Prague protocol for adenocarcinoma [8]. We decided for this protocol according to literature data and because paclitaxel regiment is not covered by health insurance in our country for cervical cancer.

Three weeks after the last chemotherapy cycle, MR was performed Figure 2.

Because of good response and down staging of the disease, the patient was operated four weeks after third cycle of NACT. Abdominal radical trachelectomy with pelvic and para-aortic lymphadenectomy was performed on May 14, 2013. Surgery time was five hours and no intraoperative and postoperative complications occurred. There was no need for blood transfusion and total blood loss during operation was 350 ml. At frozen section, lymph nodes were negative such as margins of the cervix, no infiltration of the parametria and material obtained by endocervical curettage was without tumor. The operation finished without permanent cerclage.

Abdominal trachelectomy with pelvic and paraaortic lymphnodectomy was performed according to standard procedure described by Cibula D and Ungar L. [9,10] (Figures 3,4).

Final pathological findings confirmed the tumor diameter of 18 mm and the depth of stromal infiltration of 14 mm with positive lymphovascular space and free margine, no parametrial infiltration. The distance between tumor and upper cervical resection line was 11 mm. In 40 lymph nodes, there were no metastases.

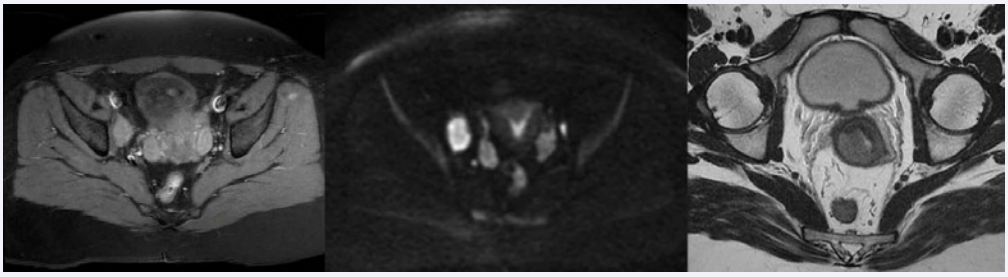

Figure 1 The pre therapy MR in a patient with cervical cancer and metastatic lymph node. Axial gadolinium-enhanced 3D fat-suppressed gradient-echo T1-weighted MR image shows an enhancing right iliac lymph node (A). Isotropic diffusion weighted image acquired using a b-value=1,000 s/mm2. Brighter areas correspond to tumor and lymph node infiltration (B). T2-weighted MR image shows a large cervical mass infiltrating the cervical stroma (C).

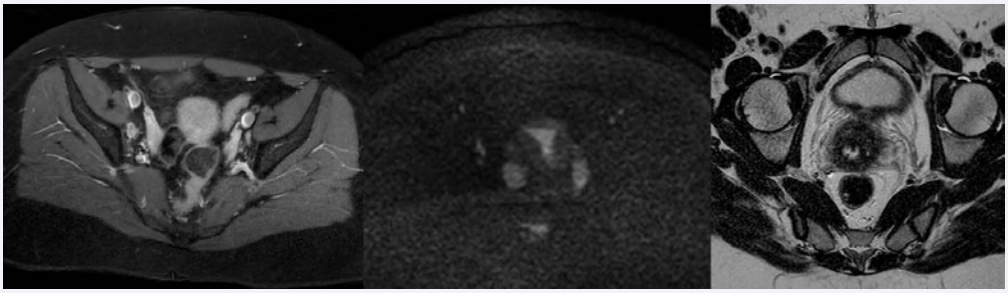

Figure 2 After therapy, no hyperintense signal is seen at sites of nodal disease on gadolinium-enhanced T1-weighted (A) and diffusion-weighted images (B), consistent with therapy response. T2-weighted image obtained after therapy shows substantial tumor volume reduction (C).

