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BRIEF REPORT

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Paratesticular desmoplastic small round cell tumors: A case report and review of the literature

Laura Sedig[1] | **James Geiger**[2] | **Rajen Mody**[1] | **Rama Jasty-Rao**[1]

[1]Division of Pediatric Hematology, Oncology and Bone Marrow Transplant, Department of Pediatrics and Communicable Diseases, University of Michigan, Ann Arbor, Michigan

[2]Division of Pediatric Surgery, Department of Surgery, University of Michigan, Ann Arbor, Michigan

Correspondence
Laura Sedig, Division of Pediatric Hematology, Oncology and Bone Marrow Transplant, Department of Pediatrics, University of Michigan, 1540 E Hospital Drive, 4204 MPB, Ann Arbor, MI 48109.
Email: lsedig@med.umich.edu

Abstract

Desmoplastic small round cell tumor (DSCRT) is a rare malignancy most often seen in the abdomen or pelvis of young men. Unfortunately, this disease is usually metastatic at diagnosis and has dismal outcomes. We describe a case of isolated paratesticular DSCRT in a 14-year-old male successfully treated with surgical resection, chemotherapy, and adjuvant radiation, and we present a review of the relevant literature. It appears that isolated, paratesticular DSCRTs have a markedly better outcome than the classic abdominal or pelvic location. We hypothesize that this is due to earlier detection and the relative ease of surgical resection.

KEYWORDS

chemotherapy, desmoplastic small round cell tumor, paratesticular, surgical resection

1 | INTRODUCTION

Desmoplastic small round cell tumor (DSRCT) is a rare, aggressive malignancy initially described by Gerald and Rosai in 1989 and most often seen in adolescent and young adult patients.[1,2] Histologically, it consists of small round blue cells with a desmoplastic reaction. The immunohistochemical profile demonstrates reactivity for cytokeratin, epithelial membrane antigen (EMA), vimentin, and desmin.[1] Fusion of the EWSR1 and WT1 genes is diagnostic for DSRCT.[2]

Patients with DSRCT are usually between 5 and 30 years of age. Males and older adolescents are more often affected.[2,3] A review of pediatric Surveillance, Epidemiology and End Results (SEER) data found 95 reported cases in patients 0–21 years of age between 1991 and 2011.[3]

DSRCT is most frequently found on abdominal or pelvic serosal surfaces, although many other locations are reported.[4] The abdominal or pelvic location can allow the tumor to grow for some time before causing symptoms. When symptoms are present, they are generally vague such as weight loss, abdominal fullness, and abdominal pain. Therefore, DSRCT is often not diagnosed until the disease burden is large and/or there is metastatic disease. In the SEER database, only 20% of patients had localized disease at presentation.[3]

The outcomes for DSRCT are quite poor with only 15–30% overall survival at 5 years.[2,3] A multimodal approach to DSRCT therapy is recommended, especially for metastatic disease. The treatment is not standardized but generally includes local control with surgical resection and/or radiation along with multiagent chemotherapy.[2,5] There are reports of hyperthermic intraperitoneal radiation and high-dose chemotherapy followed by autologous stem cell transplant but neither therapy has demonstrated a definitive survival benefit.[2,5–7] We present a case of a successfully treated isolated paratesticular DSRCT and review the literature.

2 | CASE DESCRIPTION

Our patient was a healthy 14-year-old male when he presented to the pediatric surgery clinic with an approximately 1-month history of a left groin bulge. He had no complaints of fevers, weight loss or pain. He was diagnosed with an apparent inguinal hernia and scheduled for surgical repair. In the operating room, he was discovered to have a multilobulated paratesticular mass. Frozen section revealed a small round blue cell tumor and he underwent gross total resection of the mass with left orchiectomy.

Pathology showed a malignant small round blue cell tumor with islands of poorly differentiated cells, areas of necrosis, and areas of brisk mitotic activity. The tumor was diffusely positive for neuron-specific enolase and desmin with focally positivity for EMA and pan-cytokeratin. Myogenin, CD99, CD3, CD45, CD20, and inhibin were all negative. INI-1 was retained. Further molecular testing by PCR demonstrated EWSR1/WT1 chimerism diagnostic of DSRCT. Cytogenetics demonstrated a gain of chromosome 5, also consistent with DSRCT. His testis was negative for disease.

