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Whole Abdominopelvic Intensity-Modulated Radiation Therapy for Desmoplastic Small Round Cell Tumor after Surgery

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Abstract

Purpose—Desmoplastic small round cell tumor (DSCRT) is an uncommon pediatric tumor with a poor prognosis. Aggressive multimodality therapy is the current treatment approach, however treatment toxicity is of concern. We report our results with whole abdominopelvic intensity-modulated radiation therapy (WAP-IMRT) as a component of multimodality therapy for DSCRT at a single institution.

Materials/Methods—Medical records of all patients with DSCRT who received WAP-IMRT as part of definitive treatment at MD Anderson (2006-2010) were identified and reviewed.

Results—Eight patients with DSRCT received WAP-IMRT with a median follow-up of 15.2 months. All patients received multiple courses of chemotherapy followed by surgical debulking of intra-abdominal disease; seven also had intraoperative hyperthermic cisplatin. WAP-IMRT was delivered to a total dose of 30 Gy post-operatively; four patients received a simultaneous boost (6-10 Gy) to sites of gross residual disease. Seven patients received concurrent chemotherapy during WAP-IMRT. No RTOG grade 4 nausea, vomiting, or diarrhea occurred during RT. Red cell transfusions were given to two patients to maintain hemoglobin levels of greater than 10 g/dL. Grade 4 cytopenia requiring growth factor support occurred in only one patient; no other significant cytopenias were noted. WAP-IMRT resulted in 25% lower radiation doses to the lumbosacral vertebral bodies and pelvic bones than conventional RT plans. The median time to local or distant failure after WAP-IMRT was 8.73 months in seven patients. One patient who had completed RT 20 months before the last follow-up remains alive without evidence of disease. Five patients (63%) experienced treatment failure in the abdomen. Distant failure occurred in three patients (37.5%).

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Conclusions—WAP-IMRT with concurrent radiosensitizing chemotherapy was well tolerated after aggressive surgery for DSRCT. Enhanced bone sparing with IMRT probably accounts for the low hematologic toxicity (vs. conventional WAP RT). This modality should be considered as an additional local-regional control option for DSRCT.

Keywords

Desmoplastic small round-cell tumor (DSRCT); whole abdominopelvic radiotherapy; pediatric cancer; sarcoma; peritoneal sarcomatosis; IMRT

INTRODUCTION

Desmoplastic small round cell tumor (DSRCT) is a rare and aggressive sarcoma that typically affects adolescent and young adult Caucasian males (~90%). Although fewer than 200 cases have been described in the literature, identification of a characteristic chromosomal translocation [t(11;22)(p13;q12)] and fusion protein (EWSR1-WT1) has facilitated the definitive diagnosis of DSRCT.(1, 2) Patients usually present with nonspecific abdominal symptoms, an abdominopelvic mass, and diffuse peritoneal lesions. Despite aggressive multimodality therapy, durable remissions are rare, with 3-year overall survival rates of less than 30%.(3) Because of the rarity of this disease, no general consensus has been reached regarding staging and treatment. As is true for other rare malignancies, retrospective analyses can be valuable in identifying prognostic factors and guiding disease management.

Local control achieved by complete surgical resection is desirable although usually not possible because of the tendency of DSRCTs for diffuse peritoneal seeding and omental spread. Several studies suggest, however, that gross tumor resection can prolong survival.(4-6) Multimodal therapy with surgery and aggressive combinations of chemotherapy and adjuvant radiation therapy (RT) have provided the best results to date. One retrospective study reported a 3-year overall survival rate of 55% among patients who received triple-modality therapy compared with only 27% when all three modalities were not used.(4) The most widely used treatment approach consists of “P6” chemotherapy followed by surgical debulking. This chemotherapy regimen, similar to that used for Ewing's sarcoma, comprises cyclophosphamide, vincristine, and doxorubicin alternating with etoposide and ifosfamide for seven cycles.(7)

Hyperthermic intraperitoneal perfusion with chemotherapy agents for the treatment of DSRCT in pediatric patients was recently shown to prolong survival in a selected subgroup.(8, 9) Continuous hyperthermic peritoneal perfusion has previously been effective in treating abdominal-cavity microscopic disease in adults who underwent carcinomatosis resection of mesothelioma, ovarian, colon, or appendiceal carcinoma.(10-16) Cytoreductive surgery followed by hyperthermic intraperitoneal perfusion seems to be safe in children and has the potential to improve microscopic disease control in cancers that have a tendency for aggressive peritoneal spread.