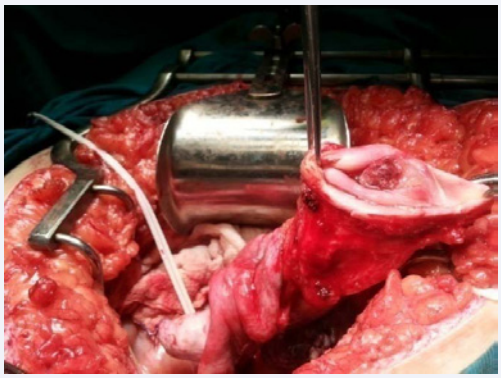

Figure 3 Uterus and resected vaginal cuf.

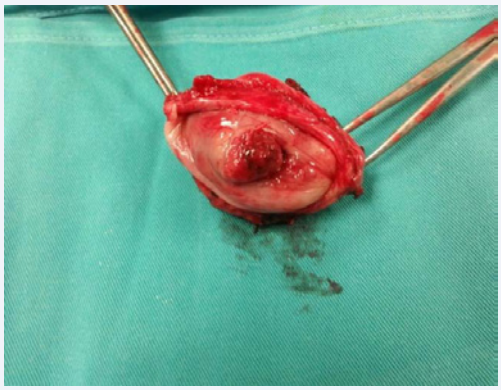

Figure 4 Specimen taken after trachelectomy showing tumor after three cycles of NACT.

The patient was discharged 10 days after operation in good condition. All findings on the follow-up visit after 24 months showed no sign of disease recurrence and patient's menstrual cycles are regular. There is no pregnancy.

DISCUSSION

The application of different therapeutic modalities in the group of patients with early stages of invasive cervical carcinoma has given different results. In most cases, a radical surgical therapy is applied, which presumes radical hysterectomy with bilateral pelvic lymphadenectomy. Standard surgical therapy has given excellent results in terms of five-year overall-survival, which is 85-91% [4]. However, a great number of young women lose their fertility permanently.

In the last three decades, the fertility-preserved approach in the group of patients with early cervical cancer presented a good oncology and pregnancy outcome [2,7]. The approaches are different and various surgical techniques in fertility preservation cervical surgery such as, vaginal, abdominal, laparoscopic or robotic have showed their respective obstetrical and oncology outcome. Even more conservative surgery showed promising results for low-risk early leasions [11].

Still we have a group of young patients who wish to preserve fertility even cervical cancer is more than 2 cm. So, further goal for gynecological oncology is to try to consider fertility-preserving approach in these groups of patients but not to compromise the oncology outcome.

Results of many recent studies concluded that cervical cancer has acceptable good response to chemotherapy. The neoadjuvant chemotherapy reduces both tumor volume and lymph node positivity and it makes surgery easier. In addition, the response to chemotherapy leads to down staging of the disease with a chance for fertility preserving in some groups of young patients with bulky tumor.

Neoadjuvant chemotherapy (NACT) followed by radical surgery (RS) has showed in several pilot studies a benefit in terms of overall survival (OS) and disease-free survival (DFS) in locally advanced cervical cancer FIGO IB-2 – IIB [8,12-16].

Marchiole P et al. presented 7 patients with large IB – IIA-1 tumor (30 mm to 45 mm). All patients underwent neoadjuvant chemotherapy followed by laparoscopic pelvic lymphadenectomy and vaginal radical trachelectomy (VRT). The patients were evaluated after NACT by clinical examination, colposcopy, and MR. The results showed a response of more than 50% of tumor volume reduction in 5 to 7 women (71%) and in two patients had a partial response with a reduction in size of the tumor of 40%. All 7 patients underwent VRT. Concerning oncology outcome in median follow up of 22 months (range 5-49 months), no relapse was observed [17]

Robova et al. presented a large serie of 15 patients with tumor more than 2 cm treated with NACT followed by vaginal trachelectomy. They received Prague protocol, 3 cycle cisplatin (75 mg/m^2) and ifosfamide (2g/m^2) in cases of sqamous cancer or cisplatin (75 mg/m^2 and doxorubicin (35mg/m^2) in case of adenocarcinoma every 10 days and then underwent simple vaginal trachelectomy with laparoscopic lymphadenectomy. Final histopathological findings were 5 patients with complete response, 6 patients with microscopic residual disease and 4 with macroscopic residual disease. Three women with a suboptimal response relapsed. They were all affected by adenocarcinoma. Patient with relaps in ovary died of the disease and two other patients presented endocervical recurrences are alive without evidence of disease. In pregnancy outcome, there were 7 pregnancies and 7 babies were born live, with two premature born in 26 and 35 gestational week [18].

