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# BRIEF REPORT
# Successful Clinical Response to Irinotecan in Desmoplastic Round Blue Cell Tumor

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**Key words:** desmoplastic round blue cell tumor; irinotecan

Desmoplastic round blue cell tumor (DRBCT) was initially described in 1991 as a rare, highly aggressive malignancy that typically occurs in adolescent males [1,2]. DRBCT most frequently occurs as multiple masses in the abdomen, usually without a definable primary lesion, although it has been described in the paratesticular region and the pleura [3]. Noninvasive imaging scans may underestimate the extent of disease because of widespread peritoneal or serosal studding. The most common extraabdominal sites of metastatic disease are the lungs and bones. Gerald et al. [2] have recently reviewed DRBCT and highlighted the heterogeneity of its clinical manifestations, histopathology, and molecular genetic abnormalities.

A variety of approaches to treatment of DRBCT have been attempted, usually involving alkylator-based aggressive chemotherapy regimens, sometimes followed by myeloablative therapy and stem cell reconstitution [3–7]. The best results have been obtained using the P6 Sloan Kettering protocol (continuous-infusion vincristine and doxorubicin with cyclophosphamide alternating with etoposide and ifsofamide), although this group has also emphasized the importance of achieving a complete remission prior to stem cell reconstitution as a significant predictor of long-term disease-free survival [8]. However, the alkylator- and etoposide-based P6 protocol has an 8% incidence of treatment-related leukemia [9]. Given the overall poor prognosis in DRBCT and the short- and long-term toxicity of the best current therapy, it seems appropriate to investigate the activity of new agents and therapeutic modalities. It was in this spirit that we used irinotecan in two patients with DRBCT.

## CASE 1

S.D. is an 18-year-old white female who presented to a local emergency room with abdominal pain at the age of 16 years. In the emergency room an ultrasound examination demonstrated a pelvic mass. Surgical exploration revealed a large pelvic tumor with extensive implantation and seeding of the lower bowel wall, the peritoneal wall, the omentum, and the left ovary and Fallopian tube. The liver and the remainder of the abdomen were free of tumor. Pathologic examination of the surgical specimens showed a small round blue cell tumor most consistent with a desmoplastic small round blue cell tumor. There was no evidence of disease outside of the abdomen. She was treated with a variation of the Memorial-Sloan Kettering P6 protocol, including myeloablation with stem cell rescue [5], and had an excellent clinical response. She did not receive radiotherapy or reexploration of her abdomen. At approximately 350 days posttransplant, the tumor recurred with peritoneal implants and a pelvic mass that mimicked her original presentation (Fig. 1). She was treated with irinotecan 50 mg/m$^2$/day for 5 days every 3–4 weeks and had a rapid response. Abdominal disease was undetectable by the third course (Fig. 1), although she continued to have significant pelvic disease. After her seventh course of irinotecan with no change in the size of the pelvic mass, she had a PET scan using $^{19}$FDG. There was no evidence of active disease anywhere within the abdomen, including the pelvic tumor, suggesting a change in the histopathology of this mass.

## CASE 2

J.D. is a 16-year-old white male with a 3-month history of gradual weight loss, increasing shortness of breath, urinary hesitancy, and recent onset of abdominal distension. He noted that his abdomen had been increasing in size daily. His physical examination demonstrated an increased respiratory rate with intercostal retractions on inspiration, coarse bibasilar rales, and a protuberant, distended abdomen that was extremely tender to touch. The liver was palpable 15 cm below the right costal margin and was rock hard. There was also a large, hard