Adjuvant RT is often a component of multimodality therapy for this highly malignant disease. In a study from Memorial Sloan Kettering Cancer Center (MSKCC) using whole

abdominopelvic (WAP) RT for DSRCT, (17) patients were treated to 30 Gy via three-dimensionally planned RT with anterior/posterior parallel opposed fields after chemotherapy and maximal surgical resection. Most patients were treated 1.5 Gy twice daily and roughly half of the patients received a boost (range 6-24 Gy). The liver dose was reduced with partial transmission blocks in patients without evidence of hepatic involvement. The renal dose was limited to 15-18 Gy in all patients via posterior blocks throughout the entire treatment or with anterior/posterior blocks after 12 fractions. Acute grade 2 upper and lower gastrointestinal (GI) toxicity was encountered in 81% and 71% of patients, respectively. One hundred percent of patients experienced some form of acute hematologic toxicity, and 33% of patients experienced long-term toxicity after surgical debulking and WAP RT.

Intensity-modulated radiotherapy (IMRT) is an attractive technique for WAP RT. Compared with conventional approaches, IMRT allows excellent dose distribution to peritoneal surfaces in the abdomen and pelvis with the potential to selectively limiting radiation doses to the organs at risk, including the vertebral column, and pelvic bones. Furthermore, dose escalation to focal areas of gross residual disease is also possible without drastically increasing toxicity or morbidity.

The objective of this study was to report the outcome of a series of eight patients treated over a 4-year period with WAP-IMRT as a component of definitive treatment for DSRCT at a tertiary care sarcoma center.

MATERIALS AND METHODS

A retrospective review of patients treated with WAP-IMRT as a component of multimodality definitive treatment at The University of Texas MD Anderson Cancer Center was performed after approval was obtained from the appropriate institutional review board. We identified eight patients as having been treated with WAP-IMRT for DSRCT between April 3, 2006 and August 13, 2010. The diagnosis of DSRCT was established by histologic and immunochemical analysis, with or without cytogenetics analysis. Pathologic specimens were reviewed centrally at the institution by pathologists specializing in sarcomatous tumors.

All patients received induction chemotherapy with an alkylator-based regimen like those used to treat Ewing's sarcoma, consisting of vincristine, doxorubicin, and cyclophosphamide alternating with ifosfamide and etoposide. Upon completion of neoadjuvant systemic chemotherapy, patients underwent debulking surgery, defined as removal of at least 90% of visible tumor. Typically surgery included partial bowel resection, omentectomy, splenectomy, and peritonectomy with complete resection of all gross disease unless it involved the porta hepatis. Most patients received hyperthermic intraperitoneal chemotherapy with 100 mg/m² of cisplatin infused into the peritoneal space at 40.5-41°C as described previously.(8, 9) Most patients had a peritoneal cancer index of greater than 12, defined by estimating tumor burden in 13 regions of the abdomen and pelvis either during surgery (as originally outlined)(18) or radiographically (as recently proposed).(9)

Consolidative therapy with IMRT was administered after chemotherapy and surgical resection. All patients underwent computed tomography(CT)- based simulation in the supine position with custom vac-loc cradles for immobilization. The isocenter was typically marked at mid-abdomen and mid-separation with the assistance of in-room lasers. Serial, non-contrasted CT images were obtained from mid-thorax to mid-femur, and these images were transferred to the treatment planning system for CT-based treatment planning. IMRT planning was performed on a Pinnacle³ treatment planning system, version 8.0m (Philips Healthcare, Andover, MA). If a boost was administered, the patient's most recent PET/CT scan was fused to the simulation CT images to assist in delineation of the target areas for focal boosting. The patient's entire peritoneal and involved retroperitoneal areas, excluding the uninvolved kidneys and liver, were contoured on the simulation CT images and comprised the clinical target volume (CTV). The CTV was expanded by 10 mm for the creation of the planning target volume (PTV) to account for set-up variability and motion. Additional structures were contoured, including the liver, kidneys, lung, heart, bladder and rectum (**Fig. 1**).

