Radioactive $^{125}\text{I}$ Seed Implantation for Recurrent Cervical Carcinoma After Surgery and Radiotherapy: A Case Report

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Case report

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Abstract

Background: The prognosis of cervical cancer is remarkable, but there are still instances of pelvic and/or extrapelvic recurrence after radical hysterectomy with platinum-based chemoradiotherapy. Sixty percent of the patients with radiotherapy (RT) failure have pelvic recurrence, and 80% of them relapse within two years after treatment. Recurrent cervical cancer seriously affects the prognosis and survival rate of patients. Due to the dose limitation for normal tissue, it is difficult to deliver a sufficient number of doses to recurrent lesions through reirradiation. With the rapid development of brachytherapy technologies such as three-dimensional afterloading brachytherapy, interstitial brachytherapy and radioactive 125I seed implantation, the overall survival (OS) of patients with recurrent cervical cancer has been improving. In the present study, a case in which the patient was successfully treated with radioactive 125I seed implantation is reported.

Case presentation: The patient, a 47-year-old woman, was initially diagnosed with International Federation of Gynecology and Obstetrics (FIGO) stage IB cervical cancer and received preoperative radiotherapy, radical hysterectomy, pelvic lymph node dissection and postoperative radiotherapy. After 95 months of follow-up, retroperitoneal lymph node metastasis and edema of the left lower limb. The size of the retroperitoneal lesion was 2.3 × 2.0 cm, and the size of the left supraclavicle lesion was 2.0 × 1.5 cm. Radioactive 125I seed implantation was performed for retroperitoneal lymph node metastasis and left supraclavicular metastasis. Paclitaxel and cisplatin chemotherapy were given after the operation. Three months after implantation, the size of the retroperitoneal focus was 1.5 × 1.1 cm, and the size of the left supraclavicular lesion was 1.0 × 0.6 cm. Thirteen months after implantation, according to the RECIST standard, the therapeutic effect reached CR. At the time of submission, the patient's progression-free survival was 6 years and 4 months.

Conclusions: CT-guided 125I seed implantation is a safe, effective, and minimally invasive method for treating patients with recurrent cervical cancer after radiotherapy. The response of this patient indicates that 125I seed implantation can be used as a complementary treatment for recurrent cervical cancer after chemoradiotherapy and may also prove to be reliable for comprehensive treatment of cervical cancer.

Background

Cervical cancer is the fourth most common malignant tumor in women and has the fourth-highest mortality rate[1]. Many patients have local recurrence or uncontrollable or distant metastasis after failure of radical hysterectomy, external irradiation and intracavitary brachytherapy. A Japanese study showed that the recurrence rate of IB~IIA cervical cancer was 11%~22% and that of IIB~IVA cervical cancer was 28%~64% based on the International Federation of Gynecology and Obstetrics (FIGO) guidelines [2]. The prognosis of patients with recurrent cervical cancer is poor, the effective rate is only 25%, and the median survival time is approximately 12 months[3]. In addition, follow-up treatment for recurrent cervical cancer after radiotherapy is a very challenging clinical problem.
In recent years, $^{125}$I seed implantation therapy has achieved good results in a variety of recurrent tumors due to its advantages of administering a high local dose, reducing the dose to surrounding normal tissue and reducing tumor reproliferation[4-6]. The present case concerning recurrence of cervical cancer involved radioactive $^{125}$I seed brachytherapy in combination with paclitaxel and cisplatin chemotherapy.

**Case Presentation**

A 47-year-old woman presented to the local hospital prior to May 2007 with menotaxis without obvious inducement. A diagnosis of cervical squamous cell carcinoma was determined by cervical biopsy. Preoperative radiotherapy for cervical cancer was performed on May 24, 2007. The total dose of external pelvic irradiation was 30 Gy/15 F, and the total dose of afterloading radiotherapy was 10 Gy/2 F. The patient underwent radical hysterectomy and pelvic lymph node dissection on June 29, 2007. Postoperative pathological results showed residual cervical squamous cell carcinoma with chronic inflammation, erosion and necrosis. Carcinoma thrombus is seen in the cervical muscularis. No cancerous cells were found in the vaginal stump, vaginal vault or parametrial tissue, and no evidence of metastasis was found in selected lymph node samples. Further treatments, including postoperative pelvic radiotherapy and chemotherapy, were administered following surgery. The total dose of postoperative pelvic radiotherapy was 20 Gy/10 F. The patient was subsequently treated with four cycles of 5-FU (0.75 g) and DDP (40 mg) chemotherapy.

