

Cervical cancer associated with genital prolapse - a brief review of the literature and long-term results of successful treatment with radiochemotherapy and surgery in a very frail patient

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Summary

Background: A case of cervical cancer associated with irreducible procidentia successfully treated with external beam radiation and extracorporeal HDR-AL with concomitant chemotherapy followed by obliterative vaginal surgery is reported for the first time. **Case:** A 73-year-old woman presented in frail condition suffering from a huge, irreducible uterovaginal procidentia combined with a squamous cell carcinoma of the cervix in FIGO Stage IIa. Successful treatment consisted of sequential application of combined radiotherapy with concurrent cisplatin chemotherapy followed by total vaginal hysterectomy and partial colectomy with colpocleisis according to the Labhardt method. The five-year follow-up documents the excellent long-term results with regard to cervical cancer and pelvic floor stability. **Conclusion:** Especially in patients ineligible for extended surgery, radiochemotherapy followed by an obliterative surgical approach is feasible without aberrant wound healing and constitutes a suitable and efficient option for treating carcinomas of the cervix associated with irreducible genital prolapse.

Key words: Cervical cancer; Procidentia; Squamous cell carcinoma.

Introduction

About one-third of the adult female population suffers from prolapse of the pelvic organs associated with urinary and fecal incontinence [1]. At 14/100,000 cases the incidence of carcinoma of the uterine cervix has remained unchanged in Europe over recent years.

The combination of both disorders is very rare and is most frequently observed in multiparous and elderly women. Since 1950, 55 cases have been published worldwide. The few cases reported during the last two decades were observed mainly in underdeveloped countries [2-9]. Although the prolapsed uterine cervix is exposed to constant irritation and ulceration, malignant changes remain a rare complication. This remarkably low risk may be explained by the displacement of the cervix from its natural environment, made harmful by exudates or viral infection [2]. Nonetheless, the continual regeneration of repetitive ulcerous injuries of the epithelium is regarded as the main causative background of malignant transformation. In general, these cancers are characterized by slow growth due to low-grade malignancy and often advanced age of patients. The majority of reported cancers were staged FIGO IIA disease or less and virtually all tumors were histologically defined as keratinizing squamous cell carcinoma. Considering all published cases, development of cervical cancer seems to be a late complication of procidentia and strongly related to its

untreated duration. In 75% of cases, procidentia had been present for ten years or more. One case was published in which a huge carcinoma of the cervix led to sudden incarcerated procidentia [9]. Schraub *et al.* pointed out a correlation between the development of cervical cancer and the treatment of uterovaginal prolapse by pessary insertion. In their series, pessary-associated cancers were again found to be a late adverse event as the mean interval between first pessary use and cancer diagnosis was 18 years. As almost all tumors occurred at the site of pessary insertion, the authors concluded that foreign body-related chronic inflammations associated with viral infection might be the main etiologic factors [9].

The curative treatment of cervical cancer is based on radical surgery and radiotherapy alone or in combination with chemotherapy. Both therapeutic principles are equivalent in early tumor Stages (Ib-IIa) [10], whereas in locally advanced Stages (IIb-IVa) radiochemotherapy is the preferred treatment [11]. By contrast, management of uterovaginal prolapse associated with a carcinoma of the cervix is not standardized and therapy strategies vary considerably between published cases. When operable, most cases were treated either by radical vaginal hysterectomy (Schauta-Amreich) with extraperitoneal lymphadenectomy as proposed by Mitra [12] or without lymphadenectomy but complemented with adjuvant radiotherapy [13]. To date, the addition of laparoscopic lymphadenectomy to the radical vaginal approach seems to be the treatment of choice, but to our knowledge this strategy remains unreported in this patient population.