Radiation was delivered to the whole abdomen and pelvis to 30 Gy in 20 1.5-Gy fractions administered once daily via IMRT with 6-MV photons. The mean liver dose was limited to less than 25 Gy. The kidneys were contoured and the dose was limited to 20 Gy to less than 33% of each kidney. Seven gantry angles were used in seven out of eight patients. The most common beam angle arrangement was 0, 40, 80, 120, 240, 280 and 320 degrees. The number of beams utilized in each plan varied (9-14 beams). A single isocenter was utilized for all plans except for one, where 2 isocenters (upper and lower) were required. Weekly port films were taken for set-up verification. Concurrent radiosensitizing chemotherapy in addition to the intraoperative perfusion therapy was offered on an outpatient basis at the discretion of the medical oncologist. For selected patients, a simultaneous integrated boost technique was used to deliver an additional 6-10 Gy to discrete areas of gross residual disease. All the patients were administered prophylactic anti- emetics (5HT3 antagonists ondansetron or granesitron) throughout the treatment.

Local failure was described as disease recurrence in the abdomen or pelvis, including liver metastasis. Distant failure was described as recurrent tumor in a site outside the abdomen and pelvis in the presence or absence of local failure. Isolated distant failure was described as disease recurrence outside of the abdominopelvic cavity, in the absence of local failure.

Conventional 3D and IMRT plans were compared dosimetrically for organs at risk. Mean doses in cGy were calculated for vertebral bodies within the treatment field, pelvic bones, bilateral kidneys, liver, bladder and spinal cord. For the evaluation of doses to the vertebral bodies and pelvic bones the percent volume receiving 5, 10, 20, 30 and 40 Gy ($V_{5\text{Gy}}$, $V_{10\text{Gy}}$, $V_{20\text{Gy}}$, $V_{30\text{Gy}}$, and $V_{40\text{Gy}}$) were calculated.

RESULTS

Patient characteristics

All eight patients who received WAP-IMRT were male; three were Caucasian, three were Hispanic, one was African American, and one was of Middle Eastern descent. The median

age at the time of diagnosis was 11.5 years (range 5-20 years), and the median age at the time of RT was 14.3 years (range 6-23 years) (**Table 1**). Two patients (25%) had liver metastasis at the time of presentation, and 75% of patients had disease confined to the abdomen. All eight patients had received multiple courses of chemotherapy followed by cytoreductive surgery and complete removal of all gross intra-abdominal, non-liver disease. Seven of eight patients had complete or near-complete (> 90%) surgical resection of intra-abdominal disease, and the eighth patient had debulking surgery (<90% disease resected). All but one patient received intraoperative hyperthermic cisplatin at the time of surgical resection. The mean number of peritoneal metastatic implants removed at surgery was 28 (range 0-402; one patient had a complete pathologic response to induction chemotherapy with no active disease removed during surgery). Seven of the eight patients received chemotherapy concurrently with IMRT (**Table 1**).

IMRT

WAP-IMRT was started a median of 66 days after surgery (range 33-182 days). An additional 6-10 Gy was administered via a simultaneous integrated boost technique to four patients (**Table 2**). The mean treatment duration was 27 days (range 25-31 days). RT was completed in all patients without a treatment break. No patient had any sites of extra-abdominal disease at the time of WAP-IMRT. Four patients received additional RT for recurrent disease (one patient was treated for recurrent liver disease, one patient was treated to the liver, esophageal lymph nodes and the skull, one patient was treated for a thoracic vertebral body metastasis and one patient was treated to the mediastinum and supraclavicular fossa). The eight patients have been followed for a median of 15.2 months (range 3-46 months) since the end of RT.

