Late Recurrence of Nonseminomatous Germ Cell Tumor Successfully Treated with Intensity-modulated Radiation Therapy

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We report the case of a 41-year-old man with a late recurrence of nonseminomatous germ cell tumor, which was successfully treated with intensity-modulated radiation therapy. For the residual retrocrural tumor invading the 11th and 12th thoracic vertebrae with an abnormal level of tumor marker (α-fetoprotein: 23.2 ng/ml) after salvage chemotherapy, chemotherapy could not be continued due to its neurotoxicity, and surgery could not be performed due to the location. In this situation, intensity-modulated radiation therapy achieved a complete response of tumor marker. The patient remained in complete clinical remission after 3 years. The efficacy of radiotherapy, especially intensity-modulated radiation therapy, for a nonseminomatous germ cell tumor is discussed.

Key words: nonseminomatous germ cell tumor — intensity-modulated radiation therapy — late recurrence

INTRODUCTION

The prognosis for nonseminomatous germ cell tumor (NSGCT) of the testis has been dramatically improved with cisplatin-based chemotherapy followed by surgical resection of the residual tumor (1). However, a small proportion of patients subsequently suffered relapses, and patients with recurrence >2 years since initial chemotherapy have been reported to have significantly poor response to salvage surgery or chemotherapy (2). Although surgical treatment for the remaining tumors after salvage chemotherapy can achieve prolonged survival (3), the tumors are occasionally unresectable. Meanwhile, although radiation therapy had been considered to have little effect on NSGCTs (4), the irradiation technology has progressed dramatically in recent years. We herein report a case with a late recurrence of NSGCT treated with an advanced irradiation method, i.e. intensity-modulated radiation therapy (IMRT).

CASE REPORT

A 25-year-old patient underwent right inguinal orchidectomy for a testicular tumor in October 1991. A mixed germ cell tumor, containing components of embryonal carcinoma, yolk sac tumor and teratoma, was diagnosed. The serum levels of tumor markers were elevated prior to orchidectomy with 10 254 ng/ml α-fetoprotein (AFP) and 376 mIU/ml human β-chorionic gonadotropin (β-HCG). A computerized tomography (CT) scan showed a huge retroperitoneal lymph node metastasis. Three cycles of chemotherapy containing cisplatin, cyclophosphamide, vinblastine, actinomycin D and bleomycin followed by retroperitoneal lymph node dissection were performed. Histopathological examination of the resected tumor showed teratoma. He had a regular follow-up with no evidence of a tumor for the first 10 years, but had been lost to follow-up for the next 5 years. In September 2007, at the age of 41, he visited our clinic with a complaint
of flank pain. CT findings showed a solitary 9 cm retrocrural mass invading the 11th and 12th thoracic vertebrae and surrounding the thoracic aorta. The serum levels of AFP and β-HCG were 2057 ng/ml and 5.2 mIL/ml, respectively. He received salvage chemotherapy with diagnosis of a late recurrence of NSGCT. After one cycle of cisplatin and etoposide and two cycles of cisplatin, paclitaxel and ifosfamide, he suffered from severe chemotherapy-induced peripheral neuropathy which had been sustained at the level of Grade 2. An additional two cycles of chemotherapy with alternative regimens containing irinotecan and nedaplatin worsened neuropathy to Grade 3, indicating difficulties for further chemotherapy. At this point, AFP still showed an elevated level (23.2 ng/ml), and the AFP-L3 fraction was also high (63.6%) although β-HCG returned to the normal value. Moreover, the residual retroperitoneal mass in positron emission tomography (PET) showed an uptake of 18F-deoxyglucose (FDG) (Fig. 1B). Although these data suggested the presence of viable tumor cells, we judged curative surgery with the resection for the invaded vertebral body and aorta to be highly challenging and difficult to perform because of a high risk of severe paraplegia and lethal bleeding.

