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Clinical features and outcomes of 20 patients with abdominopelvic desmoplastic small round cell tumor

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Abstract

Introduction: Desmoplastic small round cell tumor (DSRCT) is a rare mesenchymal malignancy. We describe our experience with treating DSRCT at a large sarcoma referral center.

Methods: A retrospective chart review was performed on DSRCT patients referred to our institution (1998–2014). Pathology specimens were reviewed to confirm the diagnosis. Clinical and imaging were extracted and summarized with descriptive statistics. Univariate analysis was performed to evaluate the association between patient, tumor, and treatment variables and overall survival (OS).

Results: In this study cohort of 20 patients, median age at presentation was 29 y (range 18–43) and 90% were male. Fifty-five percent presented with metastasis. Patients underwent chemotherapy (n = 20), radiation therapy (n = 3), and cytoreductive surgery (CRS) (n = 5). Median OS was 22 m (interquartile range: 12–28 m). Five-year OS rate was 20%. Extra-abdominal metastasis was associated with a higher hazard ratio (HR) of mortality (HR: 3.1, 95% C.I. 1.0–9.4, p = 0.04), while CRS improved OS (HR: 0.1, 95% C.I. 0.03–0.7, p = 0.02).

Conclusions: Despite aggressive treatment, less than half of the patients were dead of DSRCT within 2 years of presentation. Although a select group of patients who underwent CRS had improved OS, novel treatments are urgently needed.

Keywords: Desmoplastic small round cell tumor; Small round blue cell tumors; Multimodal management; Surgery; Chemotherapy

Introduction

Desmoplastic small round cell tumor (DSRCT) is a rare and aggressive mesenchymal malignancy.[1–4] First described in 1989,[5,6] DSRCT's name derives from its distinctive histological findings, which include clusters of undifferentiated, small round blue cells surrounded by abundant desmoplasia.[7] DSRCT cells co-express intermediate-filament proteins consistent with malignant transformation of primitive mesenchymal precursors.[8] The polyphenotypic immunoreactivity suggests a blastomatous cell of origin[9,10] that is possibly similar to the putative undifferentiated cell of origin in Ewing's sarcoma.[9,11] DSRCT is distinguished from other small round blue cell tumors by the (11; 22)

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Abbreviations

95% CI	95% confidence interval
CCR	completeness of cytoreduction scores
CRS	cytoreductive surgery
DSRCT	desmoplastic small round cell tumor
FISH	fluorescence in situ hybridization
GIST	gastrointestinal stromal tumor
HR	hazard ratio
HIPEC	heated intraperitoneal chemotherapy
IQR	interquartile range
LN	lymph node
MHS	Mount Sinai Hospital
PM	Princess Margaret Cancer Centre
OS	overall survival
PCI	peritoneal cancer index
RT	radiation therapy
RT-PCR	reverse transcription polymerase chain reaction
VAC	vincristine/doxorubicin/cyclophosphamide

(p13; q12) chromosomal translocation.[7,12] The translocation juxtaposes the EWS (22q12) and WT1 gene (11p13), creating a chimeric gene (EWS-WT1) that encodes a chimeric protein with oncogenic properties.[10,12–14]

With an annual incidence of 0.1 case per million,[15] population-based data do not exist, and so our knowledge about the clinical course and treatment of DSRCT patients is limited. In order to develop management strategies we must characterize patients and evaluate the effects of current treatment efforts. Our institution is the highest volume adult sarcoma center in Canada. Therefore we were interested in reviewing the clinical features and survival outcomes of abdominopelvic DSRCT patients treated at Mount Sinai Hospital (MSH) and Princess Margaret Cancer Centre (PM).

Material and methods

Study design

After obtaining research ethics board approval, patients were identified from the MSH/PM pathology database. A retrospective chart review was performed of patients who received treatment at PM/MHS between January 1, 1998 and January 30, 2014. Extracted data included (1) patient characteristics; (2) clinical presentation; (3) radiological findings; (4) histopathology characteristics; (5) treatment details; and (6) follow-up information.

Clinical decision-making process

Patients were referred by a medical oncologist or surgeon from an outside institution. Biopsies were performed at the referring institution and reviewed by a sarcoma pathologist at MSH. Formal consultation was initially carried out either by a surgical or medical oncologist. Patients were discussed at a sarcoma multidisciplinary tumor board that developed a recommended treatment plan. All patients received chemotherapy as the initial treatment. Radiation therapy (RT) was not routinely offered as it was mainly reserved for palliation. Cytoreductive surgery (CRS) was offered to patients who had the possibility of >90% tumor reduction at time of surgery as determined by the surgical oncologist, lacked metastases, and showed disease regression or stabilization on chemotherapy.

Histopathology and molecular methods

Diagnosis required confirmation of histopathological features, polyphenotypic immunohistochemical reactivity, and molecular/cytogenetic findings.[7] For the purpose of this study, all available original slides and pathology reports were re-reviewed by an expert sarcoma pathologist.

Immunohistochemistry was performed on using standard techniques. Markers variably included pancytokeratin (AE1/AE3; 1:175; DAKO), epithelial membrane antigen (E29; prediluted; Roche/Ventana), desmin (D33; 1:50; DAKO), smooth muscle actin (1A4; 1:200; DAKO), WTC-19 (polyclonal; 1:400; Novus), vimentin (V9; 1:200; DAKO), CD99 (EPR3097Y; 1:50; Cell Marque), neuron specific enolase (BBS/NC/VI-H14; 1:600; DAKO), synaptophysin (27G12; 1:75; Leica) and chromogranin (polyclonal; 1:2000; DAKO).

Molecular confirmation was accomplished using either reverse transcription polymerase chain reaction (RT-PCR) or fluorescence in situ hybridization (FISH). For RT-PCR, RNA was extracted from the paraffin-embedded tissue and underwent RT-PCR using primers specific for the EWS-WT1 fusion transcript that arises from the t(11; 22) (p13; q12) translocation. For FISH, EWSR1 rearrangement was confirmed using the LSI EWSR1 dual color break-apart probe (Abbott Molecular/Vysis) as outlined by the manufacturer's recommendations.

Definitions

Date of diagnosis was defined as date of biopsy-proven disease after pathology confirmation at MSH/PM. Overall survival (OS) was calculated from the date of the first treatment to the date of death or the end of the follow-up period (February 6, 2015). Completeness of cytoreduction scores (CCR) were defined as follows: CC0 as complete resection to microscopic disease, CC1 as <2.5 cm^2 gross residual tumor after resection, and CC2 as gross residual disease >2.5 cm^2. DSRCT was staged based on the Hayes–Jordan et al. classification, which combines the peritoneal cancer index (PCI), liver metastasis and extra-abdominal metastasis.[16] An experienced surgical oncologist calculated the radiological PCI using the CT scans at presentation.