Thirty cases of women diagnosed with cervical cancer ≥ 2 cm and treated with NACT followed by fertility preserving surgical management were presented in Table 1.

Lanowska et al. recently published different approach in these young patients with cervical cancer more than 2 cm. Before NACT, laparoscopic lymphadenectomy was performed to confirm no lymph node metastasis before NACT. Sentinel lymph node detection was performed in all patients. Neoadjuvant chemotherapy consist of 2-3 cycles of paclitaxel/ifosfamid/cisplatinum regiments followed by radical vaginal trachelectomy (RVT). Twenty patients were enrolled and mean tumor size was 3 cm. Radical vaginal trachelectomy was performed in 18 patients and 9 of 18 patients were with complete pathological remission. In 2 patients due to insufficient pathological response in cervical specimen chemo-radiation was recommended. In a mean follow –up of 23 months one relapse was diagnosed. Seven pregnancies

Table 1: Neoadjuvant chemotherapy and different techniques of fertility sparing surgery in literature.

	Cervical cancer ≥ 2 cm	NACT protocol	Conservative surgery	Optimal pathological response (CR+PR1) No (%)	Recurrences No.	Pregnancy No.
Marchiole et al[17]	7	TIP (or TEP for Ad.Ca)	VRT+PL	4/7 (57%)	0/7	1/7
Robova et al [18]	15	IP+(Dox for AdCa)	ST+PL	9/12* (75%)	3/12	7/12
Maneo et al [19]	8	TIP (or TEP for Ad.Ca)	Conisatio + PL	6/6& (100%)	0/6	NR
Plante et al [20]	3	TIP	VRT+PL	3/3(100%)	0/3	3/3
Palaia et al[21]	1	TIP	ST+PL	1/1 (100%)	0/1	0/1
Kobayashi et al [22]	1	BOMP	Conisatio	1/1(100%)	0/1	1/1

*, & - fertility spared number of patients, NACT: Neoadjuvant Chemotherapy; T: paclitaxel; I: Ifosfamide; P: cisplatin; E: Epirubicin; BOMP: cisplatin, bleomycin, vincristine and mitomycin; AdCa: Adenocarcinoma; VRT: Vaginal Radical Trachelectomy; ST: Simple Trachelectomy; PL: Pelvic Lymphadenectomy; CR: Complete disappearance of tumor in the cervix with negative nodes; PR1: residual disease with <3 mm stromal invasion including in situ carcinoma.

occurred in 5 women. Authors concluded that this approache, in this group of patients; laparoscopic lymphadenectomy followed NACT and RTV in patients with negative lymph node metastasis, could be safe procedure concerning oncology and obstetrical outcome [23].

Even neoadjuvant chemotherapy followed by fertility sparing surgery is performed in some centers, we must admit that there is no standardized in chemotherapy protocols and especially surgical approach in these group of patients.

These small studies point on acceptable approach with neoadjuvant chemotherapy followed conservative fertility spare surgery in young patients with bulky cervical tumor. If these group of patients are high risk group Lanowska M et al presented an oncologically safe approach to divide patients who could be consider for NACT followed fertility preserving procedure, from those who are not because of lymph node metastasis. With a developing a sentinel node detection procedure, this approach will be more acceptable. Another no standardize therapeutic approach is chemotherapy protocol. Most of them are platinum consist regiment in double or triple combination. Recent studies confirmed paclitaxel/cisplatinum regiment as most promising and have to think in consolidation of the chemotherapeutic regiments in studies. Also dose-dense interval by some authors showed good response with no increasing toxicities [18]. Another important question is the effect of chemotherapy regiments on ovarian function? Do we have to exam ovarian reserve before treatment or if these patients are young, we expect normal ovarian reserve? Pregnancy outcome in this group of patients could answer on this question.

