

Original Article

Clinical characteristics and outcomes of abdominal desmoplastic small round cell tumor: a single-center experience of 10 cases

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Abstract: Background: Desmoplastic small round cell tumor (DSRCT) is a rare and aggressive abdominal tumor typically arising in adolescent and young adult. With no large series reported, the optimal therapy modalities remain unclear. Methods: Clinical data of all consecutive DSRCT patients treated in Cancer Hospital Chinese Academy of Medical Sciences between January 2000 and December 2014 were reviewed. Results: Ten patients with a median age of 27 years (range 14-52 years) were identified; 9 male and 1 female. 9 patients underwent surgery, and the other 1 patient received biopsy. Among the 9 patients who underwent surgery, 5 patients (55.6%) underwent complete surgical removal of all macroscopic peritoneal disease and 4 patients (44.4%) underwent palliative resection. 1 patient received preoperative chemotherapy, and all the 9 patients who underwent surgery received postoperative adjuvant chemotherapy. 2 patients had intensity modulated whole abdominopelvic radiotherapy (WAP RT), and 1 patient received TARCEVA. After a median follow-up of 30 months, the median OS was 26 months. The median OS of the patients with complete surgical removal was better than the patients with no complete surgical removal (33 months: 14 months; Log Rank test, $P < 0.05$). Conclusions: A multimodal treatment combining systemic chemotherapy, complete macroscopic resection, and postoperative whole abdominopelvic-intensity modulated radiotherapy (WAP-IMRT) could improve survival.

Keywords: Desmoplastic small round cell tumor, multimodal treatment, resection

Introduction

Desmoplastic small round cell tumor (DSRCT) is a rare but highly aggressive neoplasm originated from mesenchymal tissue initially reported in 1989 [1]. DSRCT typically occurs in adolescent and young adult Caucasian men and the male/female ratio in the literature is about 6/1 [2, 3]. The age-adjusted incidence rate of DSRCT was 0.3/million, with a peak incidence of 0.74/million in persons 20-24 years old.

The pathogenesis of DSRCT is uncertain and identification of a characteristic chromosomal translocation [t(11;22)(p13;q12)] and fusion protein (EWSR1-WT1) has facilitated its definitive diagnosis [4-6]. Patients usually present with nonspecific abdominal symptoms, a large abdominal mass, and diffuse peritoneal lesions. DSRCT has a poor prognosis and long-term survival is rare, with 3-year overall survival

rates less than 30%, despite aggressive multimodality therapy [7].

Because of the rarity of this disease, no general consensus has been reached regarding the optimal therapeutic strategy. As is true for other rare malignant diseases, retrospective analyses can be valuable in guiding disease management. We reviewed the data of 10 cases of abdominal DSRCT including its clinical and radiological features, and the modalities of treatment.

Patients and methods

Patient collection

10 DSRCT patients whose median age was 27 years (14-52 years) were admitted to Cancer Hospital Chinese Academy of Medical Sciences between January 2000 and December 2014.

Desmoplastic small round cell tumor is a rare and aggressive malignant disease

Table 1. Clinical features of all the study patients with DSRCT

N	Age (year)	Sex	Symptom/signs	Tumor size (cm)	Management	Survival	OS (months)
1	24	M	pain, palpable abdominal mass	8	palliative surgery, chemotherapy (IFO+DDP, 4)	DD	5
2	29	M	pain, palpable abdominal mass	22	biopsy chemotherapy (CTX+VCR+THP+DDP, 6) palliative surgery, chemotherapy (IFO+DDP+TAX, 2)	DD	28
3	20	F	pain	5	surgery radiotherapy chemotherapy (IFO+DDP, 4)	DD	33
4	33	M	pain, palpable abdominal mass	20	palliative surgery, chemotherapy (CTX+THP+DDP, 4)	DD	20
5	26	M	abdominal mass	8	surgery, 4 chemotherapy (CTX+THP+DDP, 8)	AWD	70
6	26	M	abdominal mass	6	surgery chemotherapy (IFO+DDP+EPI, 6) radiotherapy	DD	42
7	52	M	abdominal mass	15	palliative surgery (IFO+DDP+EPI, 6)	DD	27
8	20	M	abdominal mass	15	surgery chemotherapy (IFO+DDP+EPI, 6) TARCEVA	AWD	30
9	30	M	no symptom and discovery by annual checkup	10	surgery (IFO+DDP+THP, 6)	AWND	31
10	14	M	abdominal mass	18	biopsy chemotherapy (CTX+VTR+EPI, 6) radiotherapy	DD	15

M, male; F, female; IFO, ifosfamide; DDP, Diaminodichloroplatin; CTX, cyclophosphamide; VCR, Vincristine; THP, Pirarubicin; TAX, Taxotere; EPI, Epirubicin; AWND, alive with no disease; AWD, alive with disease; DD, died disease.

