Curative intent treatment in recurrent carcinoma cervix, numbers need to increase.

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Abstract
Cervical cancer is most common cancer among females in Nepal. Majority of them presents in advanced stage and treated with definitive chemo-radiation. Fifteen to thirty percent recurs and among them 50% are localised in pelvis. The only curative treatment available at this point is surgery in selected patients and total pelvic exenteration is most common operation performed among few other surgical options. First described almost 72 years back, now the morbidity and mortality of this so-called brutal procedure has decreased and this becomes the only hope of survival in these patients. We present a case of a person from remote village of Nepal who had recurrence following primary treatment and underwent total pelvic exenteration. She recovered well and is disease free at 1-year follow up and is treatment free. The aim of this case report is to create awareness among clinicians, patient and other person involved in cancer care that treatment with curative intent is still possible after cancer recurrence.

Key words: cervical cancer, recurrence, total exenteration.

Introduction:
Cervical cancer is the most common cancer and leading cause of death among Nepalese women.\(^1\) According to the 2018 WHO report, the age-adjusted incidence rate of cervical cancer in Nepal is 21.5 per 100,000 population. Annually 2,942 new cases are diagnosed and 1,928 deaths are attributable to cervical cancer.\(^2\)

The majority of cervical cancer patient present in locally advanced stages and are amenable only to chemoradiation; among this 15-30% patients recur after completion of primary treatment.\(^3\) In majority of patients, recurrence occurs within the initial two years of treatment and in approximately 50% of patients the recurrence is localized to pelvis.\(^4\)

For these patient’s radical surgery in carefully selected patients may offer some chance for cure and chemotherapy is essentially palliative. Surgical options include radical hysterectomy, total pelvic exenteration and laterally extended endopelvic resection (LEER). The most common surgical option is total pelvic exenteration, in which uterus, ovaries, vagina, urinary bladder and rectum are removed en bloc. Alexander Brunschwig described this operation in 1948 publishing a 5-year survival rate of 19%.\(^5\) Radical hysterectomy may be an option for patients with small centrally located recurrence in the cervix with no infiltration in adjacent structures while LEER is indicated for patients with pelvic side wall disease.\(^6\)

The purpose of this case report is to create awareness that radical surgery may be a feasible option in patients who have local recurrence following chemo-radiotherapy. Such patients should be referred to specialist units which offer multimodality treatment. The consequence of surgery on quality of life vis-à-vis recurrence and survival has to be mutually decided by the patient, immediate family members and treating clinician.

Case report:
A 41-year lady hailing from a remote village of Rukum presented to this hospital in June 2018 complaining of per vaginal discharge for the last 6 months. Subsequent evaluation revealed that she was suffering from carcinoma cervix stage IIB. She was treated with definitive concurrent chemoradiation in TeleCobalt machine (2D
planning) with radiation dose of 50Gy in 25 fractions with weekly Cisplatin 50mg intravenous followed by three session of weekly brachytherapy (21Gy in 3 fractions). This treatment schedule was completed on 10 August 2018. She was kept on regular follow up. PAP smear and CT scan after 3 months showed no signs of recurrence. She presented to us after 10 months with persistent per-vaginal discharge. Clinical examination revealed a cervical mass measuring about 2 cm and subsequent biopsy showed squamous cell carcinoma. Imaging showed a mass at cervix with involvement of right parametrium and loss of fat plane with rectum and urinary bladder without pelvic or para-aortic nodes and chest was normal. This was diagnosed as a central recurrence of cervical cancer after definitive chemo-radiation (CTRT) and a total pelvic exenteration was planned with a curative intent.