The patient presented to Mindong Hospital Ningde City in April 2015 with pain in the waist and lower extremities accompanied by pitting edema of the lower extremities. A computed tomography (CT) scan revealed retroperitoneal lymph node metastasis, involvement of the left upper ureter and the left psoas major muscle, and hydronephrosis in the left kidney. A “double J” ureteral catheter was inserted, and the lumbago was relieved on April 4, 2015. After discharge, the pain in the lower back and lower extremities worsened. The patient's left lower limb edema was accompanied by decreased mobility. The PET/CT at the General Hospital of the Chinese People's Liberation Army revealed multiple enlarged lymph nodes in the left clavicular fossa and retroperitoneal lymph node metastasis, with an abnormal compensatory increase. The size of the retroperitoneal lesion was $2.3 \times 2.0 \text{ cm}$, and the size of the left supraclavicle lesion was $2.0 \times 1.5 \text{ cm}$. The patient came to the First Oncology Department of Hebei Provincial People's Hospital for further diagnosis and treatment. Left clavicular lymph node puncture was performed. Postoperative pathological findings showed middle-to-highly differentiated squamous cell carcinoma metastases in soft tissues. Thus, the patient was diagnosed with recurrent cervical cancer.

On June 1, 2015, the patient was sent to the First Oncology Department of Hebei Provincial People's Hospital for $^{125}$I seed implantation. Forty-four seeds of 0.4 mCi $^{125}$I were implanted, and particle radiation was used to treat the left abdominal aortic lymph nodes and the right abdominal aortic bifurcation lymph nodes. The following parameters were observed: Postoperative D90: 68 Gy, V90: 93.5%, V100: 89.4%, and V150: 59.8%. The edema of the left lower limb disappeared, and movement was recovered after the operation. The dose volume histogram before and after particle brachytherapy is shown in Figure 1. The image after brachytherapy shows radiation particle aggregation and effective seed distribution, as shown
in Figure 2. On June 8, 2015, under the guidance of CT, 35 seeds of 0.4 mCi $^{125}$I were implanted into the cervical cancer tumor in the left supraclavicular lymph node metastasis of cervical cancer. The following parameters were observed: Postoperative D90: 73 Gy, V90: 96.0%, V100: 90.2%, V150: 50.9%. 3 months after implantation, the size of the retroperitoneal focus was $1.5 \times 1.1$ cm, and the size of the left supraclavicular lesion was $1.0 \times 0.6$ cm. Thirteen months after implantation, according to the RECIST standard, the therapeutic effect reached CR. On April 18, 2016, 20 seeds of 0.4 mCi $^{125}$I were implanted into the cervical cancer tumor in the lumbar 5 vertebral body according to the real-time plan during the operation, and the postoperative verification dose D90 was 110.9Gy. After the operation, the patients were treated with ibanphosphate and discharged. The patient was in good physical and mental condition after $^{125}$I seed implantation. The performance status score was 0, and the patient did not complain of any discomfort.

Written informed consent was obtained from the patient for publication of this case report and any accompanying images, as was permission from the Ethics Committee of the Hebei Provincial People’s Hospital (Shijiazhuang, China).

**Discussion**

Treatment of recurrent cervical cancer is still a challenge at present, especially for those with a history of radiotherapy. After standard radical surgery or chemoradiotherapy, 20%~40% of cervical cancer patients still have local recurrence or distant metastasis\[^{7-8}\]. The choice of treatment for recurrent cervical cancer should be comprehensively evaluated according to the initial treatment, the general situation of patients and the recurrence site. Treatment regimens include targeted radiotherapy, brachytherapy and/or chemotherapy and surgery. Local palliative radiotherapy is mainly used in patients with cervical cancer with few metastases or bone metastases. Most patients with local palliative radiotherapy cannot be given a sufficient radiation dose because the radiation tolerance dose of normal tissue has not been restored. The curative effect of traditional radiotherapy and chemotherapy is poor, and complications are obvious. The tolerance and quality of life of patients are poor \[^{9-11}\]. Immunotherapy is the main treatment for recurrent cervical cancer, but its clinical application is greatly limited due to its high price. Afterloading therapy is one of the most important radiotherapy methods for patients with locally advanced cervical cancer. However, for patients with distant metastasis, due to the limitation of lumen coverage and the dose limitation of risk organs, the target dose is insufficient, rendering the patient prone to tumor recurrence and out of control growth. Because the patient could not undergo surgery and the lesion site involved distant metastasis, $^{125}$I seed implantation plus chemotherapy was selected. $^{125}$I seed implantation is a reasonable distribution, minimally invasive and repeatable procedure that has unique advantages in the treatment of locally advanced tumors \[^{12-13}\]. Clinical studies have shown that $^{125}$I seed implantation in the treatment of pelvic malignant tumors, including recurrent or metastatic colorectal cancer, ovarian cancer, and cervical cancer, can elevate the local control rate, alleviate clinical symptoms, and improve the survival time of patients\[^{14-17}\]. Qu et al. \[^{18}\] reported the treatment of
recurrent cervical cancer with $^{125}$I seed implantation in 36 patients. The median survival times for the central-type and peripheral-type patients were 6 months and 12 months, respectively, and the one-year progression-free survival (PFS) rates were 26.7% and 41.6%, suggesting that $^{125}$I seed implantation had a better effect in peripheral cervical cancer than in central cervical cancer. According to Han et al. [19], 17 patients with recurrent cervical cancer were treated with $^{125}$I seed implantation under CT guidance, and the MPD was 145 Gy. The results showed that the total effective rate was 58.0%, and the 1-year survival rate was approximately 18.3%. Two patients had symptoms of sciatic nerve injury but no other serious complications. Silva et al [20] reported that 45 patients were treated with $^{125}$I seed implantation after relapse, and 30 patients (67%) had complete clinical remission. The 5-year survival rate after relapse was 52%. $^{125}$I seed implantation in the treatment of recurrent cervical cancer has the advantages of an exact curative effect, fewer complications and good tolerance of patients. It may become an effective treatment method for recurrent cervical cancer that is not responsive to multicourse treatment.