Dosimetry

For comparison purposes, 3D conformal RT plans were generated for all eight patients in the series. A representative plan and dose volume histograms for one patient are illustrated in **Figure 2**. Anterior and posterior fields with 18 MV photons were applied to a planned dose of 30 Gy in daily 1.5-Gy fractions. The bilateral kidneys were shielded with posterior blocks beginning with the first fraction (**Fig. 2A**). Mean doses to organs at risk, including the vertebral bodies, pelvic bones, liver, bilateral kidneys and spinal cord were calculated for both the IMRT plans and the 3D conformal plans (**Fig. 3A**). Using the IMRT technique reduced the mean doses to the pelvic bones and vertebral bodies by 25.4% and 25.9% respectively (range 8.5%-55.1% lower for pelvic bones and range 9.2%-53.5% lower for vertebral bodies; **Figure 3A**). The mean spinal cord dose was reduced by 31.9% (range 12.7% - 60.2% lower, **Fig. 3A**). The mean doses to the liver, bladder and both kidneys, however, were comparable in both plans.

IMRT significantly reduced irradiated doses to the vertebral bodies and pelvic bones compared to 3D conventional plans. The mean $V_{20\text{ Gy}}$ for vertebral bodies for all 8 patients was 57.125 for the IMRT plan and 87.25 for the conventional plan (34.5% lower, **Fig 3B**). The mean $V_{20\text{ Gy}}$ for pelvic bones for the patient series was 65.38 and 91 for the IMRT and conventional 3D plans, respectively (28.1% lower, **Fig 3C**). The mean $V_{30\text{ Gy}}$ for the

vertebral bodies and the pelvic bones were 67.8% and 77.3% lower respectively for the IMRT plans compared to the 3D conventional plans (**Fig 3B, 3C**)

Concurrent radiosensitizing chemotherapy

Seven of the eight patients received simultaneous radiosensitizing chemotherapy (**Table 1**). Five patients received temozolomide-based therapy (two of whom also received irinotecan), three received bevacizumab, one received a cyclophosphamide and vinorelbine combination, and one patient received pegylated interferon.

Toxicity

Median weight loss during RT was 1.6% of the baseline pre-RT weight (range 0.8%-8.6%) (**Table 4**). Acute toxicity was graded according to the Radiation Therapy Oncology Group (RTOG) Acute Radiation Morbidity Scoring Criteria. One patient experienced grade 1 nausea and four experienced grade 2 nausea; three patients experienced grade 2 vomiting. All symptomatic nausea and vomiting were alleviated with prescribed antiemetic medication. Lower GI toxic effects included grade 1 diarrhea in one patient, grade 2 diarrhea in four patients, and grade 3 diarrhea requiring intravenous hydration in one patient. No patients experienced grade 4 upper or lower GI toxicity. Four patients (50%) had feeding tubes that had been placed for enteral nutritional support after surgery but before RT; however, no patients required feeding tube placement for symptoms during RT.

As for hematologic toxicity, four patients experienced RTOG grade 1 anemia and one patient had grade 2 anemia; packed red blood cell transfusions were administered electively for two patients to maintain a hemoglobin level of greater than 10.0 g/dL (**Table 4**). One patient had grade 1 thrombocytopenia and one patient had grade 2 thrombocytopenia; the average drop in platelet count was $131.5 \times 10^3/\mu\text{L}$ (range $21\text{-}361 \times 10^3/\mu\text{L}$). The average platelet nadir was $138 \times 10^3/\mu\text{L}$ (range $69\text{-}177 \times 10^3/\mu\text{L}$). No platelet transfusions were required. Grade 3 white blood cell count toxicity was present in three patients, and grade 4 toxicity occurred in one patient. Growth factor support was administered to the patient with grade 4 toxicity, which successfully resolved the leukopenia. All patients completed RT successfully without any breaks in treatment. Symptoms in all patients were treated on an outpatient basis; no inpatient admissions were required.

At 3 months after RT, body weight had been maintained or had increased in four of the eight patients. At 6 months, body weight was at or higher than baseline in five patients (one patient was only 3 months from completion of RT when this report was written). Two patients had experienced a 15% weight loss at 1 year, but neither had active disease. Follow-up blood urea nitrogen, creatinine, and liver function tests revealed no significant changes in six out of seven patients so tested. One patient has been followed for only 3 months, and another patient has had elevated liver function tests with active hepatic disease. Of the seven out of eight patients followed for greater than 3 months after WAP-IMRT no long-term grade 3 or 4 toxicity was noted. One patient, however was treated 3 years after his original WAP-IMRT therapy to the esophagus for a peri-esophageal lymph node recurrence and later developed esophageal strictures related to this treatment requiring intermittent dilatations.