Abbreviations: COG, Children's Oncology Group; DSCRT, desmoplastic small round cell tumor; EMA, epithelial membrane antigen; SEER, Surveillance, Epidemiology and End Results

TABLE 1 Isolated paratesticular desmoplastic small round cell tumors reported in the literature

First author	Number of patients[a]	Patient age (years)	Treatment	Patient outcome at time of report
Bisogno	1	17	Complete surgical resection with orchiectomy, chemotherapy (VCR, D, I)	NED 63 months after diagnosis
Cummings	4	17	Orchiectomy[b], chemotherapy (CDDP, D, CPM)	Lost to follow up
		28	Orchiectomy[b] chemotherapy[c]	Relapse in cervical lymph nodes at 7 months after diagnosis, DOD 16 months after diagnosis
		28	Orchiectomy[b], chemotherapy[c]	Relapse with pulmonary disease at 24 months after diagnosis, NED at 36 months after diagnosis
		37	Orchiectomy[b]	Relapse in the retroperitoneum 36 months after diagnosis, lost to follow up
Farhat	1	NR	Orchiectomy[b], chemotherapy (CDDP, Epi, CPM, VP16)	NED 32 months after relapse (unclear if metastatic disease at diagnosis, widespread disease at relapse)
Furman	1	21	Surgical resection[b], chemotherapy (Carbo, I, VP16, VCR, CPM, A)	NED 33 months after diagnosis
Garcia-Gonzalez	1	23	Surgical resection[b], chemotherapy (Initial: MTX, Dacarb, CPM, D, VCR; subsequent: D, VCR, A, CPM)	NED 72 months after diagnosis
Ordonez	1	28	Orchiectomy[b], chemotherapy (CDDP, VP16)	AWD: regional metastatic disease 12 months after diagnosis (unclear if metastatic disease at diagnosis)
Roganovich	1	17	Complete surgical resection, chemotherapy (I, D, VCR)	NED 60 months years from diagnosis
Saab	1	19	Complete surgical resection, chemotherapy (Carbo, VCR, A, CPM, I, VP-16)	NED at 120 months from diagnosis
Sha	1	27	Orchiectomy[b], chemotherapy (CDDP, VP16, I, Epi)	NED 36 months from diagnosis

A, doxorubicin; AWD, alive with disease; Carbo, carboplatin; CDDP, cisplatin; CPM, cyclophosphamide; D, dactinomycin; Dacab, dacarbizine; DOD, dead of disease; Epi, epirubicin; I, ifosfamide; MTX, methotrexate; NED, no evidence of disease; NR, not reported; VCR, vincristine; VP16, etoposide.
[a]Only newly reported patients are included.
[b]Unclear if complete surgical resection.
[c]Unclear which chemotherapy used and if it was given up front, at relapse or both.

Our patient was enrolled on a prospective integrative clinical sequencing trial (PEDS-MIONCOSEQ) and underwent paired tumor/normal whole exome sequencing and tumor transcriptome sequencing (RNA-Seq). Specifics of the sequencing procedure and bioinformatics analysis have been previously described.[8] The study detected the characteristic EWSR1-WT1 gene fusion, copy gains in of chr1q, 3, 5, 9, 15 and 21, as well as a somatic mutation of MAP3K13 at a low alleic frequency of 5.7%; the significance of which remains unknown in this tumor.[9] Our patient had microscopic positivity at the tumor margins and the remainder of his staging evaluation including abdominal/pelvic laparoscopic exploration, computerized tomography chest/abdomen/pelvis, and positron emission tomography scan was negative.

Our patient was then treated with chemotherapy and adjuvant radiation. His chemotherapy was in accordance with Children's Oncology Group (COG) protocol AEWS1031 arm B with vincristine, topotecan, cyclophosphamide, doxorubicin, etoposide, and ifosfamide. He received 50.4 Gray of adjuvant radiation to the tumor bed after cycle six of chemotherapy due to his microscopically positive margins. He tolerated radiation and all 17 cycles of chemotherapy without any significant side effects. At the time of manuscript submission, he is 24 months from diagnosis and 13 months from completion of chemotherapy without evidence of disease.

3 | DISCUSSION

Paratesticular DSRCT is rare with only 20 such cases reported in the literature (review limited to literature with at least an abstract available in English). Like DSRCT in general, it is seen in older adolescents and young adults. The youngest patient previously reported in the literature was 17. Our patient was 14 at the time of diagnosis.