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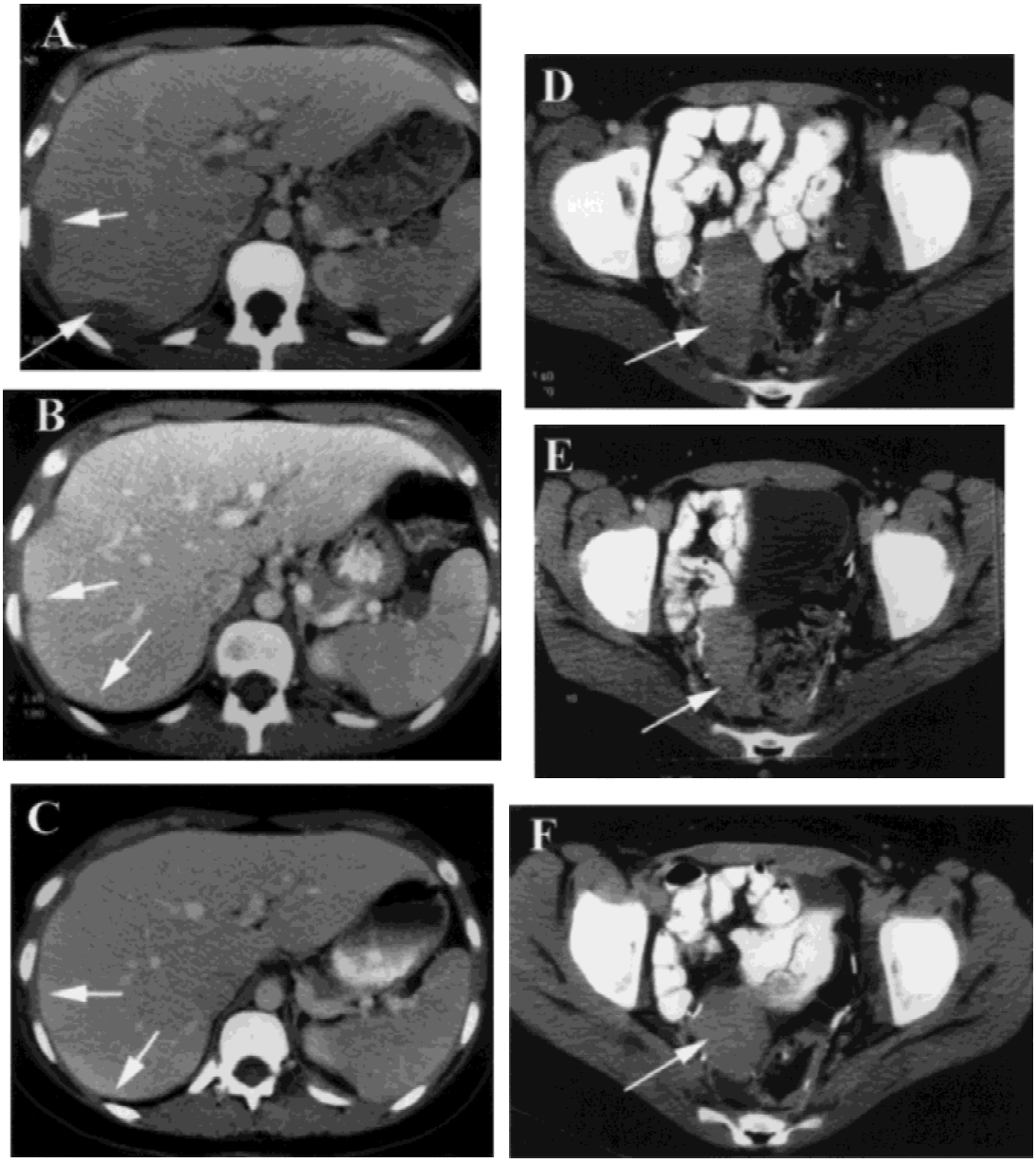


**Fig. 1.** CT scans of the liver and upper abdomen (**A–C**) and lower pelvis (**D–F**) in Case 1. The arrows point to areas of gross disease. Scans A and D, pretreatment; scans B and E, after the first course or irinotecan; scans C and F, after the second course of irinotecan. The large pelvic mass seen in scans D–F was negative on PET scan (see text for details), suggesting lack of active tumor.

suprapubic mass extending to the umbilicus. CT scans of the chest, abdomen, and pelvis demonstrated extensive abdominal tumors and diffuse pulmonary involvement (Fig. 2). A bone scan also revealed metastatic disease. Core biopsies of one of the abdominal masses demonstrated a round blue cell tumor with extensive desmoplasia and immunoreactivity for desmin, consistent with a diagnosis of DRBCT. He was treated with irinotecan 50 mg/m$^2$/day for 5 days for two courses, with a decrease in the dyspnea, stabilization of the abdominal disease, and some decrease in the pulmonary lesions (Fig. 2), after which he was switched to the P6 protocol.

## DISCUSSION

Irinotecan (CPT-11) is a selective topoisomerase I inhibitor that is a member of the camptothecan class of drugs [10] that may also possess antiangiogenic activity [11]. Irinotecan is a prodrug that must be metabolized to the active SN-38, which is up to 100 times more cytotoxic than the parent agent [12]. Irinotecan has shown significant preclinical activity against a variety of pediatric tumor xenografts, including neuroblastoma, several types of brain tumors, rhabdomyosarcoma, and primitive neuroectodermal tumor [13–19]. The related topoisom-