Overall survival and patterns of failure

At the time of last follow-up (median 30.7 months, range 12-64 months), three patients had died of disease progression, four were alive with active disease, and one was alive without evidence of disease (**Table 2**). Five patients (63%) experienced treatment failure in the abdomen: in the liver, spleen, rectosigmoid colon and para-aortic lymph nodes. Distant failure occurred in three patients (37.5%). Isolated distant failure, involving the mediastinum/supraclavicular fossa or the thoracic vertebral body (T3), occurred in two patients (25%). The median time to local or distant failure after WAP-IMRT was 8.73 months (range 2.76- 16.5 months) in seven patients (**Table 2**). One patient who had completed RT 20 months before the last follow-up remains alive without evidence of recurrent disease.

DISCUSSION

In this retrospective study of patients with DSRCT who received WAP-IMRT as a part of aggressive multimodality therapy, we found that IMRT was well tolerated with no evidence of significant GI, renal, or hepatic injury, suggesting that WAP-IMRT is an additional option for patients with refractory disease. DSRCT is an aggressive tumor characterized by specific histochemical and immunochemical features. Although the recent discovery of a unique disease-specific translocation involving the fusion of the Wilms tumor gene product WT1 and the Ewing's sarcoma gene product EWS has facilitated diagnosis, outcomes after treatment unfortunately remain poor.(7, 19-22) Recent efforts have focused on improving disease control without increasing treatment-related morbidity.(4, 22-24)

The current treatment approach for patients with DSRCT, particularly young patients, is aggressive and typically includes chemotherapy, surgical debulking, and RT, often with concurrent systemic treatment. At MD Anderson, after biopsy-confirmed diagnosis and initial chemotherapy similar to that used for Ewing's sarcoma, patients undergo maximal surgical debulking; some patients with diffuse peritoneal disease also undergo hyperthermic intraperitoneal chemotherapy (clinical trials identifier: NCT00436657).(2) The goal of this approach is control of peritoneal microscopic disease. Patients then go on to receive adjuvant WAP-RT, with or without concurrent chemotherapy, after surgery. In the study reported here, patients were treated with induction chemotherapy, maximal debulking surgery, hyperthermic intraperitoneal chemotherapy, and WAP-IMRT with or without simultaneous chemotherapy; seven of the eight patients in our study received systemic therapy concurrently during RT.

The addition of concurrent chemotherapy to RT has been used in an attempt to improve outcome for many different types of malignancies, including sarcomas, and has proven to be superior to RT alone.(25, 26) The choice of chemotherapy agents depends on multiple factors, including efficacy for a particular tumor type, potential for radiosensitization, and additive toxicities. In the patients reviewed here, non-anthracycline-based regimens were used because of their effectiveness in refractory sarcoma and because they can be tolerated during RT. The addition of bevacizumab, a vascular endothelial growth factor inhibitor, also provides radiosensitization.(25, 27, 28) For patient convenience, these concurrent therapies are given on an outpatient basis because of the availability of effective antiemetic therapies,

portable pumps for continuous infusions, and better hematologic support, which has significant implications for the quality of life of these young patients.(23, 25)

Even in the setting of aggressive surgical resection and induction, operative, and concurrent chemotherapy, the toxicity of WAP-IMRT was fairly limited. Grade 1 anemia occurred in four patients and grade 2 anemia in one patient. Red blood cell transfusion was administered electively to two patients to maintain hemoglobin levels greater than 10 g/dL. No platelet transfusions were required, as only grade 1 and 2 thrombocytopenia occurred in two of eight patients. There was, however, one instance of grade 4 leukopenia in a patient receiving concurrent weekly interferon. This patient was treated with growth factor support and responded appropriately, with no requirement for inpatient hospitalization or breaks in RT.