Prehabilitation in the form of nutritional support, physiotherapy and social services (financial assistance) was started in out-patient basis. The patient and her husband were primed and trained for stoma management by the dedicated Stoma-Care nurse. Total pelvic exenteration was performed in June 2019 wherein rectum, uterus with both the ovaries, fallopian tubes, upper vagina and urinary bladder were removed en-bloc. Rectum was stapled using TX 60 blue (Ethicon) at low rectal level and perineum was not disturbed. End sigmoid colostomy was done over left iliac fossa and a urostoma with ileal conduit urinary diversion with bilateral ureteric stents was brought out through right iliac fossa. The surgery lasted for six and a half hours and the estimated blood loss was 200ml. There were no adverse intraoperative events and no blood product was transfused. She was extubated and shifted to ICU. Her post-operative recovery was uneventful and was discharged home on the 14th post-operative day. At the time of discharge her complications were Grade II by Clavien Dindo classification. The final histopathology report showed a 5 cm moderately differentiated squamous cell carcinoma arising from the cervix which was infiltrating the lower uterine segment, urinary bladder and rectum. All the resection margins were free and no nodal metastases were noted. The final stage was ypT3aN0. Tumour board decided to keep her on regular follow-up. She went back to her home at Rukum and is doing all her routine household work and taking care of children. She is asymptomatic, has gained weight and is disease free at 1-year follow-up.

**Discussion:**

Survival of patients with recurrent cervical cancer is dismal and the only treatment modality associated with long term survival benefit is radical surgical excision. Patients with small central recurrences involving cervix or only the fornice are amenable to radical hysterectomy. Another procedure is total exenteration which was first described in 1948 by Alexander Brunshwig. The author published a case series of 22 patients with 23% operative mortality and longest survival, as reported, was 8 months. Over the years the 5-year survival has increased to 50-60% and mortality and morbidity has decreased. In a study from Germany, 70.2% had at least one major complication including

Figure 1: The empty pelvis seen after removal of urinary bladder, uterus with parametrium, paracolpos, upper half of vagina, adnexa, distal colon and rectum. Levator ani inferiorly, iliac vessels and plevic wall laterally shows a good loco-regional clearance.

Figure 2: En-bloc specimen of total exenteration showing Urinary bladder, uterus with ovary, sigmoid colon and rectum. Three orifices seen from left to right namely, urethral cut margin, vaginal cut margin (portion of cervical mass is seen, tip of artery pointing the mass) and rectum.
ileus (8.5%), fistula (29.8%), ureteral anastomotic leak (6.4%) and cardiothrombotic event (23.4%) where authors also noted that complete tumor resection was associated with significantly higher overall and progression free survival. Morbidity and mortality has decreased considerably due to meticulous surgical techniques, improved intraoperative care, good intensive care unit and new antibiotics to combat fatal infections. This patient developed fever on the 6th post-operative day. Blood culture grew Salmonella sp and she was treated with Piperacillin (Grade II Clavien Dindo complication).

To offer the prospect of satisfactory long-term outcome, patients for total exenteration need to be selected properly. The most commonly used imaging is CT scan. Positron emission tomography (PET) is also suggested by some studies and this has a sensitivity of 93-96% and a specificity of 93-95%. The results of PET scan often lead to changes in plan by sparing women from extensive surgical procedure in the setting of widely metastatic disease. In a study from Taiwan, 22 (55%) out of 40 patients had their treatment modified due to PET scan finding and they concluded that PET was superior to CT/MRI in restaging of recurrent cervical carcinoma. This patient was evaluated by pelvic MRI and CT scan of chest and upper abdomen for local and systemic evaluation respectively.

Total exenteration as the only option for curative intent treatment brings with it a lot of issues which need to be discussed with the patient and relatives viz. operative mortality of 3-5%, major changes in body image, altered sexual function, life-long management of double stoma and family support, without the assurance of a cure. Though this patient hailed from a remote village in Nepal, she had accepted all the consequences and her husband was immensely supportive. This encouraged the surgical team to proceed with radical operation. At one year follow up she is free from disease.

Although total exenteration was described 72 years back there seems to be a reticence on the part of the clinician-community in accepting this operation. This hesitancy is also shared by the patients and relatives mainly because of the prospect of managing stoma for urine and faeces. Given the burden of cervical cancer in Nepal and late presentation needing definitive CTRT, clinicians are poised to witness increasing number of patients with recurrent disease. The aim of this case report is to bring in the awareness in cancer care that curative intent surgery is still possible in a selected group of patients with recurrent disease. In the future, surgeons should aim to perform continent urinary diversion, create neo-vagina and restore gastrointestinal continuity after total exenteration which will vastly improve the quality of life of these patients.

**Conclusion:** Curative intent surgery is possible in appropriately selected patient with recurrent carcinoma cervix. The treating clinician should be well versed with the procedure to achieve optimal peri-operative and long-term outcome.

**References:**