Revised manuscript accepted for publication October 23, 2007

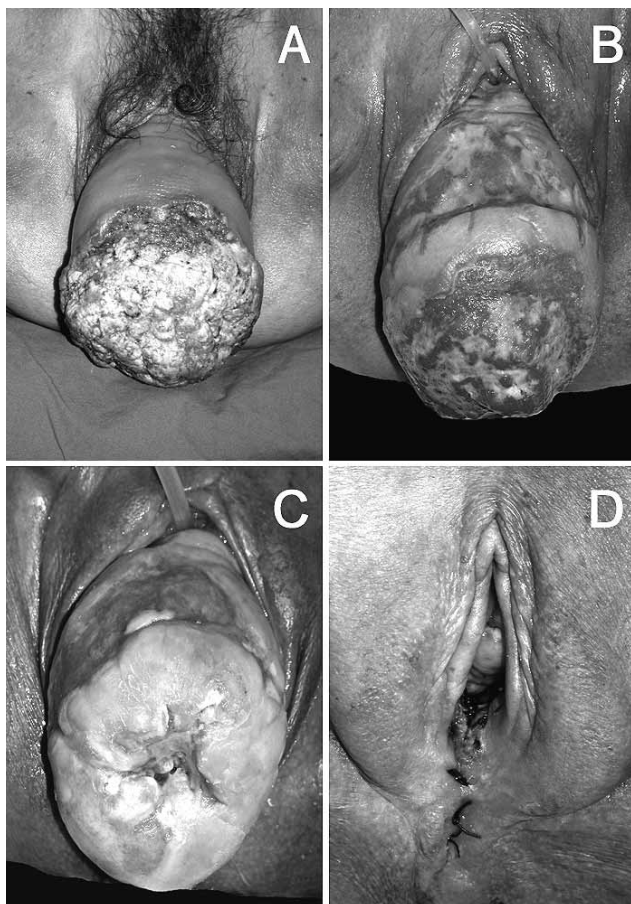


Fig. 1

We report the long-term results of a case involving a 73-year-old very frail patient suffering from irreducible uterovaginal prolapse combined with FIGO Stage IIa squamous carcinoma of the cervix, who was successfully treated with combined radiotherapy and concomitant chemotherapy followed by obliterative vaginal surgery.

Case Report

A 73-year-old cachectic patient with ten births in her anamnesis presented at our oncological outpatient unit with severe vaginal bleeding from a uterovaginal prolapse persisting for more than ten years. The patient complained of pain, lack of appetite, increasing malodor and anuresis. Gynecological examination revealed that the prolapse was irreducible and that the entire surface of the cervix was a ragged exophytic tumor showing verrucous hyperkeratotic features with punctual bleeding (Figure 1A). The tumor extended to the proximal vagina and had a horizontal and vertical diameter of 14.3 and 12.5 cm, respectively. Rectovaginal examination gave no evidence of parametrial or rectal tumor involvement. According to FIGO classification, the disease was clinically Stage IIa. Performed biopsies resulted in the histological diagnosis of a well-differentiated, keratinizing squamous cell carcinoma. No pathologically enlarged mediastinal or retroperitoneal lymph nodes or signs of distant metastatic disease were detected by computed tomography (CT) scan. However, bilateral hydronephrosis was diagnosed. Pelvic magnetic resonance (MR) imaging showed a

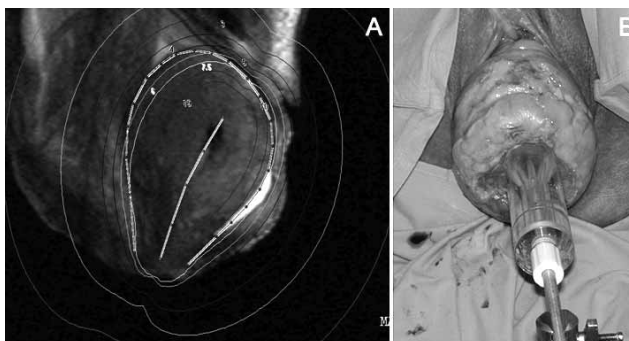


Fig. 2

Figure 1. — Macroscopic alteration during therapy. A) the unreducible uterovaginal prolapse associated with a carcinous distention of the uterine cervix; B) after completion of external radiochemotherapy; C) after completion of brachytherapy; D) after vaginal hysterectomy and colpocleisis.

Figure 2. — A) the patient's radiation portal adjusted by MRT-based planning. B) Adjustment of extracorporeal intracavitary brachytherapy.

large prolapse comprising the entire uterus, the caudal parts of the urinary bladder, the parametria as well as extracorporeal parts of the peritoneal cavity (Figure 2A). Serum creatinine was elevated to 1.7 mg/dl, and SCC was 3.1 ng/ml.

Because of inoperability due to the patient's frail general condition on the one hand and the tumor extension on the other, the decision was made to administer neoadjuvant radiochemotherapy: pelvic external irradiation at a total dose of 52.2 Gy, subdivided into 29 fractions of 1.8 Gy each, was administered with concomitant weekly cisplatin therapy at a dose of 40 mg/m². On completion of external irradiation the tumor mass showed partial regression (Figure 1B). External radiotherapy was complemented with three sessions of extracorporeal high-dose-rate intracavitary brachytherapy (HDR-AL) of 7.5 Gy per session at point A. To minimize irradiation-induced injury of adjoining pelvic organs because of the altered anatomical situation caused by the still irreducible procidentia, the patient's radiation portal was adjusted by MRT-based planning. Despite meticulous computerized planning, hemorrhagic cystitis could not be avoided after an administered dose of 36 Gy. After radiotherapy had been discontinued for three weeks, all symptoms of radio-cystitis improved and finally resolved. Recurrent grade 1 anemia was treated with recombinant erythropoietin. One episode of grade 2 neutropenia that occurred towards the end of radiochemotherapy was promptly treated with filgrastim to avoid further protraction of treatment.