The minimal hematologic morbidity in this series stands in contrast to the hematologic toxicity documented in another series of patients with DSRCT treated with WAP-RT via conventional techniques.(17) In that series of 21 patients, 76% experienced grade 4 thrombocytopenia, 62% required platelet transfusions, and almost half required granulocyte colony-stimulating factor support. Grade 4 leukopenia and anemia occurred in 29% and 33% of patients, respectively. One likely explanation for the lesser hematologic toxicity in our series is the lower bone marrow dose administered with IMRT compared with conventional 3D conformal RT techniques. Indeed, when we compared the dose distribution to lumbosacral vertebral bodies and pelvic bones for IMRT with those for conventional WAP plans, the mean bone doses were roughly 25% lower with the IMRT plan. The enhanced bone-sparing nature of IMRT may account for the lesser observed hematologic toxicity. It has been documented that hematologic toxicity correlates with bone marrow radiation dose in patients undergoing chemoradiotherapy for anal cancer and cervical cancer (29, 30). Our data show that IMRT results in a significant reduction of bone marrow volume irradiated between 10 and 30 Gy. This may account for the low observed rate of grade 3 and 4 hematologic toxicity in this series of patients since bone marrow activity declines after radiotherapy and bone marrow regeneration is influenced by volume and dose (31, 32). It is also likely that chemotherapy agents utilized in this series may have contributed to the bone marrow sparing nature of this multi-modality therapy. Of note is that 57% of the patients in the series reported by Goodman and colleagues¹⁷ received high-dose chemotherapy and autologous bone marrow or peripheral stem-cell transplant before RT. No patient in our study had received a transplant immediately before RT.

The upper and lower GI toxicity was also fairly limited in this patient cohort. Grade 1 or 2 nausea, vomiting and diarrhea occurred in five patients (63%), three patients (38%), and four patients (50%), respectively. Patients who did experience nausea, vomiting, or diarrhea were treated in an outpatient setting with symptomatic medications; one patient experienced grade 3 diarrhea requiring outpatient intravenous fluid administration. No RTOG grade 4 upper or lower GI toxicity was noted. This is quite remarkable, considering that the GI morbidity rate in another series of adult patients who received hyperthermic intraperitoneal chemotherapy was as high as 40% and included bowel obstruction, pancreatitis, gastroparesis, abdominal abscess, and enterocutaneous fistulae.(13) In the MSKCC study, 33% of patients experienced grade 4 upper GI toxicity with small bowel obstruction.(17) Since the upper and lower GI tracts are contained within the peritoneal cavity and are targets

for radiotherapy regardless of the radiation therapy delivery technique it is unclear whether IMRT technique itself contributes to the lower observed GI toxicity. We did treat our patients prophylactically with anti-emetic agents throughout radiotherapy and this may be largely responsible for the reduced upper GI toxicity.

At time of last follow-up, liver function tests were normal in six of seven patients. One patient with progressive hepatic metastasis had persistently elevated liver serologic findings at 6 months after RT. Renal function remained stable and within normal limits in all patients after RT.

Unfortunately, despite aggressive multimodality therapy, the overall prognosis for patients with DSRCT remains poor. Of the eight patients reported in this series, five experienced intra-abdominal recurrence within the RT field, and the mean time to local or distant recurrence after RT was only 262 days (8.73 months). Two other patients experienced distant recurrence, and one other patient is alive without evidence of recurrent disease. The high in-field failure rate suggests that a WAP dose of 30 Gy may be insufficient for adjuvant RT in DSRCT. There is little room for escalation of other local therapies; these patients underwent aggressive surgical debulking with intraperitoneal chemotherapy. Unfortunately, the enthusiasm for radiation dose escalation in this setting is minimal given the potential for life-threatening complications. Targeted therapies are urgently needed to augment the effects of radiation for this disease.

Activation of the insulin-like growth factor 1 receptor (IGF-1R) has been implicated in the tumorigenesis of DSRCT, as it has been in Ewing's sarcoma.(33, 34) Clinical trials are underway to test several forms of IGF-1R-inhibitor-based therapy, with either antibodies or small molecule inhibitors.(35) The addition of an IGF-1R inhibitor to RT as a radiosensitizer may prove superior to current treatment strategies and offers renewed hope for the management of refractory DSRCT in the future.(36)

In summary, DSRCT is a radiosensitive tumor. WAP-IMRT is an additive and surprisingly well-tolerated option for patients with DSRCT and diffuse abdominopelvic disease after surgery. Patients may benefit from aggressive tri-modality therapy, however unfortunately abdominopelvic failure is the rule. WAP-IMRT may reduce radiation toxicity compared to conventional WAP radiation allowing for further treatment intensification/incorporation of novel systemic agents. This manuscript is limited by its retrospective nature, small patient number, and use of a variety of concurrent chemotherapeutic agents with WAP-IMRT which may have varying hematologic effects themselves. However, DSRCT is in itself a very rare disease with an aggressive nature; therefore any attempt to improve the outcome for these young patients would be of interest. This information from this series will undoubtedly be useful in designing a prospective study with homogenous chemotherapy regimens combined with WAP-IMRT in this cohort.