The clinical, pathological data and therapy modalities including the type of surgery, perioperative radiotherapy and/or chemotherapy of the 10 patients were reviewed. All cases underwent contrast-enhanced CT and/or MRI examination. Multimodal treatment was defined as a combination of two or more subsequent therapeutic treatments (surgery, chemotherapy, radiotherapy and molecular targeted therapy).

Follow-up

All patients were followed after operation at 3-month intervals for the first year and at 4- to 6-month intervals thereafter. The follow-up pro-

gram included blood routine and blood biochemistry examination, abdominal ultrasonography, and chest X-ray examination. Enhanced computed tomography (CT) or magnetic resonance imaging (MRI) was performed every 6 months for surveillance of recurrence. In cases where a suspicious recurrent or metastatic lesion was detected, MRI or CT was employed to consolidate the diagnosis.

Statistical analysis

Statistical analysis was performed by using SPSS 17.0 software. Continuous variables of normal distribution are presented as mean \pm

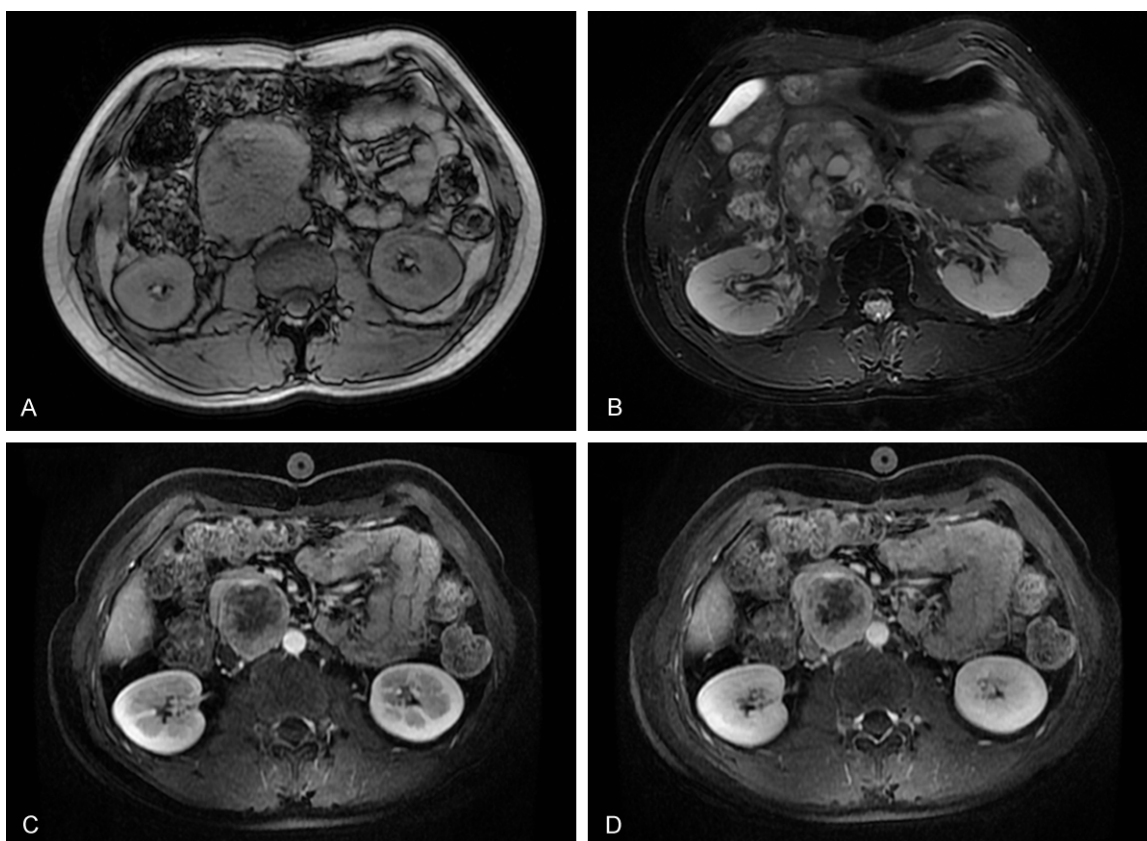


Figure 1. Magnetic resonance images show a soft-tissue mass with 7.6×6.2 cm in size within the retroperitoneal region around the inferior vena cava. The mass shows low signal intensity on T1-weighted image (A), and slightly long signal intensity on T2-weighted images (B). Enhancement scans show multiple cystic necroses inside the mass (C and D).

standard deviation (SD) and compared by using the independent *t* test. Continuous variables of non-normal distribution are presented as medians and were compared by using the Mann-Whitney *U* test. Categorical variables were compared by using Fisher's exact test. In all cases, statistical significance was defined as $P < 0.05$.