On completion of radiochemotherapy no macroscopic tumor residues were visible and the prolapse was reducible (Figure 1C). As the patient was widowed and no longer sexually active,

a simple vaginal hysterectomy was performed with a two-third colpectomy and a colpocleisis according to the Labhardt method (Figure 1D). Histologic examination revealed minor residues of the squamous cell carcinoma with no lymphatic space involvement. All margins of the specimen were found to be clear.

The patient has been followed-up in accordance with our aftercare program over the past five years. On her last visit, the patient was in very good physical condition with excellent quality of life; her considerable weight gain of 14 kg, reached 18 months after treatment was completed, remained unchanged. Neither CT scan nor gynecologic examination revealed evidence of recurring cervical cancer or any signs of weakness of the pelvic floor. Serum SCC was 0.1 ng/ml.

Discussion

Although treatment concepts are well-established for the various stages of cervical cancer [10, 11] as well as for assessment of uterovaginal prolapse and related pelvic floor disorders, the best standard of care remains unclear when both conditions coincide. The completely changed anatomical situation in the case of a massive, irreducible uterovaginal prolapse and the frequently associated severe comorbidity, especially in frail geriatric patients, often make radical surgery impossible.

We have reported the case of an elderly and very frail patient suffering from a huge, irreducible uterovaginal prolapse associated with cervical cancer. Despite the existing bilateral hydronephrosis at diagnosis, we classified the tumor as FIGO Stage IIA and not Stage IIIB, because we were convinced that the hydronephrosis was not related to tumor spread but rather due to third-degree procidentia as recently reported [13, 14]. Even though the tumor was operable, the patient's severely compromised general condition, the recurring hemorrhage and the onset of renal failure prompted us to adapt the available therapy modalities to meet the requirements of the special situation. We therefore decided to concomitantly administer radiotherapy of the lower pelvis and chemotherapy as a first measure with the intention to significantly down-stage the tumor and make the procidentia reducible.

In the literature, successful treatment with external beam therapy was reported only by Kriplani *et al.* in an incarcerated procidentia secondary to a huge cervical cancer. However, in that case, prior to therapy, the prolapse was successfully reduced manually under deep sedation and remained in situ during radiotherapy [9]. In contrast, the uterovaginal prolapse in our patient was irreducible due to the bulky tumor. On completion of radiochemotherapy successful down-staging was achieved, the prolapse became reducible and no residual tumor was visible.

In all reported cases so far, reduction of genital prolapse prior to radiation therapy was clearly recommended and the authors pointed out an increased risk of visceral injury and vesico- or rectovaginal fistula formation from ionizing radiation in the case of persisting uterine prolapse [6, 7]. Accordingly, in our case, cautious MR-based planning of radiotherapy with patient-specific adjustment

of the radiation fields for external beam treatment and extracorporeal HDR-AL was not able to prevent an episode of severe hemorrhagic cystitis and a subsequent treatment delay of three weeks. We wonder if hyperfractionized scheduling with smaller single doses per session would have been able to prevent this complication without compromising oncologic outcome. On the other hand, no late adverse events have been recorded during the five-year follow-up. Taken together, the radiochemotherapy-induced early side-effects were manageable and ultimately acceptable in this special case.

In our frail and sexually inactive patient we opted for an uncomplicated surgical procedure consisting of a simple vaginal hysterectomy and a colpocleisis according to the Labhardt method to enable safe reconstruction of the pelvic floor. It is worth noting that the patient had an unremarkable postoperative recovery without aberrant wound healing as a potential consequence of previous radiotherapy.

Although a radical vaginal surgical approach with either laparoscopic or extraperitoneal lymphadenectomy should be the treatment of choice for operable cervical cancer associated with procidentia, we conclude from our own experience that in elderly and frail patients considered ineligible for radical surgery, an up-front radiochemotherapeutic approach is a valuable treatment option, even in the case of unreduced genital prolapse. This may also be true for the neoadjuvant approach in primary inoperable locally advanced cervical cancers associated with procidentia.

Initial surgery of huge tumor masses in combination with an altered anatomical situation is often associated with excessive hemorrhage and involves great effort. Preceding radiochemotherapy could ease subsequent surgery and prevent unforeseen complications by reducing tumor mass. Moreover, prior administered external irradiation including the pelvic lymph nodes reduces the extent of required surgery and the risk of postoperative complications.

Although literature is available on the best quality therapy for cervical cancer, the question of a standard therapy concept for uterovaginal prolapse associated with cervical cancer remains unsolved. Reports on the treatment of several cases involving this problem and critical appraisal thereof will be helpful in choosing the best therapeutic strategy.

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