Paratesticular DSRCT can present with an isolated mass or with metastatic disease. Of the 20 reported cases, 12 had localized disease (see Table 1)[4,5,10–16] and eight had metastatic disease at the time of diagnosis (see Table 2).[10,17–21] Most patients presented due to a mass or testicular pain. Our patient presented with a painless mass and his staging evaluation did not find any metastatic disease.

TABLE 2 Metastatic paratesticular desmoplastic small round cell tumors reported in the literature

First author	Number of patients[a]	Patient age (years)	Location of metastasis (at diagnosis)	Treatment	Patient outcome at time of report
Cliteur	1	32	Abdomen	Orchiectomy, chemotherapy (VCR, VP16, I, A)	DOD 24 months after diagnosis
Cummings	2	32	Retroperitoneal mass	Orchiectomy	Lost to follow up
		26	Lungs, lymph nodes	Orchiectomy, chemotherapy[b], bone marrow transplant	NED 30 months after diagnosis
Prat	1	22	Lungs, lymph nodes (regional and distant)	Orchiectomy, chemotherapy[b]	DOD 17 months after diagnosis
Rais	1	27	Abdomen	Surgical resection, chemotherapy[b]	NED 6 months after diagnosis
Thuret	1	34	Retroperitoneal	Orchiectomy, chemotherapy[b]	Not reported
Yue	2	25 and 35	Abdominal and retroperitoneal	One received orchiectomy, hepatic artery embolization, and chemotherapy (CPM, Pir, Vind, Dacarb), the other received chemotherapy alone (CPM, Epi, Vinp) (unclear which patient received surgery)	Unclear but appears they both are DOD

A, doxorubicin; AWD, alive with disease; CDDP, cisplatin; CPM, cyclophosphamide; Dacarb, dacarbazine; DOD, dead of disease; Epi, epirubicin; I, ifosfamide; NED, no evidence of disease; NR, not reported; Pir, pirarubicin; VCR, vincristine; Vind, vindesine; Vinp, vinpocetine; VP16, etoposide.
[a]Only newly reported patients are included.
[b]Unclear which chemotherapy used.

There is no standardized treatment approach for DSRCT but surgery is the preferred means of local control.[2] All of the reported paratesticular DSRCT patients underwent surgical resection, often with orchiectomy. The ubiquity of surgery is likely because the paratesticular location makes surgery feasible sooner after diagnosis and less morbid. Our patient underwent a gross total excision with high inguinal orchiectomy.

Radiation therapy is also commonly used for local control in DSRCT, especially for those unable to undergo surgical resection.[2] The dose and field of radiation administered varies.[2,4,5] Interestingly, none of the reported patients with paratesticular DSRCT received radiation therapy. We opted to give our patient adjuvant local radiation therapy due to his microscopically positive margins. In our review, the postsurgical margin status was not addressed for any of the cases.

Multiagent chemotherapy is considered standard therapy for DSRCT in the neoadjuvant or adjuvant setting. A variety of chemotherapy regimens have been used and most are similar to approaches used for Ewing sarcoma.[2] Based on the limited literature for DSRCT treatment, we chose the most recent pediatric Ewing protocol, the COG protocol AEWS1031.

Despite multimodal therapy, patients with DSRCT overall have very poor survival rates of 15–30% at 5 years.[2,3] Patients with paratesticular DSRCT appear to have far better outcomes. Out of the 20 previously reported cases of paratesticular DSRCT, 17 had follow-up data available. Of those 17, 10 (~60%) were alive without evidence of disease between 6 and 120 months off therapy. When only patients with metastatic disease are considered, two of six (33%) were alive 6–30 months after diagnosis. However, for those patients with isolated paratesticular disease, eight of 10 (80%) were alive without evidence of disease 33–120 months after diagnosis. One patient was alive with disease 12 months after diagnosis. This review suggests that the survival rate for isolated paratesticular disease is better than metastatic paratesticular disease and the outcomes in paratesticular location in general are much better than the DSRCT outcomes overall. Accordingly, our patient is alive and well without evidence of disease 24 months after diagnosis.

The dramatically improved survival of isolated paratesticular DSRCT compared to DSRCT overall is likely due to its location. The location of the mass renders itself to early detection by patients that leads to earlier medical intervention. The paratesticular location also improves the feasibility of complete surgical excision.

It is unclear if paratesticular DSRCT tumors are biologically distinct from the more typical, widely metastatic DSRCT. While the tumor sequencing did not show any actionable targets in our case, ongoing studies will hopefully identify novel targeted therapies that are less toxic and more effective for this disease.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

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