The most frequent histopathological finding in cervical cancer is squamous type; however, in 20% to 25% of the cases adenocarcinoma is diagnosed with increased incidence in young population [24,25]. Based on the recent clinical recommendation for trachelectomy, the histological type does not influence in decision-making except in the case of small, neuroendocrine cervical cancer [2]. An interesting article was published by Galic V *et al*. showing that adenocarcinoma histology had negative impacts survival for both early and advanced-stage of the disease [26]. Still we are required studies with a larger number of patients and adequate follow-up to validate this conservative approach and to define a group of patients in "bulky" cervical cancer for this treatment.

REFERENCES

1. Covens A, Rosen B, Murphy J, Laframboise S, DePetrillo AD, Lickrish G, et al. Changes in the demographics and perioperative care of stage IA(2)/ IB(1) cervical cancer over the past 16 years. Gynecol Oncol. 2001; 81: 133–137.
2. Schneider A, Erdemoglu E, Chiantera V, Reed N, Morice P, Rodolakis A, et al. Clinical Recommendation Radical Trachelectomy for Fertility Preservation in Patients With Early- Stage Cervical Cancer. Int J Gynecol Cancer. 2012; 22: 659–666.
3. Rob L, Pluta M, Strnad P, Hrehorcak M, Chmel R, Skapa P, et al. A less radical treatment option to the fertility-sparing radical trachelectomy in patients with stage I cervical cancer. Gynecol Oncol. 2008; 111: 116 –120.
4. MandicP, Novakovic D. Nincic. Surgical approaches towards fertility preservation in young patients with early invasive cervical carcinoma. Journal of BUON. 2009; 14: 581-586.
5. Novak F. Radical abdominal subcor poreal extir pation of the cervix with bilateral pelvic lymph nodes dissection in cancer in situ of the cer vix uteri. Acta Med Iugosl. 1952; 6: 59 -71.
6. Dargent D, Brun J, Roy M, Mathevet P. La trachelectomie elargie. Une alternative a l'hysterectomie radicale dans le traitement des cancers in filtrants developpes surla face externe du col uterin. J Obstet Gynecol. 1994; 2: 285 –292.
7. Wethington SL, Cibula D, Duska Lin da R, Garrett Leslie, Kim C, Chi DS, et al. An International Series on Abdominal Radical Trachelectomy. 101 Patients and 28 Pregnancies. Int J Gyne col Can cer. 2012; 22: 1251–1257.
8. Robova H, Rob L, Halaska MJ, Pluta M, Skapa P, Strnad P, et al. High-dose density neoadjuvant chemotherapy in bulky IB cervical cancer. Gynecologic Oncology. 2013; 128: 49– 53.
9. Cibula D, Slama J, Fischerova D. Update on abdominal radical trachelectomy. Gynecologic Oncology 2008; 111: 111–115.

10. Ungar L, Palfalvi L, Hogg R, Siklos P, Smith R, Del Preori G. Abdominal radical trachelectomy: a fertility-preserving option for woman with early cervical cancer. BJOG. 2005; 112: 366–369.

11. Plante M. Evolution in fertility-Preserving options for early- stage cervical cancer. Radical trachelectomy, Simple Trachelectomy, Neoadjuvant chemotherapy. Int J Gynecol Cancer. 2013; 23: 982-989.

12. Neoadjuvant chemotherapy for cervical cancer meta-analysis collaboration. Neoadjuvant chemo therapy for locally advanced cervix cancer: a systematic review and meta-analysis of individual patient data from 21 randomized cont rolled trials. Neoadjuvant Chemotherapy for Locally Advanced Cervical Cancer Meta-analysis Collaboration. E ur J Canc er. 2003; 39: 2470-2486.