Results

Patient characteristics

The patients, tumor characteristics, therapy modalities and outcomes are reported in **Table 1**. The 10 patients with DSRCT in this study were included 9 male and 1 female. The clinical presentations of all 5 cases were not very specific; most of them had vague abdominal pain and/or abdominal mass. 5 patients (50%) were symptomatic at the time of diagnosis with clinically palpable abdominal mass, 3 patients (30%) with clinically palpable abdominal mass and

abdominal pain, 1 patient (10%) with abdominal pain only, and 1 patient (10%) with no symptom and diagnosed by annual checkup. Pre-operative biochemical data, including ALT, albumin (ALB), TBIL, and international normalized ratio (INR) of prothrombin time (PT), were not noticeably abnormal. No ascites were observed, and all patients were in Child-Pugh Class A. The size of the tumors ranged from 5 to 22 cm (median: 12.5 cm; mean: 12.7 ± 6.09 cm). Pre-operative imaging data were available for all 10 cases: these patients all underwent CT and/or MRI examinations (**Figure 1**).

Surgical procedures

Nine patients underwent surgery, and the other 1 patient received biopsy. Among the 9 patients who underwent surgery, 5 patients (55.6%) underwent complete surgical removal of all macroscopic peritoneal disease and 4 patients (44.4%) underwent palliative resection. No

Desmoplastic small round cell tumor is a rare and aggressive malignant disease

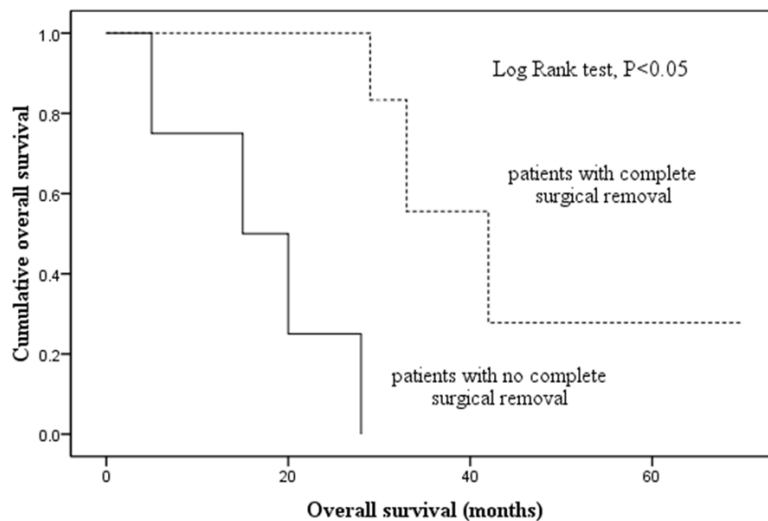
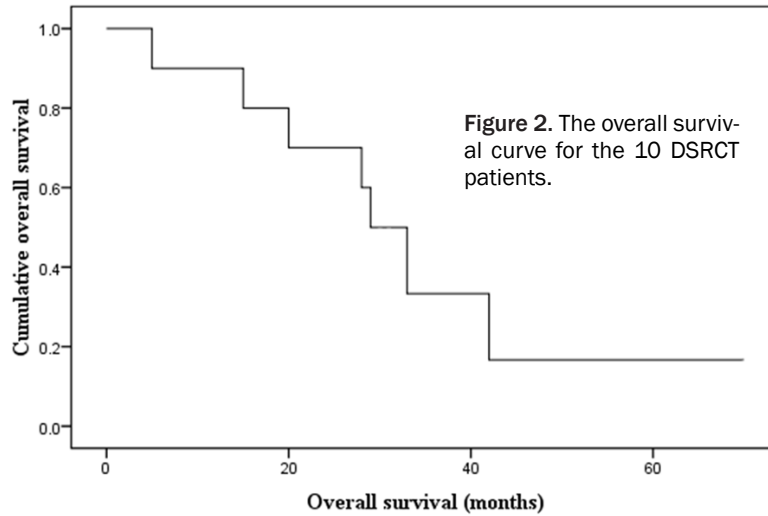


Figure 3. The overall survival curves for the patients with complete surgical removal and the patients with no complete surgical removal.

patient developed severe postoperative complications, which required reoperation. There were no postoperative deaths.