The most common sites of extrapelvic metastasis are the para-aortic lymph nodes (81%), lung (21%) and supraclavicular lymph nodes (7%)[21]. In this patient, the metastatic sites were the retroperitoneal lymph nodes and supraclavicular lymph nodes. It is impossible for interstitial brachytherapy or afterload to treat this kind of lymph node metastasis. With CT guidance, $^{125}$I seed implantation was successfully implanted into the lymph nodes. One month after $^{125}$I seed implantation, a pelvic CT scan showed that the lymph nodes were smaller than before. After 3 months, the patients were hospitalized again. Pelvic CT and chest CT showed that the particles accumulated at the site of retroperitoneal lymph node metastasis, and the size of lymph nodes was significantly smaller than before. The enlargement of the supraclavicular lymph nodes disappeared. Thirteen months after implantation, the patient was readmitted to the hospital for CT review. According to the RECIST standard[22], the therapeutic effect reached CR. In the second half of the year, no progress was observed. The latest evaluation of the patient showed that the PFS time had reached 6 years and 4 months. The PFS of this patient was significantly higher than that observed in other studies. The following three reasons were considered possible explanations: First, the clinical stage of this patient was early IB, and the prognosis was good. Second, although some studies have shown that the site of cervical cancer recurrence is one of the factors influencing the survival time of patients[23], the metastatic site of the patient indicates poor prognosis, and the metastatic focus in this case was given a radical dose, which may prolong the survival time of patients. Last, the patient was given 6 cycles of TP Regimen adjuvant chemotherapy after particle implantation, suggesting that particle combined chemotherapy can effectively improve the survival time of the patient. The depressed edema of the left lower limb disappeared after the operation, and the pressure of the lymph node metastasis on the blood vessels was relieved, effectively alleviating the symptoms of poor movement, suggesting that particle implantation can effectively improve the quality of life and survival time of patients.

This case showed that $^{125}$I seed implantation is an effective treatment for recurrent lymph node metastasis of cervical cancer that can effectively alleviate the symptoms of edema and left lower limb movement limitation and achieve a good therapeutic effect. As it is a local treatment, $^{125}$I seed
implantation can be used as a supplementary treatment for recurrent cervical cancer. It is a reliable means for comprehensive treatment of primary cervical cancer. At present, there are still deficiencies. A large sample size and more clinical trials and studies are needed to obtain more reliable evidence-based recommendations.

**Declarations**

**Ethics approval and consent to participate**

Not applicable.

**Consent for publication**

Not applicable.

**Competing interests**

The authors declare that they have no competing interests.

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**Authors’ contributions**

SQ performed the bibliographic search and wrote the manuscript; SQ, XD and HZ revised the manuscript; JZ took part to the equipment preparation and follow-up; JW made the decision to submit the article for publication. All authors read and approved the final manuscript.

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Page 6/10
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Figures

Figure 1

(A) Dose volume histogram (DVH) before retroperitoneal 125I seed implantation (B) Dose volume histogram (DVH) after retroperitoneal 125I seed implantation
Figure 2

CT images (A-B) acquired following interstitial 125I seed implantation. CT image (C) immediately after seed brachytherapy. CT image (D) 13 months after 125I seed implantation. The images following brachytherapy showed radiation particle aggregation and effective seed distribution.