13. Lissoni AA, Colombo N, Pellegrino A, ParmaG, Zola P, Katsaros D, et al. A phase II, randomized trial of neo-adjuvant chemotherapy comparing a three- drug combination of paclitaxel, ifosfamide, and cisplatin (TIP) versus paclitaxel and cisplatin (TP) followed by radical surgery in patients with locally advanced squamous cell cervical carcinoma: the Snap- 02 Italian Collaborative Study. Ann Oncol. 2009; 20: 660-665.

14. Eddy GL, Manetta A, Alvarez RD, Williams L, Creasman WT. Neoadjuvant chemotherapy with vincristine and cisplatin followed by radical hysterectomy and pelvic lymphadenectomy for FIGO stage IB bulky cervical cancer: a Gynecologic Oncology Group pilot study. Gynecol Oncol. 1995; 57: 412-416.

15. Leone B, Vallejo C, Perez J, Cuevas MA, Machiavelli M, Lacava J, et al. Ifosfamide and cisplatin as neoadjuvant chemotherapy for advanced cervical carcinoma. Am J Clin Oncol. 1996; 19: 132-135.

16. Zanetta G, Lissoni A, Pellegrino A, Sessa C, Colombo N, Gueli-Alletti D, et al. Neoadjuvant Chemotherapy with cisplatin, ifosfamide and paclitaxel for locally advanced squamous-cell cervical cancer. Ann Oncol. 1998; 977-980.

17. Marchiole P, Tigaud Jean-Dominique, Costantini S, Mammoliti S, Buenerd A, Moran E, et al. Neoadjuvant chemotherapy and vaginal radical trachelectomy for fertility-sparing treatment in women affected by cervical cancer (FIGO stage IB – IIA1). Gynecologic Oncology. 2011; 122: 484–490.

18. Robova H, Halaska M, Pluta M, Skapa P, Strnad P, Lisy J, et al. The role of neoadjuvant chemotherapy and surgery in cervical cancer. Int J Gynecol Cancer. 2010; 20: 42 –46.

19. Maneo A, Chiari S, Bonazzi C, Mangioni C. Neoadjuvant chemotherapy and conservative surgery for stage I B1 cervical cancer. Gynecol Oncol. 2008; 111: 438–443.

20. Plante M, Lau S, Brydon L, Swenerton K, LeBlanc R, Roy M. Neoadjuvant chemotherapy followed by vaginal radical trachelectomy in bulky stage IB1cervical cancer: case report. Gynecol Oncol. 2006; 101: 367 –370.

21. Palaia I, Musella A, Loprete E, Achilli C, Perniola G, Panici PB. Neoadjuvant chemotherapy plus fertility-sparing surgery in locally advanced cervical cancer: case report. J Minim Invasive Gynecol. 2011; 18: 121–122.

22. Kobayashi Y, Akiyama F, Hasumi K. A case of successful pregnancy after treatment of invasive cervical cancer with systematic chemotherapy and conisation. Gynecol Oncol. 2006; 100: 213 –215.

23. Lanowaska M, Mangler M, Speiser D, Bockholdt C, Schneider A, Kohler C et al. Radical Vaginal trachelectomy after laparoscopic staging and neoadjuvant chemotherapy in women with early-stage cervical cancer over 2 cm. Int J Gynecol Cancer. 2014; 24: 586-593.

24. Young RH, Clement PB. Endocervical adenocarcinoma and its variants: their mor-phology and differential diagnosis. Histopathology. 2002; 41: 185–207.

25. Chan PG, Sung HY, Sawaya GF. Changes in cervical cancer incidence after three decades of screen ing US w om en less than 30 years ol d. Obstet G lynec. 2003; 102: 76 5–773.

26. Galic V, Herzog TJ. Lewin SN, Neugut AI, Burke WM, Lu Yu-Shiang, et al. Prognostic significance of adenocarcinoma histology in women with cervical cancer. Gynecologic Oncology. 2012; 125: 287– 291.

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