We selected radiation therapy with a simultaneous integrated boost IMRT (SIB-IMRT) technique (Fig. 2) to deliver enough doses to all targets, including vertebral lesions, while sparing the spinal cord and kidneys. The clinical target volume definition was based on the PET/CT and magnetic resonance imaging. The planning target volume (PTV) was created by adding an automatic isotropic 5 mm margin. Briefly, seven equidistant 6 MV beams (incident at angles of 50°, 80°, 150°, 180°, 210°, 280°, 310°) were used, and intensity-modulated beams were delivered using a dynamic multileaf technique. A dose of 60 Gy was delivered to the FDG-PET-positive lesions, while 54 Gy was prescribed to other PTV (the lesion bounched by a red line in Fig. 2) in 30 fractions simultaneously using the SIB-IMRT technique. Dose–volume histogram analysis showed that the mean dose delivered to the PTV was 61.2 Gy. The maximal doses to the spinal cord and duodenum were 50.2 and 49.6 Gy, respectively. The mean doses to the pancreas, left kidney and right kidney were 31.8, 10.6 and 12.6 Gy, respectively, indicating within tolerance doses to those tissues.

Acute toxicity, evaluated according to the Common Terminology Criteria for Adverse Events Version 3.0, was only Grade 1 anorexia. There was no neurological adverse effect induced by the IMRT. AFP returned to the normal value, and AFP-L3 fraction also fell to an undetectable level 2 months after the radiotherapy. The patient had no signs of elevated serum markers and growth of the residual mass with negative PET examination (Fig. 3) 3 years after the salvage radiation therapy.

DISCUSSION

To our knowledge, this is the first report of an NSGCT successfully treated with IMRT. The clinical course of this case suggested the possibility of curative radiation therapy for NSGCTs despite previous reports showing a poor response. Kersh et al. showed that radiation therapy with a mean dose of 40 Gy was effective in patients with seminomas, but not in those with NSGCTs (4). However, no clinical study of radiation therapy for NSGCTs with doses of >60 Gy, which is generally considered to be curative for solid tumors, has been

![Figure 1](image1.png)

Figure 1. (A) Computed tomography (CT) image of the residual retroperitoneal tumor (arrow) invading the 11th and 12th thoracic vertebrae. (B) 18F-deoxyglucose (FDG) uptake of the residual retroperitoneal tumor in positron emission tomography (PET) (arrow).

![Figure 2](image2.png)

Figure 2. Dose distribution of intensity-modulated radiation therapy (IMRT) treatment planning. The pink line indicates the PTV for FDG-PET-positive lesions planned to deliver the higher dose than the other part of the PTV (red line). A dose of ≥60 Gy was delivered to the central whitish area using the SIB-IMRT.
reported. One previous case report showed that occult lumbar vertebral body metastasis of an NSGCT was eliminated by radiation with a total dose of 61 Gy (5), suggesting that dose escalation could be correlated with a good outcome in NSGCT as well as prostate cancer (6). Meanwhile, dose escalation is generally limited by severe complication resulting from damages to the surrounding organs. An IMRT contributes not only to dose escalation to the target lesions but also to reduction in toxicity because it works to conform to the shape of the target lesions, minimizing the radiation dose to surrounding normal tissues. This suggests that the IMRT could be a valuable tool for treating retroperitoneal tumors surrounded by important intraperitoneal organs. Actually, the IMRT has been applied to less radiosensitive tumors such as head and neck sarcoma or melanoma than NSGCTs through its advantages of local dose escalation and limited toxicity (7). In our case, dose escalation by using the IMRT could contribute to local control of the residual tumor.

The feature in our case was sole elevation of AFP. This suggests the possibility that the residual tumor was teratoma which was more radiosensitive than other NSGCTs (4,8–10). However, the limitation in our case was that there was no pathological evidence of the residual tumor because resection of the tumor was impossible. Therefore, it remains to be elucidated whether radiotherapy has equivalent efficacy for patients with elevation of AFP.

In conclusion, for localized residual tumors after salvage chemotherapy, high-dose salvage radiation therapy by using the IMRT might be an alternative treatment option to salvage surgery.

Conflict of interest statement
None declared.

References

Figure 3. Negative PET examination 3 years after the salvage radiation therapy.