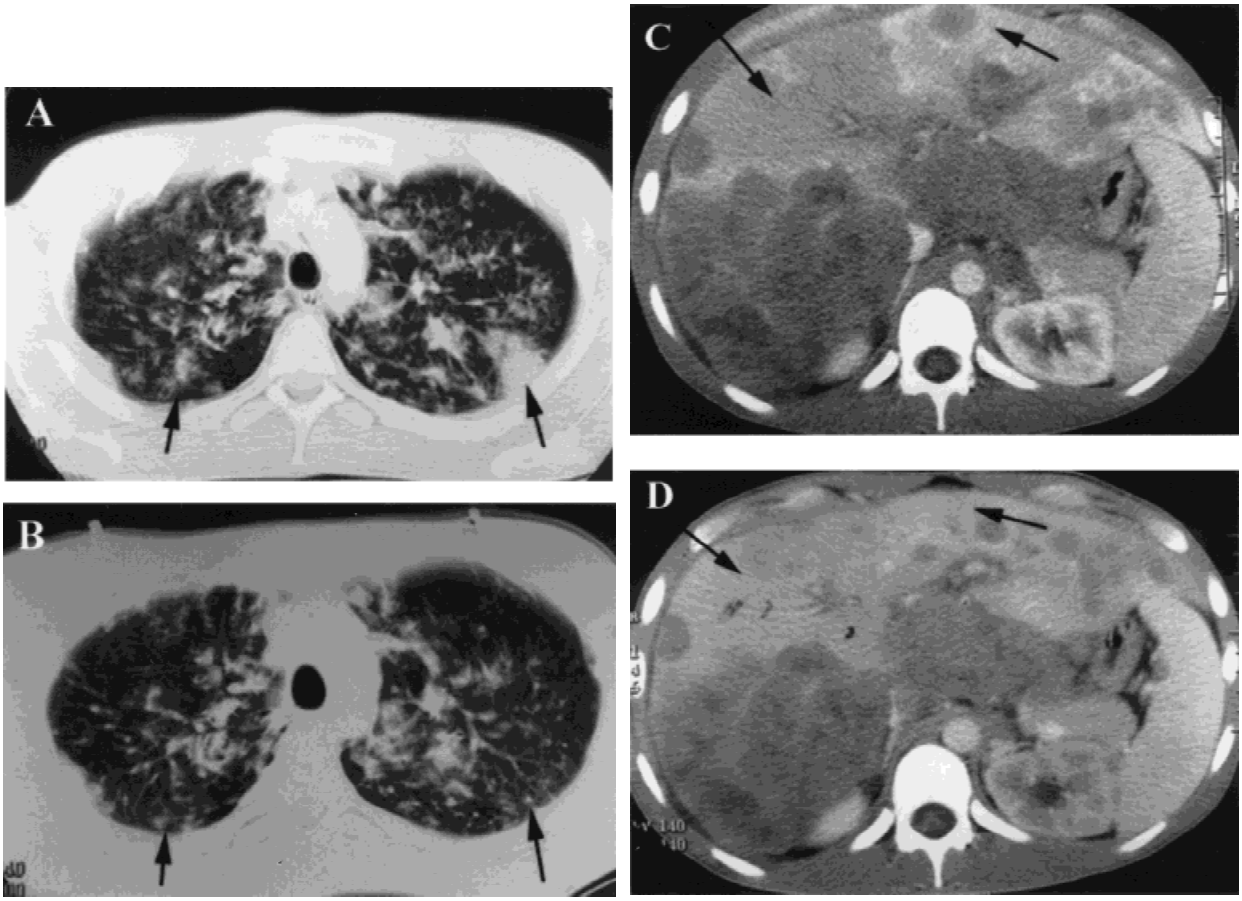


**Fig. 2.** CT scans of the lungs (**A,B**) and upper abdomen (**C,D**) in Case 2. The arrows point to areas of gross disease. Scans A and C, pretreatment; scans B and D, after the first course of irinotecan.

erase I inhibitor topotecan also has significant antitumor activity in children and is currently being used in several Phase II trials in solid tumors. In Phase II clinical trials in adults, both alone and in combination with other agents, irinotecan has demonstrated efficacy in nonsmall cell lung cancer, non-Hodgkin lymphoma, and metastatic colon cancer, among others [20–26]. The Pediatric Oncology Group has recently completed a Phase I trial of five daily doses of irinotecan. Phase II trials are planned depending on the results of this study.

DRBCT is a rare, highly aggressive cancer, and long-term survivors are few. It tends to be initially quite responsive to chemotherapeutic agents, especially alkylators, but usually recurs 12–24 months after diagnosis [1,2]. The group at Memorial-Sloan Kettering Hospital has reported the best survival data using a combination of their P6 protocol, abdominal radiation, aggressive surgery, and myeloablation, followed by autologous stem cell reconstitution [5,8]. However, other groups have been unable to replicate this success [6].

Because irinotecan has been found to be active against a broad range of malignant tumors, in particular primitive neuroectodermal tumor and rhabdomyosarcoma, which bear some similarity to DRBCT, we believed that it was reasonable to attempt to use this agent in the two patients described in this report. Both patients responded to treatment. The first achieved a complete response; the other had stabilization of his disease and, at some anatomic sites, a minor partial response. This is particularly noteworthy in case 1, who has been heavily pretreated. These responses may be similar to those observed in adult patients with relapsed or refractory small cell lung cancer, among whom the overall response rate to irinotecan plus etoposide was 71% [23]. Similarly impressive results have been seen in metastatic colon cancer [21,24,25]. Indeed, its greatest activity may be found when used in combination with another DNA-damaging agent, such as platinum-containing intercalating agents [21,22,26,27]. The responses reported here for our two patients suggest that irinotecan should be explored as an active agent in DRBCT.

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