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Figure 1.

Whole-abdominopelvic intensity-modulated radiation therapy plans for desmoplastic small round cell tumor. Blue lines indicate prescribed 30-Gy dose area. Panels A and B are axial images illustrating sparing of the pelvic bone (A) and both kidneys (B); panels C and D are sagittal images illustrating sparing of the vertebral body (C) and hepatic tissue (D).

(C)

Figure 2.

Dose distributions for intensity-modulated radiation therapy (IMRT) and three-dimensional conformal radiation therapy (3D CRT) plans for patient #1. Panel A shows the anteroposterior and posteroanterior fields for the 3D CRT plan, with kidney shields placed on the posterior field beginning with the first fraction. Panels B and C show the dose-volume histogram analyses for both plans; dotted lines indicate IMRT doses and solid lines, 3D CRT doses.

a)

b)

c)

Figure 3.

Dosimetric Comparison between intensity-modulated radiation therapy (IMRT) and three-dimensional conformal radiation therapy (3D) plans for organs at risk. Panel A illustrates mean doses for lumbosacral vertebral bodies, pelvic bones, spinal cord, liver, bladder and bilateral kidneys for the 8 patient series. Error bars indicate 5% error. Panel B and C demonstrate the average $V_{5\text{Gy}}$, $V_{10\text{Gy}}$, $V_{20\text{Gy}}$, $V_{30\text{Gy}}$ and $V_{40\text{Gy}}$ values for all 8 patients in the series for the vertebral bodies (B) and pelvic bones (C).

Patient and treatment characteristics

Table 1

Demographics			Disease		Treatment					
Patient Number	Sex	Age at Dx	Race	Presentation	Liver Mets? *	Extraabdominal Mets? *	Surgery	HIPEC	WAP-IMRT Dose / Boost Dose (Gy)	Concurrent Chemo?
1	M	5	H	Abd pain, constipation	N	N	Complete	Y	30/-	Temozolomide
2	M	10	ME	Palpable abd mass	Y	N	Complete	Y	30/-	None
3	M	10	H	Right hip pain	N	Y-right hip	Complete	Y	30/-	Temozolomide, bevacizumab
4	M	18	C	Palpable abd mass, early satiety	N	N	Complete	Y	30/-	Cyclophosphamide, vinorelbine, bevacizumab
5	M	20	C	Abd pain	N	N	Complete	Y	30/40	Temozolomide, bevacizumab, rapamycin
6	M	8	H	Abd pain, nausea, vomiting	N	N	Near complete (>90%)	Y	30/40	Temozolomide, irinotecan
7	M	17	AA	Abd pain, constipation	Y	Y-mediastinum	Debulking (<90%)	N	30/36	Temozolomide, irinotecan
8	M	13	C	Abd pain	N	N	Near complete (>90%)	Y	30/36	Interferon

Dx, Diagnosis; Mets, Metastasis; HIPEC, hyperthermic intraperitoneal chemotherapy; WAP-IMRT, whole abdominopelvic intensity-modulated radiation therapy; H, Hispanic; ME, Middle Eastern; C, Caucasian; AA, African-American

* At diagnosis.