Chemotherapy

1 patient received preoperative chemotherapy, and all the 9 patients who underwent surgery received postoperative adjuvant chemotherapy. 1 patient, who was not amenable to surgery and received biopsy, was treated exclusively with systemic chemotherapy. Chemotherapy regimens were based on the combination of doxorubicin and ifosfamide or cyclophosphamide.

Radiotherapy

2 patients including case 6 and case 10 received preoperative radiotherapy. The two patients had intensity modulated WAP RT, with 9-field modulated beam arrangement, with 6 MV photons. The clinical target volume included the whole peritoneal cavity and the retroperitoneum, treated up to a dose of 60 Gy in 2.0 Gy daily fractions.

Molecular targeted therapy

Case 8 received TARCEVA (Erlotinib hydrochloride) 150 mg once per day for 6 months with no serious adverse events. The other 9 patients did not receive molecular targeted therapy.

Overall survival

At the time of analysis, 7 patients (70.0%) had died and 3 patients (30.0%) were alive including 2 with disease progress and 1 with no recurrence. After a median follow-up of 30 months (range 5-70 months), the median overall survival (OS) was 26 months (range 5.0-70.0 months). The overall survival

curve for the entire population is reported in **Figure 2**. The median OS of the patients with complete surgical removal was better than the patients with no complete surgical removal (33 months: 14 months; Log Rank test, $P < 0.05$) (**Figure 3**).

Discussion

This study found that DSRCT was more prevalent in males (male to female ratio is 9:1), and this finding was similar to the previously reports [8-10]. The origin of DSRCT is yet unknown, but it is speculated that it arises from the mesothelium (or from submesothelial or

Desmoplastic small round cell tumor is a rare and aggressive malignant disease

subserosal mesenchyme), which is most extensive in the peritoneum [11, 12]. The primary site is frequently unknown, as it is most often discovered at the stage of a disseminated tumor within the abdomen [13].

After a median follow up of 30 months, the median OS of our series was 26 months, consistency with the previously studies [14, 15]. Studies have shown that complete surgical resection is a major determinant for patient survival [16-18]; however, DSRCT most commonly presents as a multicentre abdominal mass, complete resection is not often feasible. Our study found that survival time of the patients with complete surgical removal was longer than the patients with no complete surgical removal (33 months: 14 months; $P < 0.05$). However, only 5 patients underwent complete surgical resection.

Multimodal treatment combining complete macroscopic resection of the disease, systemic pre- and/or postoperative chemotherapy, and postoperative radiotherapy could prolong survival of patients with DSRCT [10, 14, 19]. The 10 patients in this series received multimodal treatment, while, the benefit could not appraise for the small sample. There is no standard chemotherapy regimen for DSRCT at present. Most chemotherapy combinations used for DSRCT are based on cyclophosphamide or ifosfamide, similar to those used in Ewing's sarcoma and Wilms tumor, which share the same EWS-WT1 translocation [18, 20].

Adjuvant radiotherapy is often a component of multimodality therapy for this highly malignant disease, as it could contribute to improve outcomes [14, 21]. Some researchers found that whole abdominopelvic-intensity modulated radiotherapy (WAP-IMRT) is an option for patients with refractory DSRCT [21, 22]. Compared with 2D or even 3D WAP radiotherapy, WAP-IMRT resulted in less hematologic, renal, and gastrointestinal toxicity, with the possibility of focal dose escalation in specific areas, which could affect local control [21-23].

Targeted therapies to the specific identified mutation (translocation $t(11:32)(p13;q12)$) could become an option part of the therapeutic strategy in the future. Anti-ILG R1, trabectedin, tyrosine kinase inhibitors, ganitumab, temsirolimus alone, and temsirolimus combined with cixutumumab (a fully human IgG1 monoclonal

antibody directed against insulin growth factor 1 receptor, IGF-1R) have reported interesting results in DSRCT [24, 25].

To summarize, desmoplastic small round cell tumor (DSRCT) is a rare and aggressive malignant abdominal tumor, a multimodal treatment combining systemic chemotherapy, complete macroscopic resection, and postoperative whole abdominopelvic-intensity modulated radiotherapy (WAP-IMRT) could prolong survival. Our study is a retrospective study performed at a single center, and further studies at multiple centers are needed to confirm our conclusions.

Disclosure of conflict of interest

None.

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Desmoplastic small round cell tumor is a rare and aggressive malignant disease

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