Table 2

Treatment characteristics and outcome

Treatment										Outcome		
Patient Number	WAP Dose, Gy / Fraction Size, Gy	Boost Dose, Gy / Site	Energy, MV	Mean Liver Dose, Gy	V30, Liver	Mean Right Kidney Dose, Gy	Mean Left Kidney Dose, Gy	Time to RT Failure, months	Site of Failure	Status at Follow-Up		
1	30 / 1.5	no	6	24.2	33%	14.2	16.7	8.73	Diffuse abdominal	DOD		
2	30 / 1.5	no	6	20.2	24.0%	14.1	14.2	7.23	Liver	AWD		
3	30 / 1.5	no	6	12.7	3.0%	14.4	15.0	1.65	Para-aortic LN	DOD		
4	30 / 1.5	no	6	24.5	21.0%	20.5	19.0	2.8	Spleen, SCV	DOD		
5	30 / 1.5	40 / 5 abd nodes	6	22.9	27.0%	21.6	24.6	8.83	Rectosigmoid	AWD		
6	30 / 1.5	40 / pelvic node	6	23.7	10.0%	14.3	18.0	—	none	NED		
7	30 / 1.5	36 / liver	6	30.5	35.0%	24.7	20.5	14.9	Mediastinum, SCV	AWD		
8	30 / 1.5	36 / pelvic LN	6	22.8	18%	19.2	19.8	2.77	Bone (T3)	AWD		

Abbreviations: WAP, whole abdominopelvic; RT, radiotherapy; abd, abdominal; LN, lymph node; SCV, supraclavicular fossa; DOD, dead of disease; AWD, alive with disease; NED, no evidence of disease.

Table 3

Dose characteristics of intensity-modulated RT vs 3D Conformal RT for a patient with desmoplastic small round cell tumor

Region of Interest	Minimum Dose, Gy IMRT (3D Conformal)	Maximum Dose, Gy IMRT (3D Conformal)	Mean Dose, Gy IMRT (3D Conformal)
Bladder	13.71 (23.22)	36.144 (33.115)	27.868 (31.383)
Left kidney	7.26 (11.485)	30.664 (18.908)	16.671 (13.631)
Liver	7.576 (12.731)	37.452 (33.812)	24.198 (24.983)
Right kidney	7.687 (10.944)	27.867 (19.857)	14.18 (13.165)
Spinal cord	2.062 (19.11)	19.943 (33.515)	14.471 (29.796)
Stomach	19.837 (15.146)	40.215 (31.529)	29.243 (20.892)
Pelvic bones	8.938 (13.892)	34.856 (34.991)	19.60 (32.765)
Vertebral bodies	6.632 (11.265)	30.072 (33.669)	17.932 (30.02)

Treatment-related toxicity

Table 4

Pt #	Nausea, RTOG Grade	Vomiting, RTOG Grade	Diarrhea, RTOG Grade	Hgb Start, g/dL	Hgb Nadir, g/dL	Anemia, RTOG Grade	Plt Start, ×10 ³ /μL	Plt Nadir, >×10 ³ /μL	Plt, RTOG Grade	WBC Start, ×10 ³ /μL	WBC Nadir, ×10 ³ /μL	WBC, RTOG Grade	ANC Nadir, ×10 ⁹ /L	Baseline Weight, kg	3 mo Weight, kg (% change)	6 mo Weight, kg (% change)
1	0	0	2	12.5	11.3	0	208	138	0	8.50	2.90	2	2.37	19.5	21.4 (110%)	20.8 (107%)
2	0	0	0	11.0	10.5	1	219	123	0	4.80	1.90	3	3.59	47.6	50.0 (105%)	59.9 (126%)
3	1	0	2	13.7	14.1	0	198	177	0	5.40	3.00	1	1.91	43.6	42.2 (97%)	47.0 (108%)
4	2	2	1	10.4	10.1	* 1	223	175	0	2.30	1.80	3	1.44	61.6	64.8 (105%)	61.7 (100%)
5	2	0	2	13.1	13.0	0	510	149	0	6.50	2.60	2	1.82	73.0	61.2 (84%)	61.3 (84%)
6	2	2	0	12.1	10.2	1	467	137	0	7.30	3.60	1	2.28	25.6	24.6 (96%)	24.6 (96%)
7	0	0	0	10.2	8.2	* 2	385	97	1	10.50	1.60	3	1.06	64.0	72.4 (113%)	69.9 (109%)
8	2	2	2	11.0	10.7	1	236	69	2	2.10	0.90	** 4	0.50	54.4	49.5 (91%)	Not reached

Abbreviations: Pt, patient; RTOG, Radiation Therapy Oncology Group (Acute Radiation Morbidity Scoring Criteria); Hgb, hemoglobin; Plt, platelet; WBC, white blood cell; ANC, absolute neutrophil count; Mo, month

* erythrocyte transfusion given

** growth factor support given.